UNIT 7 VITAMINS, COENZYMES AND MINERALS

Structure

7.1 INTRODUCTION

You have already learnt from the preceding units that proteins, carbohydrates, fats and nucleic acids are the major constituents of living cells. In Unit 6 we described a specialised class of protein, the enzymes. You are aware by now that enzymes function as biological catalysts and through enzyme regulation, metabolism in the living organism is also regulated. Life, as we mentioned earlier, would not be possible without the invaluable role of these molecules. However, you will recall that many enzyme molecules require cofactors for their functioning. These cofactors can be small organic molecules (coenzymes) or simple metal ions. In this unit you will learn about vitamins and minerals, as many of these molecules perform the role of cofactors. However, the role of vitamins and minerals, in general, is not only limited to being cofactors of enzymes. It is only a part of their job. The cell, for its proper functioning also requires vitamins and some other elements, in trace amounts. These molecules are essential for normal growth, well being and proper functioning of human beings. In this unit we shall briefly describe the vitamins, their deficiency symptoms, and dietary sources, their relationship with coenzymes and their biochemical functions. We shall also discuss the role of minerals and trace elements in the physiology and biochemistry of humans. With the knowledge gained from the study of various biomolecules, especially carbohydrates, lipids and proteins, it will be easier for you to learn about bioenergetics and metabolism. This we shall describe in Block 3, where you will learn how the body converts food into energy. You will be able to relate, more clearly, the role of enzymes, coenzymes and other trace substances in metabolism, after studying Block 3.

Objectives

After studying this unit, you should be able to:

- define vitamins and explain their biological significance,
- classify vitamins into water soluble and fat soluble types,
- describe the biochemical functions of water soluble vitamins and also their role as coenzymes in intermediary metabolism,
- describe the role of fat soluble vitamins, and
- explain the significance of minerals and trace elements in human beings.

7.2 BIOLOGICAL SIGNIFICANCE AND CLASSIFICATION OF VITAMINS

Vitamins are small organic molecules which function in trace amounts in the body. They are required for the proper functioning of the cell, normal growth and reproduction. The importance of these organic compounds became obvious when it was observed that certain organisms do not synthesise them on their own, but have to get them from various food materials. Their absence from foodstuffs results in diseases, which have been recognised since ancient times. Thus a disease known as 'scurvy' could be prevented by lime juice. Scurvy is characterised by swollen gums, painful joints, loss of weight, haemorrhages under the skin, and muscular weakness. These conditions are prevented by vitamin C, contained in lime juice. This vitamin was first isolated in 1930. Likewise, symptoms of beriberi could be alleviated by a compound present in rice polishings, and night blindness could be avoided by consumption of liver. The compounds present in these food materials, which are responsible for curing various diet related diseases, came to be known as vitamins. This name was derived from "vital amines", as one of the earlier compounds, thiamine, that was discovered to prevent beriberi, was identified as an amine. However, you should note that not all of the vitamins are amines.

British sailors got their slang name "limeys" from the lime juice they drank to prevent scurvy, when out on the sea for long periods.

A great advance in our understanding of vitamins came in the 1930s, when these compounds were isolated in large quantities, and their molecular structures determined. It was found that many vitamins or their derivatives were principal components of coenzymes. You will recall from Section 6.2, that coenzymes are small molecular weight nonprotein, organic compounds which are bound to the protein portion of the enzyme molecule, and are absolutely essential for the enzyme function. Such enzymes can be considered as conjugated proteins, consisting of an inactive protein portion, called the apoenzyme, which is complexed with a coenzyme (or a prosthetic group, if the coenzyme is tightly bound to it). It was established that biochemically, many of the vitamins or their derivatives function as coenzymes or prosthetic groups of enzymes, participating in the various reactions of intermediary metabolism. We shall now discuss the classification of vitamins, which is based on their solubility.

Classification of Vitamins

All the known vitamins can be classified into two groups, depending on their solubility. These are the **water soluble vitamins** and the **fat soluble vitamins.** The former group comprises of the B vitamins and vitamin C, where as the fat soluble group consists of vitamins A,D,E and K. Most of the water soluble vitamins have well identified coenzyme functions. The coenzyme function of vitamin C, however, is not clear. But nonetheless, you will recall from Section 2.3.5 that this vitamin undergoes oxidation - reduction and participates in biological redox reactions, probably as a cofactor. The fat soluble vitamins, on the other hand, are not known to have any coenzymic properties. We shall discuss separately, the above mentioned two vitamin groups. Let us first describe the water soluble vitamins.

7.3 WATER SOLUBLE VITAMINS

We have already mentioned that this group comprises of the B vitamins and vitamin C. Because of their solubility in water, these vitamins are regularly eliminated from the body in the urine. The body, therefore, requires replacement of these vitamins. For this reason they must be present in our daily diet. Fruits and vegetables are a good source of water soluble vitamins. These vitamins are destroyed by prolonged heat. This implies that there is an appreciable loss of vitamin activity during the cooking process.

With the exception of vitamin B_{12}, all water soluble vitamins can be synthesised by plants. Therefore, green leafy vegetables, whole grains, legumes and yeast, are a good source of these vitamins.

You will now learn about the chemical structure of the B group of vitamins. Besides, you will also learn about the source, and the physiological functions of these vitamins. We shall also briefly discuss the biochemical role of some of these vitamins as coenzymes.

7.3.1 The B Vitamins

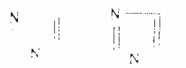
The B vitamins comprise thiamine, riboflavin, niacin, pantothenic acid, pyridoxine, biotin, folic acid and cyanocobalamin. All these individual vitamins have been grouped under the B vitamins, because, around the start of this century it was wrongly thought that the B group consisted of a single vitamin. Let us study the individual members of the B group.

Vitamin B_1 (Thiamine)

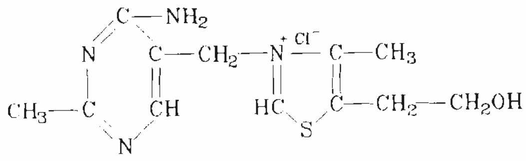
Thiamine or vitamin B_1 is essential in the diet of most vertebrates and some microorganisms. Its absence in the diet causes a disease, known as beriberi in man, and polyneuritis in animals. This disease involves peripheral nerves, causing muscle cramps, nerve pain, numbness of the extremities and circulatory disorders. There is also a reduction in appetite. Vitamin B_1 is present in yeast, whole grain, cereals, eggs and pork. This vitamin has to be obtained from many food items. This is because no single food source is rich enough to meet our daily requirement.

You will recall that water soluble vitamins are eliminated from the body in the urine, and need to be continuously replaced.

Vitamin B_1 or thiamine is made up of a substituted pyrimidine, which is joined by a methylene bridge to a substituted thiazole, as shown below:

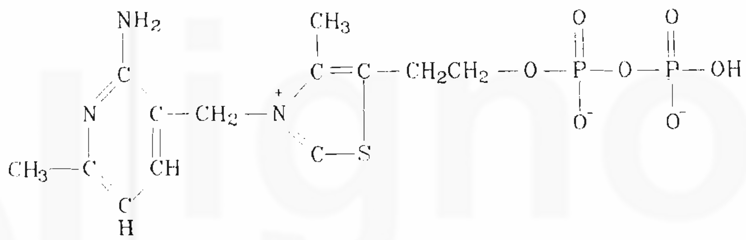


Pyrimidine Thiazole



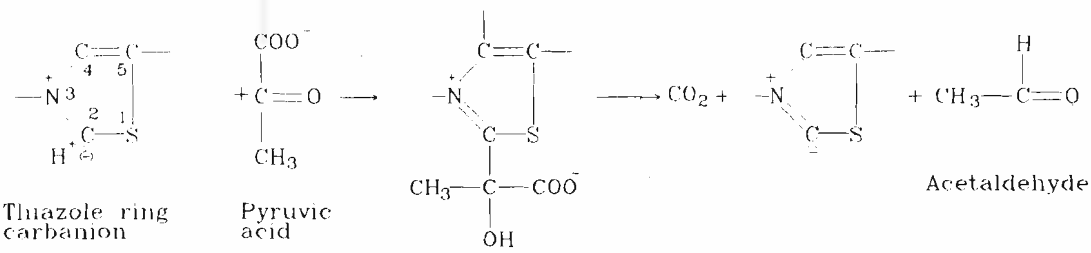
Thiamine chloride

The active coenzymic form of this vitamin that occurs in cells, is, thiamine pyrophosphate or TPP. This coenzymic form is also known as **cocarboxylase.**



Thiamine pyrophosphate (cocarboxylase)

Biochemically, cocarboxylase participates in the decarboxylation of α-keto acids, such as pyruvic acid. This is an important reaction in the glycolytic pathway. During this reaction the thiazole ring, which is the main site of action of the coenzyme, forms a carbanion by dissociation of a proton from carbon number 2. Pyruvic acid then reacts with the carbanion, forming an intermediate, which then releases CO_2 and acetaldehyde, regenerating the thiazole ring. This reaction is depicted below :



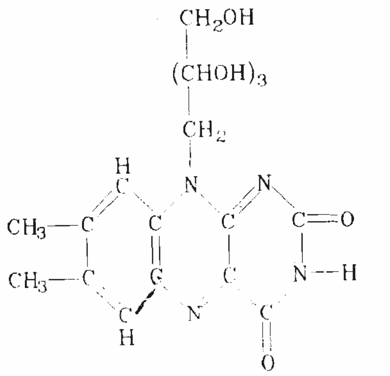
Thiazole ring carbanion; Pyruvic acid; Intermediate; Acetaldehyde

The physiological symptoms of thiamine deficiency can be ascribed to the failure of this reaction, which transforms pyruvic acid to acetaldehyde.

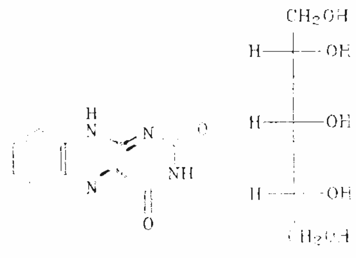
Vitamin B_2 (Riboflavin)

Riboflavin, an important member of the vitamin B family, is relatively heat stable, but sensitive to light. Deficiency of this vitamin in the diet of animals leads to inadequate growth, loss of hair and cataract in the eyes. In human beings, decrease in the intake of this vitamin leads to abnormal vision and corneal inflammation. Yeast, milk, liver, eggs and leafy vegetables are good sources of this vitamin. It is also present in cereals. Polishing the cereals leads to the loss of this vitamin, as well as of vitamin B_1.

Riboflavin is made up of a yellow pigment called **flavin** and a pentose alcohol, called **ribitol.**

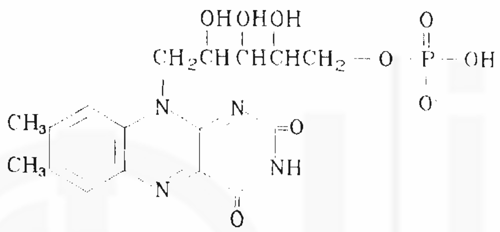


Riboflavin

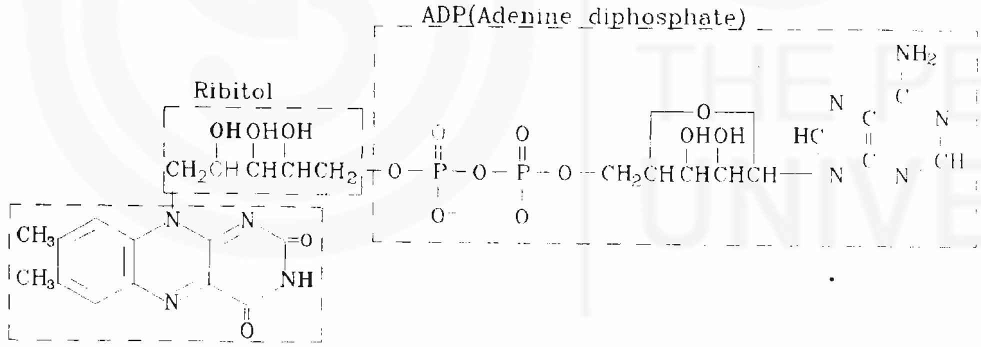


Flavin (isoalloxazine)   Ribitol

The coenzymic forms of this vitamin, which also occur in some foodstuffs, are **flavin mononucleotide (FMN)** and **flavin adenine dinucleotide (FAD)**. Their structures are shown in Fig. 7.1



Flavin mononucleotide(FMN)



Flavin adenine dinucleotide (FAD)

Fig. 7.1 : Coenzymic forms of Vitamin B₂

Biochemically these flavin nucleotides function as coenzymes for some oxidation-reduction enzymes, known as flavoenzymes. Some flavoenzymes are succinic dehydrogenase, D-amino acid oxidase and some other enzymes linked to electron transport. The oxidation-reduction reaction occurs on the flavin portion of the molecule, in which reduced flavin nucleotide is an intermediate.

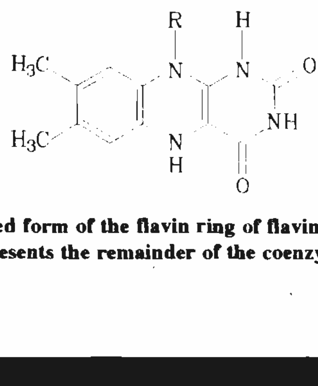


Fig. 7.2 : Reduced form of the flavin ring of flavin nucleotides. R represents the remainder of the coenzyme molecule.

As an example, we have represented below a reaction catalysed by the enzyme, D-amino acid oxidase :

E, in the reaction shown here represents the apoenzyme part and FAD or $FADH_2$ the coenzyme portion. FAD in D-amino acid oxidase is a prosthetic group i.e. it is tightly bound to the apoenzyme.

$$\underset{NH_2}{R-\overset{}{CH}}-COOH + H_2O + E-FAD \longrightarrow R-\underset{O}{\overset{}{\underset{\|}{C}}}-COOH + NH_3 + E-FADH_2$$

D – amino acid	D – amino acid oxidase	α–keto acid	Reduced form of D – amino acid oxidase

The reduced form of D-amino acid oxidase then reacts with molecular oxygen to form hydrogen peroxide and thus releases the oxidised form of the enzyme :

You will recall from subsection 1.5.6 that H_2O_2 is decomposed by catalase, which is contained in peroxisomes.
$2H_2O_2 \longrightarrow 2H_2O + O_2$

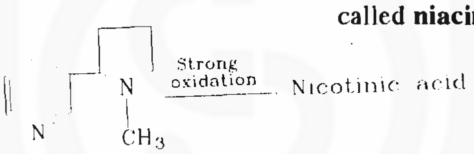
$$E-FADH_2 + O_2 \longrightarrow E-FAD + H_2O_2$$

Different flavoenzymes in their oxidised state are coloured yellow, red or green. On reduction, these enzymes lose their colour. This property can be used to assay their activity.

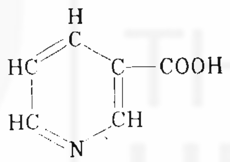
Niacin

Insufficiency of niacin in the diet causes **pellagra** in humans. The symptoms of this disease are loss of appetite, sore tongue, diarrhoea and mental disturbances. In this disease, parts of the body that are exposed to sunlight develop skin lesions. Meat, eggs and milk are good sources of this vitamin.

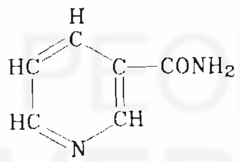
Niacin is the nontoxic derivative of the toxic tobacco alkaloid, nicotine. There are two forms of this vitamin, which are **nicotinic acid** and **nicotinamide.** These are collectively called **niacin.**



Nicotine

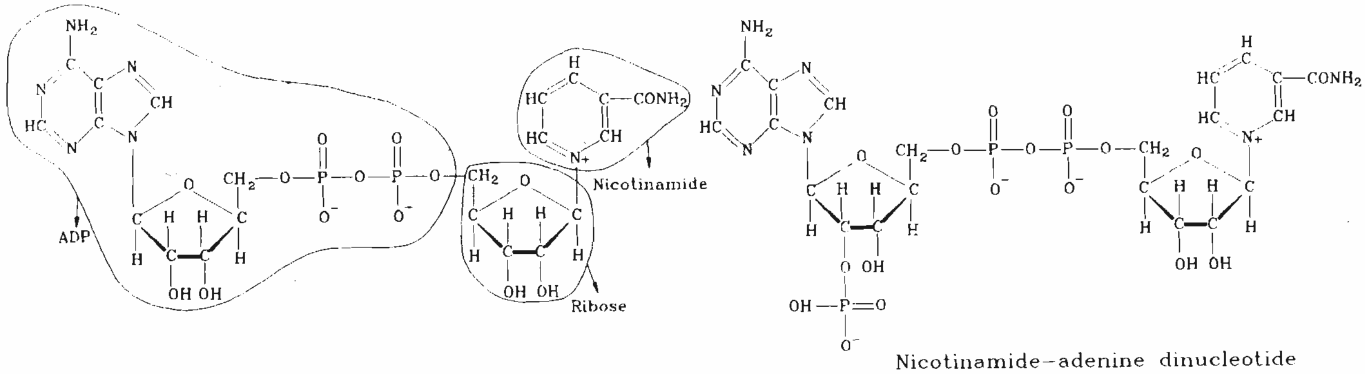


Nicotinic acid



Nicotinamide

The amide form of this vitamin forms part of two very important coenzymes, **nicotinamide adenine dinucleotide or NAD** and **nicotinamide adenine dinucleotide phosphate** or **NADP (Fig. 7.3).**

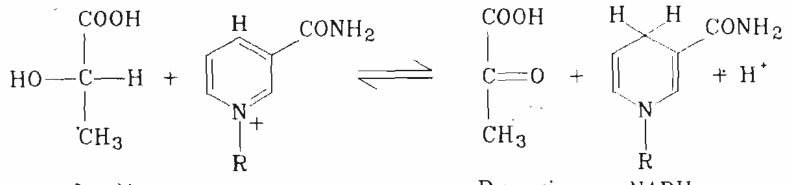


Nicotinamide-adenine dinucleotide (NAD)

Nicotinamide-adenine dinucleotide phosphate (NADP)

Fig. 7.3 : Coenzyme forms of nicotinamide

These coenzymes are called pyridine nucleotides. They function as coenzymes of several oxidoreductases, also called pyridine linked dehydrogenases. In these enzymes, the linkage between the coenzyme portion and the protein (apoenzyme) is weak. The active part of these coenzymes is the nicotinamide portion. The function of the coenzyme can be well illustrated in the lactate dehydrogenase catalysed reaction shown below :

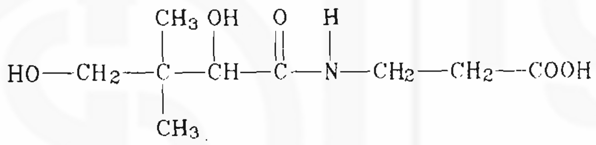


You would observe that two hydrogen atoms are transferred from the substrate, lactate. One hydrogen atom is transferred in the form of a hydride ion (:H^-) to the 4 position of the oxidised nicotinamide portion. The other hydrogen atom is released as a hydrogen ion (H^+). The reduced nicotinamide portion can be regenerated by the reversal of this reaction or by other metabolic reactions.

Vitamin B_5 (Pantothenic acid)

The deficiency symptoms of this vitamin in human beings are emotional disturbances, burning sensation in hands and feet, and distress in the gastrointestinal tract. Rats fed on diets, containing insufficient amounts of pantothenic acid, show subnormal growth, dermatitis, greying of hair and failure of adrenal cortex. Good sources for this vitamin are milk, eggs, yeast, liver and kidney. It is also present in whole grain cereals and legumes.

Structurally pantothenic acid is an amide of pantoic acid and β-alanine.



Pantothenic acid

The structure of the coenzyme form of this vitamin is quite complex.

It consists of an adenosine diphosphate part, linked to pantothenic acid through a phosphoester bond. This in turn is joined to β-mercaptoethylamine, through an amide linkage. The coenzymic form is known as **coenzyme A**, to denote its role in acetylation

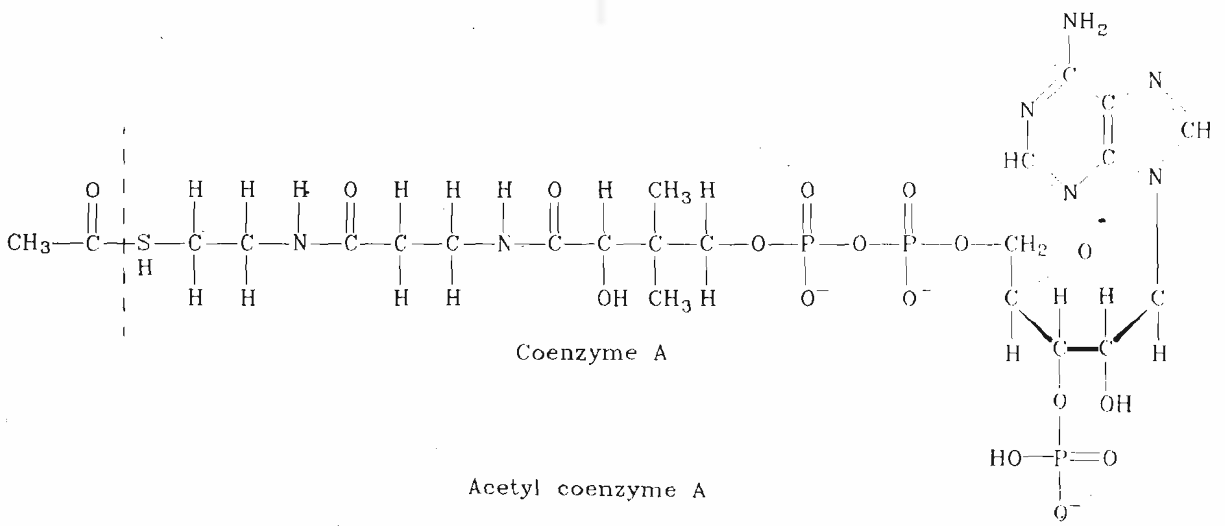
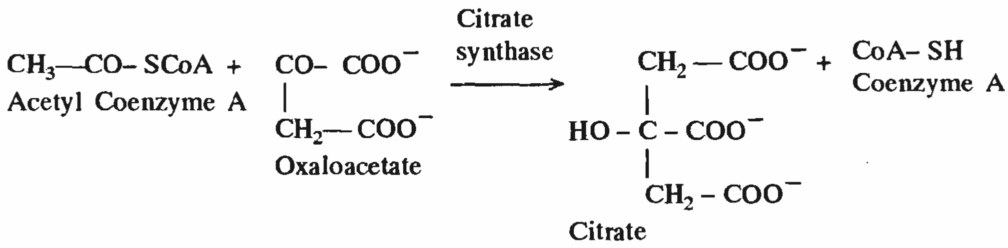


Fig. 7.4 : Coenzyme A and acetyl coenzyme A. Note that in the formation of acetyl coenzyme A, the hydrogen of the thiol group is replaced by the acetyl group.

Biomolecules-II

You will learn about krebs cycle in Unit 10 of this course.

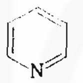
reactions occuring in fatty acid synthesis and oxidation, and in other metabolic transformations. During the enzymatic reactions involved in these biochemical processes, the thiol group of the coenzyme, functions as its active centre and becomes esterified with an acetate group, to yield the thioester, **acetyl coenzyme A**, which transfers its acetyl group to acceptor compounds. For example, acetyl coenzyme A, reacts with oxaloacetate to yield citrate in one of the reactions of the Krebs cycle

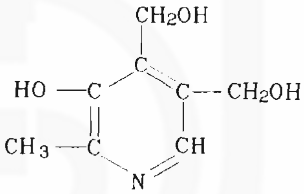


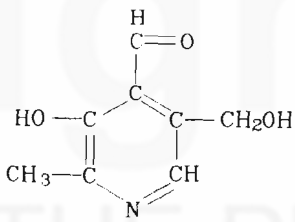
Vitamin B_6 (Pyridoxine)

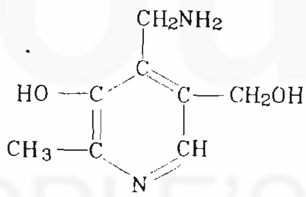
The lack of this vitamin in the diet of young rats causes dermatitis, known as acrodynia, the symptoms of which are swelling and edema of the ears, nose and paws. Other animals, such as cows and dogs, show disturbances of the central nervous system, on a diet defficient in pyridoxine. In human beings, deficiency of this vitamin results in convulsions, chronic anemia and peripheral neuropathy. The vitamin is present in eggs, liver, yeast, cereals, legumes and milk.

Though pyridoxine was the first compound to be identified as having vitamin B_6 activity, two other related compounds, pyridoxal and pyridoxamine, share the same activity. All the three compounds are naturally occuring pyridine derivatives.

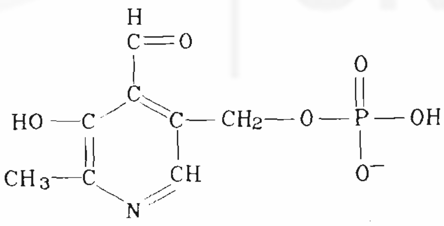

Pyridine

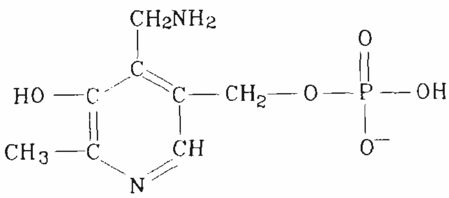

Pyridoxine


Pyridoxal


Pyridoxamine

The coenzymic forms of the vitamin are **pyridoxal** phosphate and **pyridoxamine phosphate.**


Pyridoxal phosphate


Pyridoxamine phosphate

These compounds participate as coenzymes for a number of enzymes involved in amino acid metabolism, catalysing the transfer or transformation of amino groups. In the transamination reactions the α–amino group of an amino acid is transferred to the α–carbon atom of a α–keto acid. The aldehyde group of pyridoxal phosphate is the reactive part of the coenzyme. It reacts with the α–amino group of an amino acid substrate, forming a Schiff's base. This is followed by transfer of the amino group from the amino acid to the coenzyme forming a α–keto acid, which is then released. Pyridoxamine phosphate remains bound to the enzyme (Fig. 7.5a). A different α-keto acid now binds to the enzyme and accepts amino group from pyridoxamine phosphate, resulting in the formation of a different α–amino acid, and regenerating pyridoxal phosphate for another similar cycle of reactions (Fig. 7.5b).

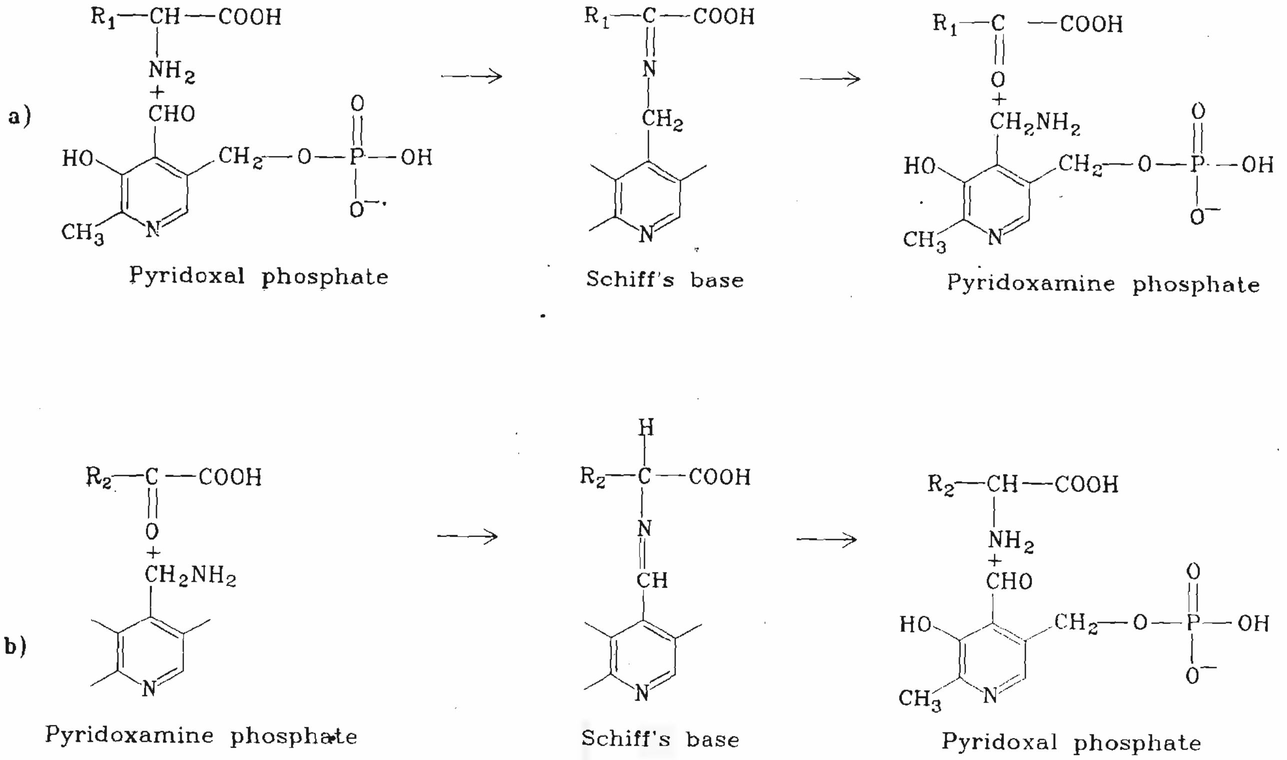
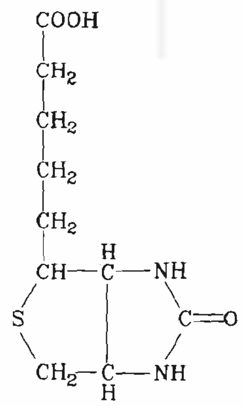


Fig. 7.5 : The function of the pyridoxal coenzymes in the general reaction of transamination

Biotin

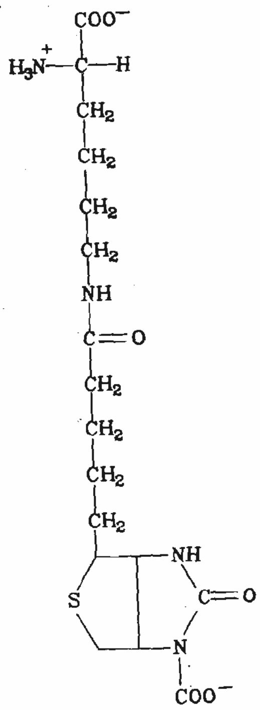
The deficiency of this vitamin results in dermatitis, nausea and depression. In animals, this vitamin is needed to protect them against the toxicity generated, when they are fed raw egg white. The raw egg white contains a protein, avidin, which binds biotin very strongly. This reduces its availability for the animal and causes the symptoms of vitamin deficiency. Liver is a good source of this vitamin. Other sources are yeast, kidney, nuts, tomatoes and egg yolk. Intestinal bacteria also produce this vitamin and hence its deficiency cannot be easily produced.

Biotin is an imidazole derivative. Its structure is shown below.



Biotin

As a coenzyme it is present in a combined state, as a substituted amide. The amide is formed with the ε– amino group of a particular lysine residue of the apoenzyme. Biotin so bound is called **biotinyllysine.**



N-Carboxybiotinyllysine

Fig. 7.6 : N-Carboxybiotinyllysine as the intermediate carrier of carboxylate group derived from a molecule of carbon dioxide

This coenzyme functions in the transfer or incorporation of carbon dioxide as a carboxylate group, catalysed by carboxylating enzymes, such as propionyl CoA carboxylase. During the reaction, the labile carboxybiotin derivative serves as an intermediate. The reaction is represented by the following equations :

$$\text{ATP} + \text{HCO}_3^- + \text{Biotinyl} - \text{enzyme} \rightleftharpoons \text{ADP} + \text{P}_i + \text{Carboxybiotinyl enzyme}$$

The term P_i stands for inorganic orthophosphate.

$$\text{Carboxybiotinyl} - \text{enzyme} + \text{Substrate} \rightleftharpoons \text{Biotinyl} - \text{enzyme} + \text{Carboxylated substrate}$$

Folic acid (Pteroylglutamic acid)

Folic acid deficiency in the diet of animals leads to anemias and failure of growth. Treatment with folic acid alleviates the symptoms of macrocytic anemias. Folic acid is present in many plant tissues, especially in leaves. For example, spinach leaves are a good source of this vitamin. It is also present in yeast, soybeans, kidney, liver, eggs, wheat and mushrooms.

Folic acid is composed of three major components. These are a substituted pteridine, p-amino benzoic acid and glutamic acid. Hence it is also called **pteroylglutamic acid** (Fig. 7.7).

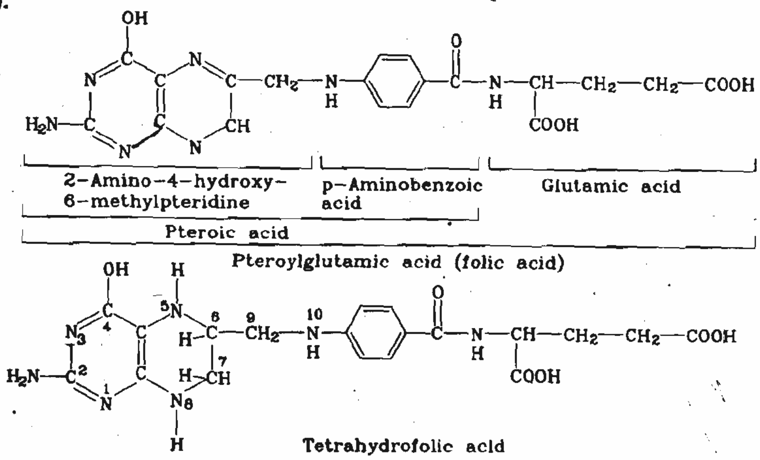


Fig. 7.7 : Structures of folic acid and tetrahydrofolic acid

The reduced form of this compound, 5,6,7,8-tetrahydrofolic acid (FH_4), is the coenzyme form of folic acid. Biochemically the coenzyme functions as a carrier of one-carbon fragments for the biosynthesis of purines, pyrimidines, serine, glycine and methyl groups. The one-carbon fragment may be hydroxymethyl, formyl or methyl groups, which are either transferred from one compound to another or are converted into one another. The nitrogen atoms at 5 and 10 positions in FH_4 i.e. N^5 and N^{10} participate in the shuffling of one carbon groups. The following reaction shows the participation of FH_4, in which the hydroxymethyl group of serine is enzymatically transferred to FH_4 to form N^5, N^{10}methylene-FH_4, and glycine:

$$\underset{\text{Serine}}{\overset{NH_2}{\underset{OH}{CH_2}-CH-COOH}} + FH_4 \xrightleftharpoons{\text{Serinehydroxymethyl transferase}} \underset{\text{Glycine}}{\overset{NH_2}{CH_2-COOH}} + N^5, N^{10}\text{-methylene}-FH_4 + H_2O$$

Vitamin B_{12} (Cyanocobalamin)

Cyanocobalamin is a heat stable vitamin. Its deficiency causes pernicious anemia. Administration of vitamin B_{12} cures this disease. Liver is the best source of vitamin B_{12}. It is also found in oysters, salmon and kidney. Vitamin B_{12} deficiency also affects myelin formation and leads to degradation of nerves, spinal cord and brain.

Pernicious anemia causes general weakness and fatigue, due to lack of erythrocytes or red blood cells, and not due to lack of haemoglobin. Recall that the erythrocytes contain haemoglobin molecules, which carry oxygen to the cells.

Myelin sheath is the protective coating which surrounds the nerves.

Vitamin B_{12} has a very complicated structure, in which cobalt (III) atom is bound to four nitrogen atoms of a corrin ring, a nitrogen atom of 5,6-dimethyl benzimidazole moiety and a cyanide group (Fig. 7.8).

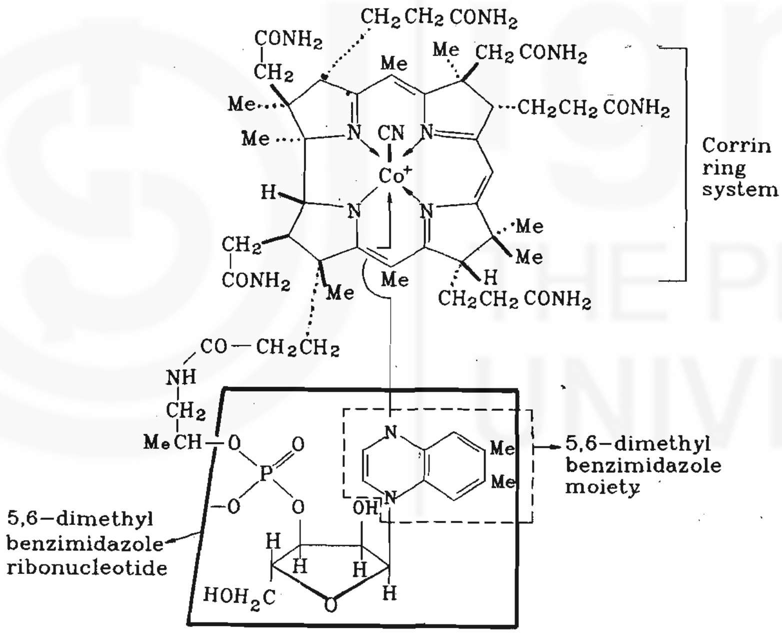
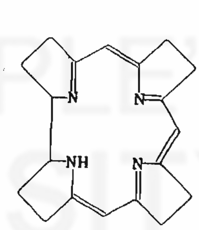


Fig. 7.8 : Vitamin B_{12} (cyanocobalamin)



corrin

In one of the coenzymic forms of this vitamin, the cyanide group is replaced by a 5-deoxyadenosyl group (Fig. 7.9).

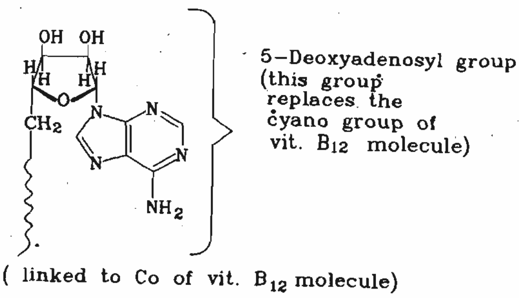
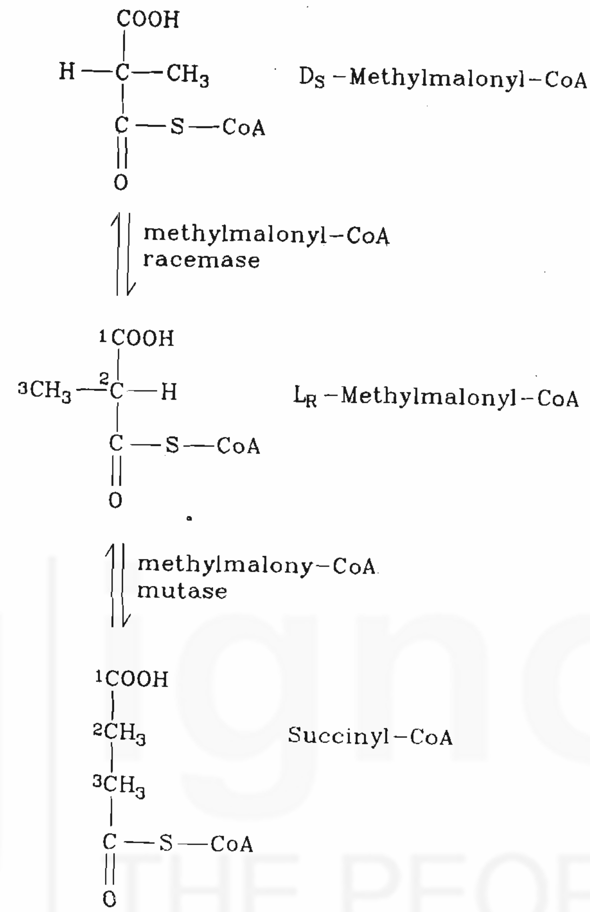


Fig. 7.9 : Coenzymic form of vitamin B_{12}

Biochemically, the B_{12} coenzyme is associated with enzymes such as methylmalonyl-CoA mutase, glutamate mutase and dioldehydrase. Methylmalonyl-CoA mutase, catalyses the isomerisation of methylmalonyl-CoA to succinyl CoA. In this isomerisation, $\overset{\overset{O}{\|}}{C} - S - CoA$ group is transferred from carbon atom 2 to the methyl carbon atom as depicted below.



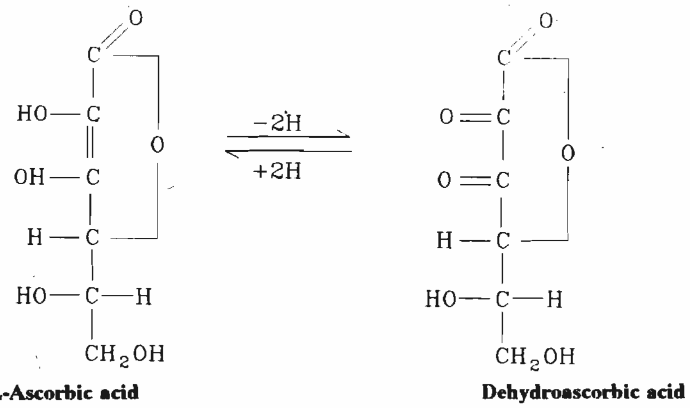
In general, this coenzyme functions in the enzymatic migration of a hydrogen atom from one carbon to an adjacent one, with the simultaneous transfer of a group X from the neighbouring carbon atom to the one which carried the original hydrogen.

We shall now describe the least stable of the water soluble vitamins, which is ascorbic acid.

7.3.2. Vitamin C (Ascorbic Acid)

Vitamin C is least stable to heating, particularly in the presence of trace metals, such as copper. Lack of this vitamin in the diet leads to scurvy, a disease characterised by anemia, loss of weight, feeling of tiredness, swollen and bleeding gums, and haemorrhages in the mucous membrane. Man, monkeys and guinea pigs are the only animals sensitive to a lack of this vitamin, since they do not possess the biosynthetic machinery for making this vitamin. Other animals can synthesise this vitamin and hence do not suffer from its deficiency. Citrus fruits, green leafy vegetables and tomatoes are rich sources of this vitamin. The activity of this vitamin is lost on cooking.

Vitamin C or ascorbic acid has a simple structure, which resembles a monosaccharide to some extent. It is an enediol of a hexose sugar acid, and is a naturally occurring lactone. This is the reduced form of the vitamin, the oxidised form being dehydroascorbic acid.



Vitamin C is easily oxidised in air, especially in presence of cu^{++} or Fe^{+++} ions. Both the forms of vitamin C are biologically active, due to the conversion of dehydroascorbic acid to ascorbic acid, and are found in body fluids.

The coenzyme form of the vitamin C is unknown and its specific biochemical function is not clear. Being a powerful reducing agent, it may participate in the oxidation-reduction processes in the body. It is also involved in the hydroxylation reactions, such as hydroxylation of proline to hydroxyproline, which is an amino acid found exclusively in collagen. However, the requirement of vitamin C for these reactions is not specific, since other reducing agents, which have no action against scurvy, can also function in these reactions. Vitamin C, over the last two decades, has been attributed with properties such as prevention of colds, heart diseases and cancer. However, nothing is certain regarding these claims as yet.

SAQ 1

Name the water soluble vitamins. Which of the water soluble vitamin is not identified with a coenzyme function ?

....

....

....

....

....

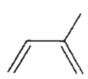
....

We shall now describe the fat soluble vitamins.

7.4 FAT SOLUBLE VITAMINS

It was observed, several decades ago, that young rats which were fed purified diets, did not show satisfactory growth. However, addition of animal fats, such as, butter and cod liver oil to these purified diets, resulted in normal growth. The growth promoting factors in these fats were collectively named as Vitamin A. Later work, however, showed that these factors consisted of Vitamin A, D, E and K, collectively known as **fat soluble vitamins**. These vitamins are nonpolar, hydrophobic molecules i.e., they are not soluble in water. Fat soluble vitamins are fairly stable and are not destroyed by heat.

Fat soluble vitamins are isoprene derivatives that require normal fat absorption in the human beings, so that they are absorbed themselves. They are transported by lipoproteins or other specific binding proteins in the blood, since unlike water soluble vitamins, they are not soluble in water, which is the normal biological solvent. The body is able to store excess of fat soluble vitamins in the liver and as such toxicity occurs with overdosage of these vitamins. We may point out that no coenzyme functions have yet been ascribed to any of the fat soluble vitamins.



Isoprene

We shall describe the importance of these vitamins for our health, their chemical structures and the biochemical functions they perform.

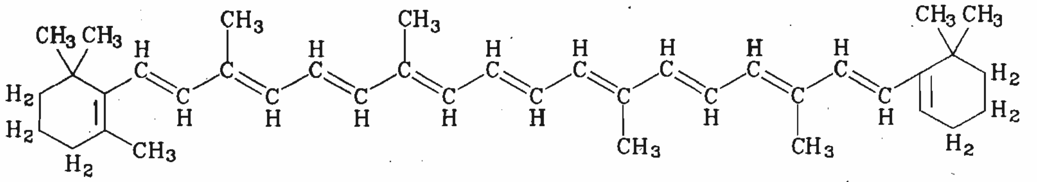
Vitamin A (Retinol)

Lack of this vitamin in the diet leads to inadequate growth. The development of bones and nervous system is also affected. Various mucous membranes harden and dry up, leading to degeneration of kidneys and sterlity. The effect of vitamin A deficiency on the eyes is conspicuous and leads to dry eyes or **xerophthalmia** and finally to **blindness**. In adults vitamin A deficiency shows up as **night blindness** in its early stages. This symptom is due to failure of the eyes to adapt to dark.

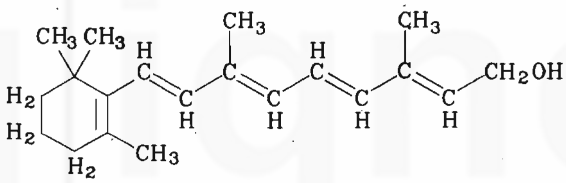
Fish liver oils are the best sources of vitamin A. Green and yellow vegetables such as spinach, lettuce, carrots and tomatoes are also very good sources of this vitamin.

Structurally vitamin A is an isoprene derivative which is related to carotenoid pigments, α, β and γ carotene, found in plants. These carotenoid pigments are precursors of vitamin A and are known as **provitamin A**. Vitamin A contains a six membered carbocyclic ring and a polyunsaturated eleven carbon side chain.

The structures shown here are called all *trans* because each $-CH_3$ group bears a *trans* relationship to the H atom on the adjacent C atom, along the aliphatic chain.



β-Carotene(all-*trans*)

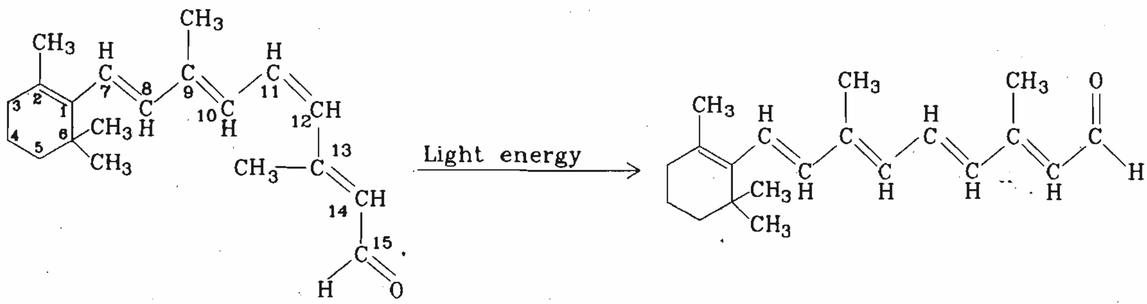


Vitamin A (all-*trans*)(Retinol)

You would observe from the above structures, that β—carotene has a symmetrical structure. It can give rise to two molecules of vitamin A. This process involves a symmetrical oxidative cleavage of the molecule, which occurs enzymatically.

Though a general biochemical function of vitamin A is not yet clear, its role in the visual process is well understood and can be explained as follows:

The retina of the mammals has two types of photo receptor cells, rod cells for vision in low light intensity and cone cells for vision in bright light. Rod cells, which participate in the visual process in the night contain a light absorbing conjugated protein called, **rhodopsin**, made up of a protein part **opsin** and a firmly bound **11-*cis*-retinal**, which is the aldehyde of vitamin A. This bound 11-*cis*-retinal, isomerises into all *trans*-retinal, in response to light.



11-*cis*-Retinal　　　　all-*trans*-Retinal

This isomerisation leads to the dissociation of all *trans*-retinal, which triggers the nerve impulse. During the process of reconstitution of rhodopsin, all trans-retinal is enzymatically reduced to all *trans*- vitamin A, which then isomerises in an enzymic reaction to 11-*cis*-vitamin A. This compound is then enzymatically oxidised to 11-cis-retinal, which now combines with opsin, to regenerate the rhodopsin. The visual cycle is thus complete. We have represented this visual cycle in the rod cells, diagrammatically in Fig.7.10.

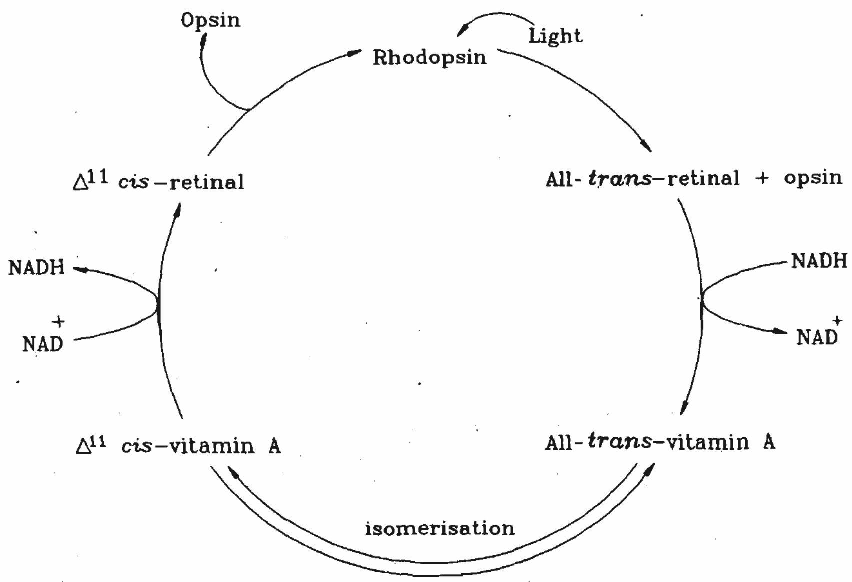


Fig. 7.10 : Visual cycle in the rod cells

Vitamin D

This vitamin is required for the formation of healthy bones. Its absence in the diet causes rickets or abnormal formation of bones. It is also involved in the formation of teeth. A rich source of vitamin D is fish liver oil. The D vitamins are actually sterol compounds, which occur in animals and plants. Preformed vitamin D is generally not required in diet, excepting for individuals who are not exposed to sunlight. In normal cases, exposure of the skin to sunlight brings about the formation of this vitamin from its provitamins, which are ergosterol (a plant sterol) and 7-dehydrocholesterol (an animal sterol). There are, as such, two main compounds which are known for their vitamin D activity, namely calciferol and cholecalciferol.

Calciferol or Vitamin D_2 is produced by the UV irradiation of ergosterol, present in yeast and moulds.

Cholecalciferol or Vitamin D_3 is produced by the UV irradiation of 7 - dehydrocholesterol, present in the skin. These conversions and structure of vitamin D_2 & vitamin D_3 are shown in Fig.7.11.

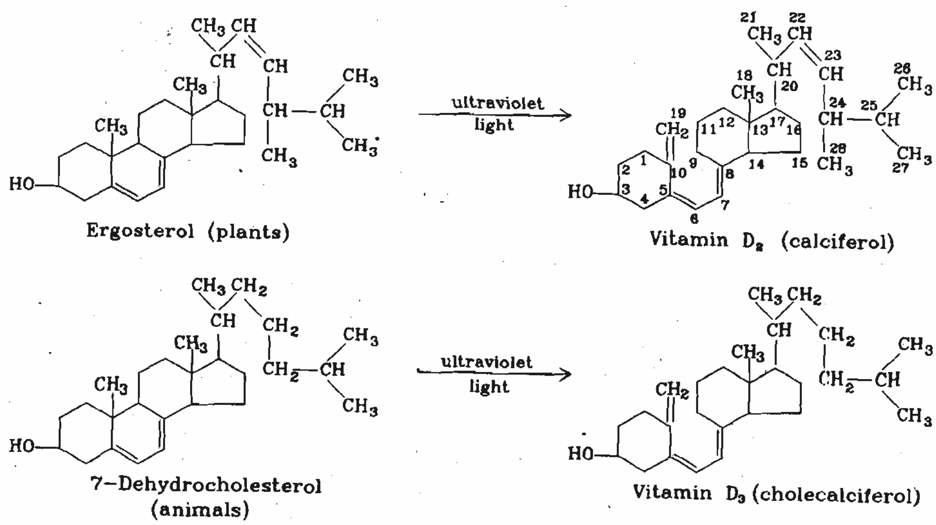
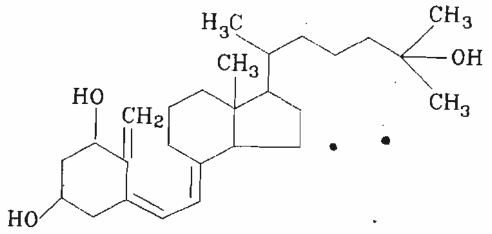


Fig. 7.11 : UV induced conversions of ergosterol and 7-dehydrocholesterol to vitamin D_2 and vitamin D_3 respectively

It is for these UV induced convertions of provitamin D, that human beings need to be exposed to sunlight for some time, to get their supply of vitamin D. In humans, two hydroxyl groups are introduced in cholecalciferol (vitamin D_3) molecule in liver and kidney, converting it into 1,25-dihydroxy cholecalciferol, also called **calcitriol,** which is the biologically active form. Since calcitriol is produced in the body, rather than being ingested, it is frequently referred to as a hormone.



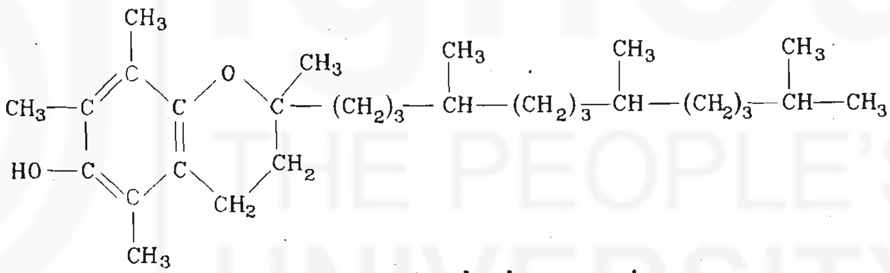
1,25 – dihydroxy cholecalciferol
(Calcitriol)

Biochemically vitamin D is involved in the utilisation of calcium and phosphorus for the normal formation of bones and teeth. It stimulates the absorption of calcium and phosphorus from the intestine.

Vitamin E (Tocopherols)

Animals fed on diets deficient in this vitamin suffer from infertility. The other symptoms are musculor dystrophy, degeneration of the kidneys and necrosis of the liver. Wheat germ oil is a rich source of vitamin E. Other sources are corn and cottonseed oils, egg yolk, meat and green leafy vegetables.

Vitamin E belongs to a group of compounds called tocopherols. α-tocopherol is the most important of these, both in terms of availability and effectiveness.



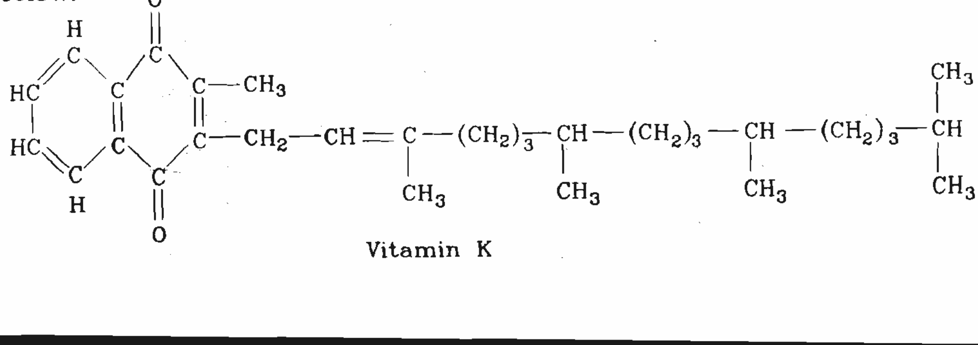
α-tocopherol

Tocopherols are powerful antioxidants, and one of their main functions is possibly to protect highly unsaturated fatty acids in biological membranes, against the damaging effects of oxidation. It also provides protection to vitamin A against oxidation. Vitamin E is destroyed by oxidising agents and UV light, but it is fairly resistant to heat (up to 200°C).

Vitamin K

A deficiency of this vitamin in the diet increases the clotting time of blood, leading to haemorrhages. Spinach, cabbage, alfalfa, are good sources of this vitamin. The vitamin is also synthesised by intestinal bacteria, hence, its deficiency cannot occur easily in mammals.

Vitamin K was the last of the four fat soluble vitamins to be discovered and characterised. This vitamin is derived from 1,4-naphthoquinone and its structure is shown below.



Vitamin K

The importance of this vitamin in the blood clotting mechanism is derived from its participation in the synthesis of prothrombin by the liver. It may also be involved in the electron transport system, because of the ease with which it can be reversibly reduced.

SAQ 2

Tick [√] mark the following statements as true or false.

a) Rhodopsin is dependent on vitamin A for its regeneration. [True / False]

b) Tocopherols are associated with antioxidant action. [True / False]

c) Blood clotting requires vitamin K. [True / False]

d) Vitamin D_3 is produced by the UV irradiation of 7-dehydrocholesterol present in the skin. [True / False]

In the preceding sections we described the biochemical significance of vitamins. You will now learn about minerals and trace elements, which are necessary for proper functioning of the organism.

7.5 MINERALS AND TRACE ELEMENTS

You are already familiar with the role of bulk constituents of our diet such as, proteins, fats and carbohydrates, in nutrition. The crucial function which vitamins play in the physiology and biochemistry of the organism has.already been discussed in Sections 7.3 and 7.4. However, these are not the only components of food, which are important for the functioning of an organism. Minerals, such as calcium and phosphorus are present in the body in bulk amounts and are important for the formation of bodily tissues. Similarly trace elements such as zinc, copper, manganese and molybdenum, function as cofactors for several enzymes, just as various derivatives of vitamins do. You will recall from the study of carbohydrates, proteins, lipids and nucleic acids, that carbon, hydrogen, oxygen and nitrogen form the bulk of the atoms in our bodies. Infact they constitute 99.3% of all the atoms in our bodies. The rest of the 0.7% atoms belong to about twenty one elements. They perform critical functions that are essential for life. These essential elements can be divided into two groups — the **macrominerals,** which are found in bulk concentrations in the body, and the **trace elements,** which are present in very small concentrations (ppm or ppb). Both these groups, which play an important nutritional role, are found either as ions or covalently bonded to organic molecules, in the living system. Except sodium and potassium, most of these minerals are not readily absorbed, and are generally excreted in feces. Kidneys also excrete many absorbed minerals.

You shall now learn about the nutritional significance of these minerals and trace elements. We shall also discuss their sources in food and their biochemical functions. Let us first describe the individual members of macrominerals.

7.5.1 Macrominerals

This group of minerals comprises of calcium, phosphorus, sodium, potassium, magnesium, sulphur and chlorine.

Calcium

This is one of the most essential and widespread elements present in the body and is found as the stable Ca^{2+} ion. Calcium is required for several life processes, such as growth and maintenance of the skeletal system, tooth formation, muscle contraction, mental activity and blood clotting. Calcium is the main mineral constituent of our bones and teeth, which account for 99% of the calcium in the body. Release of Ca^{2+} across synaptic membranes is involved in signal transmission. Calcium also participates in the blood clotting mechanism. It also regulates the flow of other mineral ions in and out of the cell.

Milk and milk products, such as butter milk, skim milk, cheese and green leafy vegetables, are the richest sources of calcium. Amaranth and drumstick leaves are important sources among leafy vegetables. Tapioca is also a good source. Children require more calcium than adults for their growing bones. Pregnant and lactating women also require a lot of calcium to meet the needs of the fetus and to replace the calcium secreted in breast milk.

Phosphorus

This element is abundantly present in bones and teeth, in the form of basic calcium phosphate. In the form of phosphodiester linkage,it is an important constituent of nucleic acids. As nucleotides, such as ATP and ADP, it participates in a large number of crucial biochemical transformations including energy metabolism. As nucleotides, it is a component of some coenzymes. In the form of dihydrogen phosphate ($H_2PO_4^-$) and monohydrogen phosphate ion (HPO_4^{2-}), it acts as a buffer, helping to maintain the proper pH of the biological fluids. Foods, such as nuts, oil seeds, pulses and cereals are rich sources of phosphorus.

SAQ 3

Tick [√] mark the appropriate answer. Utilisation of calcium and phosphorus in the formation of bones is dependent on

a) Pyridoxal phosphate [ ]

b) Carboxybiotin [ ]

c) Pantothenic acid [ ]

d) Vitamin D [ ]

Sodium, Potassium and Chlorine

Sodium and potassium are present in large concentration in the extra and intracellular fluids, and are involved in the maintenance of osmotic pressure and cell volume. Sodium and potassium ions contrib e to some extent in the maintenance of membrane potential and are involved in neuro conduction. Potassium ions are also implicated in the mechanism of short te emory. Sodium ions are also involved in the active transport of sugars and amino ac ls. Sodium and potassium ions are generally present in the form of their chloride salts in the body. Na^+, K^+, Cl^- ions are also necessary for the production of digestive secretions and for normal eye response to light.

All foodstuffs contain sodium and potassium. Fruits and vegetables are rich sources of these minerals. Our daily vegetarian food is adequate to meet bodily requirements of potassium. However, sodium content of natural food is insufficient for our bodily needs and hence extra sodium in the form of common salt has to be added to the food. This is because the body loses a large part of its sodium through urine and sweat, and this loss has to be made good.

Magnesium

Magnesium along with calcium and phosphorus is a constituent of the bones. It is required as a cofactor in many enzymatic reactions and is crucial for metabolism. Mg^{2+} ions are also essential for nerve impulse transmission and muscular contraction. It forms part of the chlorophyll molecule, found in plant cells. Magnesium is present in cereals, pulses, nuts and also in green vegetables. Normal diet is adequate for the supply of this metal.

Sulphur

This macromineral is found as a constituent of some amino acids, which are the basic units of proteins. For example, amino acid cysteine contains sulphur in the form of a sulphydryl group (-SH), and methionine contains a thioether group (CH_3 — S — CH_2 —) One important sulphur compound present in the body is coenzyme A (abbreviated as CoA-SH, showing the sulphydryl group). Coenzyme A on esterification forms acetyl CoA, which contains a thioester functional group.

$$CH_3-\overset{\overset{\displaystyle O}{\|}}{C}-S-CoA$$

Acetyl CoA

Acetyl CoA is an important intermediate in the metabolism of carbohydrates, lipids and proteins. You will note that sulphur is present in a bound form in the body.

We shall now briefly describe the trace elements.

7.5.2 Trace Elements

In addition to the above elements which are needed in relatively large concentrations for a healthy body, there are 14 other elements which are required in trace amounts. These are iron, zinc, copper, manganese, molybdenum, fluoride, iodine, cobalt, chromium, selenium, arsenic, nickle, silicon and boron. We shall describe some of these elements.

Iron

Bulk presence of iron in the body is in haemoglobin, the red pigment of erythrocytes, where it is present as the central atom of the haem portion of the haemoglobin molecule. As part of haem it plays a crucial role in the transport of oxygen. As part of haem portion of cytochromes, it forms a part of the electron transport system, participating in various oxidation reduction reactions. Iron is also stored in spleen.

Cereals, millets, pulses and green leafy vegetables are principle sources of iron. However, because of the limited capacity of our body to absorb dietary iron, our food should supply 10-25 fold more iron than needed by the body. It must be noted that the availability of iron from foodstuffs depends more on the total composition of the diet, than the iron content of individual foods. Even a small reduction in the level of iron results in anemia. Iron deficiency also causes increased heart and respiratory rates.

Zinc

A deficiency of zinc leads to subnormal growth and deficiency in gonadal function. It is present in adequate concentrations in cereals and pulses, and is also present in leafy vegetables, roots, tubers and fruits. Some nuts and spices have high concentration of this metal.

At the biochemical level, zinc is a constituent or a cofactor for carbonic anhydrase, carboxypeptidase and alcohol dehydrogenase. It is also crucial for the structural integrity of sequence-specific DNA binding proteins.

Copper

A deficiency of this metal leads to pathological conditions in organs, that are enriched in connective tissue. Other symptoms are impaired myelination and defective metabolism of the neurotransmitter, catecholamine, leading to disturbances in the central nervous system.

Copper is well distributed in various types of foodstuffs such as cereals, pulses, leafy vegetables, nuts, spices and fruits. Biochemically, copper is involved in the absorption of iron. It also participates in the metabolism of the neurotransmitter, catecholamine, and in the formation of connective tissues. It is an important constituent of oxidative enzymes such as, cytochrome oxidase. Copper circulates in the plasma as ceruloplasmin. In plants it forms part of the structure of plastocyanin, which participates in the transfer of electrons during photosynthesis.

Manganese

Inadequate intake of this metal can lead to defective mineralisation of the skeletal bones. Manganese is present in almost all types of foods and is abundant in nuts, cereals, fruits and vegetables. At the biochemical level manganese functions as a cofactor for a number of enzymes such as phosphotransferases and arginase. Manganese is present at the active centre of water-splitting enzymes of the photosynthetic apparatus of plants.

Molybdenum

This metal is a cofactor for xanthine and aldehyde oxidases, and functions in uric acid metabolism. It is also a constituent of nitrogen fixing systems. Since no symptoms of molybdenum deficiency are detected in humans, its intake through food appears to be adequate. It is found in peas, cereals, organ meat and yeast.

Fluoride

This is an important ion for the prevention of dental caries. However, excess intake through water results in fluorosis which is characterised by hardening of bones.

Iodine

Inadequate intake of this element, either through food or water, leads to goitre, which is characterised by swelling of the thyroid gland in the neck. Iodine deficiency at the prenatal stage may result in mental retardation. Insufficient intake of iodine in later life may lead to inadequate body growth.

The biochemical role of iodine derives from its presence in thyroxine, the hormone secreted by the thyroid gland. This hormone regulates body's chemical activity, and is important for normal growth. In the absence of adequate iodine, thyroid gland cannot synthesise enough thyroxine, and hence it responds by increasing its size to make more thyroxine.

Cobalt

A lack of this element results in pernicious anemia. Cobalt is also a part of vitamin B_{12}. Dietary sources of cobalt are dairy products and meat.

Chromium

This element plays a role in lowering the blood sugar level in the body. It has also been found to lower total serum cholesterol in human beings. Good source of chromium are brewers yeast, whole grain cereals and liver.

Other trace elements, i.e. selenium, arsenic, nickle, silicon and boron, have been found to be essential to animals. However, their role in human beings is not as yet clearly established.

SAQ 4

Tick [√] mark the following statements as true or false.

a) Cobalt is associated with vitamin B_{12}. [True / False]

b) Iron is involved in haemoglobin formation. [True / False]

c) Maintenance of osmotic pressure and cell volume depends on sodium and potassium ions. [True / False]

d) Magnesium is important as a cofactor for many enzymatic reactions. [True / False]

7.6 SUMMARY

- For proper functioning, an organism not only requires proteins, fats, carbohydrates and nucleic acids, but also some organic compounds, known as vitamins.
- Vitamins are required in trace amounts. They must be obtained from the food we eat, as some organisms including humans do not synthesise them.
- Deficiency of vitamins result in various diseased states.
- Vitamins have been classified, on the basis of their solubility, into water soluble and fat soluble types. The water soluble type comprise of vitamin B group and vitamin C, where as the fat soluble type are vitamins A, D, E and K.
- The B group of vitamins also exist in coenzymic forms, which participate in various reactions of intermediary metabolism.
- Deficiency of B group of vitamins, comprising of thiamine, riboflavin, niacin, pantothenic acid, pyridoxine, biotin, folic acid and cyanocobalamin, causes various diseases, such as beriberi, pellagra, inadequate growth, cataract in eyes, dermatitis etc.
- Vitamin C is required for the prevention of scurvy. No coenzymic form for this vitamin is known as yet. However, it is involved in the oxidation reduction processes in the body.
- Fat soluble vitamins are not identified with any coenzymic functions, but they have important physiological functions. For example, a derivative of vitamin A is involved in the visual cycle in dim light, vitamin D is involved in the utilisation of calcium and phosphorus for the normal formation of bones and teeth, vitamin E as a powerful antioxidant prevents oxidative damage to biological membranes, and vitamin K participates in blood clotting mechanism.

- In addition to vitamins, humans also require some minerals and trace elements for proper functioning. Their absence in the diet also results in various diseased states.
- Some elements as ions, act as cofactors for many enzymatic reactions.
- Minerals such as calcium and phosphorus are required in bulk and are known as macrominerals, where as some elements such as zinc and copper are required in small amounts and are called trace elements.
- Both macrominerals, as well as the trace elements perform crucial functions in the organism.

7.7 TERMINAL QUESTIONS

1. Identify the biochemical reactions associated with the following vitamins: niacin, folic acid, riboflavin, biotin and pantothenic acid.
2. What is the biochemical reaction in which vitamin B_{12} participates as a coenzyme?
3. Describe the component parts of coenzyme A and folic acid.
4. What are the physiological roles of calcium ?
5. What is the relationship between vitamin A and vision ?
6. Give one principal source for each of the following vitamins: vitamin A, vitamin D, vitamin C, vitamin B_{12}, vitamin E.

7.8 ANSWERS

Self Assessment Questions

1. Vitamin C and the B group of vitamins are water soluble. The B group comprises of vitamin B_1 or thiamine, vitamin B_2 or riboflavin, niacin, vitamin B_5 or pantothenic acid, vitamin B_6 or pyridoxine, biotin, folic acid, and vitamin B_{12} or cyanocobalamin.
   Vitamin C or ascorbic acid does not have any known coenzymic function.
2. a - true ; b - true ; c - true ; d - true
3. d
4. a - true ; b - true ; c - true ; d - true

Terminal Questions

1. Niacin is associated with oxidation-reduction reactions. Folic acid is associated with the reactions involving transfer of one carbon fragments. Riboflavin is associated with some oxidation-reduction reactions. Biotin is associated with carboxylation reactions. Pantothenic acid is associated with acetylation reactions occurring in fatty acid synthesis.
2. Vitamin B_{12} coenzyme functions in the enzymatic migration of a hydrogen atom from one carbon atom to an adjacent one, with the simultaneous transfer of a group x from the neighbouring carbon to the one to which the hydrogen atom was originally bound.
3. Component parts of coenzyme A are adenosine diphosphate, pantothenic acid and mercaptoethylamine. Components of folic acid are pteridine, p-amino benzoic acid and glutamic acid.
4. Physiological roles of calcium are : (a) growth and maintenance of the skeletal system and teeth (b) muscle contraction (c) nerve signalling and (d) blood clotting.
5. Retinal rod cells which participate in the visual process in dim light contain a light absorbing conjugated protein, called rhodopsin, made up of a protein part opsin and a firmly bound11-*cis*-retinal, which is the aldehyde of vitamin A. The transformations that rhodopsin undergoes, in response to light, form the biochemical basis of vision.

6. Fish liver oils are important sources of vitamin A and D. Important source of vitamin C are citrus fruits and that of vitamin B_{12} is liver. Wheat germ oil is a rich source of vitamin E.

FURTHER READINGS

1. *Harper's Review of Biochemistry* (18th ed.)
D.W. Martin, P.A. Mayes and V.W. Rodwell
Lange Medical Publications, Maruzen Asia (Pte.) Ltd.
Singapore
1981

2. *Outlines of Biochemistry* (4th ed.)
Eric E. Conn and P.K. Stumpf
Wiley Eastern Limited, New Delhi
1976

3. *Principles of Biochemistry*
Albert L. Lehninger
CBS Publishers and Distributors, Delhi
1984

NOTE