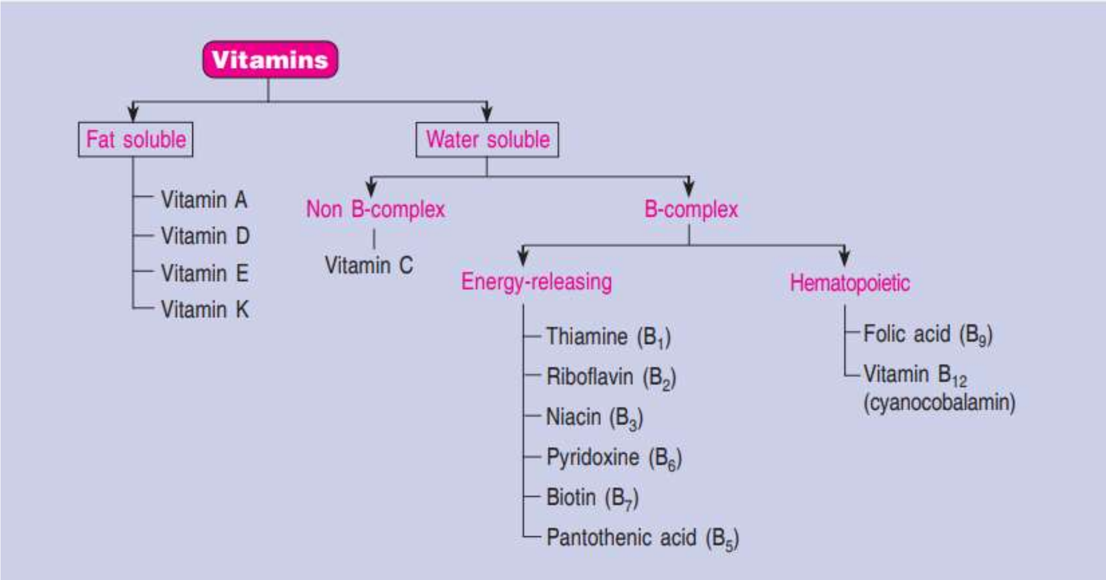
Vitamins may be regarded as organic compounds required in the diet in small amounts to perform specific biological functions for normal maintenance of optimum growth and health of the organism. The bacterium E.coli does not require any vitamin, as it can synthesize all of them. The ability to synthesize vitamins was lost. Hence, the higher organisms have to obtain them from diet. The vitamins are required in small amounts, since their degradation is relatively slow

Classification of vitamins

There are about 15 vitamins, essential for humans. They are classified as fat soluble (A, D, E and K) and water soluble (C and B-group) vitamins as shown in the Table 4.1. The B-complex vitamins may be sub-divided into energy-releasing (B1, B2, B6, biotin etc.) and hematopoietic (folic acid and B12). Most of the water soluble vitamins exert the functions through their respective coenzymes while only one fat soluble vitamin (K) has been identified to function as a coenzyme. Synthesis of vitamins by intestinal bacteria

Vitamins, as per the definition, are not synthesized in the body. However, the bacteria of the gut can produce some of the vitamins, required by man and animals. The bacteria mainly live and synthesize vitamins in the colon region, where the absorption is relatively poor.. As far as humans are concerned, it is believed that the normal intestinal bacterial synthesis, and absorption of vitamin K and biotin may be sufficient to meet the body requirements. For other B-complex vitamins, the synthesis and absorption are relatively less. Administration of anitibiotics often kills the vitamin synthesizing bacteria present in the gut, hence additional consumption of vitamins is recommended.

TABLE 4.1: Classification of vitamins



Fat soluble vitamins—general

The four vitamins, namely vitamin A, D, E, and K are known as fat or lipid soluble. Their availability in the diet, absorption and transport are associated with fat. They are soluble in fats and oils and also the fat solvents (alcohol, acetone etc.). Fat soluble vitamins can be stored in liver and adipose tissue. They are not readily excreted in urine. Excess consumption of these vitamins (particularly A and D) leads to their accumulation and toxic effects. All the fat soluble vitamins are isoprenoid compounds, since they are made up of one or more of five carbon units namely isoprene units (CH C.CH3 CH CH). Fat soluble vitamins perform diverse functions. Vitamin K has a specific coenzyme function.

Water soluble vitamins—general

The water soluble vitamins are a heterogenous group of compounds since they differ chemically from each other. The only common character shared by them is their solubility in water. Most of these vitamins are readily excreted in urine and they are not toxic to the body. Water soluble vitamins are not stored in the body in large quantities (except B12). For this reason, they must be continuously supplied in the diet. Generally, vitamin deficiencies are multiple rather than individual with overlapping symptoms. The water soluble vitamins form coenzymes that participate in a variety of biochemical reactions, related to either energy generation or hematopoiesis. It may be due to this reason that the deficiency of vitamins results in a number of overlapping symptoms. The common symptoms of the deficiency of one or more vitamins involved in energy metabolism include dermatitis, glossitis (red and swollen tongue), cheilitis (rupture at the corners of lips), diarrhea, mental confusion, depression and malaise. Deficiency of vitamins B1, B6 and B12 is more closely associated with neurological manifestations

VITAMIN D

Vitamin D is a fat soluble vitamin. It resembles sterols in structure and functions like a hormone. The symptoms of rickets and the benefical effects of sunlight to prevent rickets have been known for centuries. Vitamin D was isolated by Angus (1931) who named it calciferol.

Chemistry

Ergocalciferol (vitamin D2) is formed from ergosterol and is present in plants (Fig.4.1). Cholecalciferol (vitamin D3) is found in animals. Both the sterols are similar in structure except that ergocalciferol has an additional methyl group and a double bond. Ergocalciferol and cholecalciferol are sources for vitamin D activity and are referred to as provitamins. During the course of cholesterol biosynthesis , 7-dehydrocholesterol is formed as an intermediate. On exposure to sunlight, 7-dehydrocholesterol is converted to cholecalciferol in the skin (Fig.4.2). Vitamin D is regarded as sun-shine vitamin. The synthesis of vitamin D3 in the skin is proportional to the exposure to sunlight. Dark skin pigment (melanin) adversely influences the synthesis of cholecalciferol. (Note : The term vitamin D1 is no more in use. It was originally used for fat soluble crystalline material, which later turned out to be a mixture).

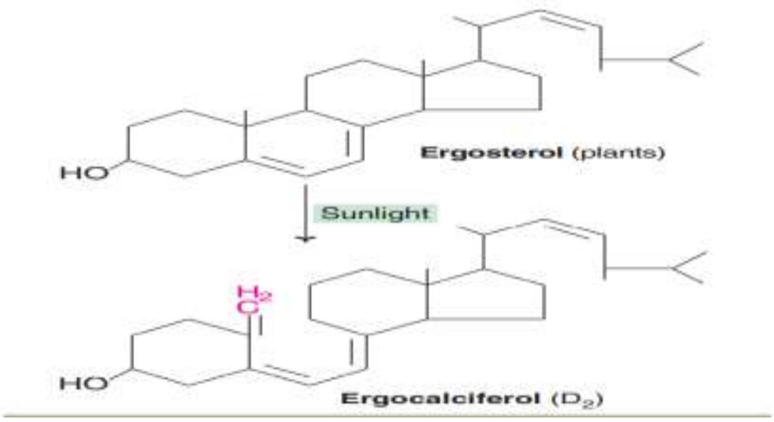


Figure 4.1: Formation of ergocalciferol from ergosterol.

Absorption, Transport and Storage

Vitamin D is absorbed in the small intestine for which bile is essential. Through lymph, vitamin D enters the circulation bound to plasma D2-globulin and is distributed throughout the body. Liver and other tissues store small amounts of vitamin D.

Synthesis of 1,25-DHCC active form

Cholecalciferol is first hydroxylated at 25th position to 25-hydroxycholecalciferol (25-OH D3) by a specific hydroxylase present in liver. 25-OH D3 is the major storage and circulatory form of vitamin D. Kidney possesses a specific enzyme, 25-hydroxycholecalciferol (calcidiol) 1-hydroxylase which hydroxylates 25-hydroxycholecalciferol at position 1 to produce 1,25- dihydroxycholecalciferol (1,25-DHCC). 1,25 DHCC contains 3 hydroxyl groups (1,3 and 25 carbon) hence referred to as calcitriol. Both the hydroxylase enzymes (of liver and kidney) require cytochrome P450, NADPH and O2 for the hydroxylation process. The synthesis of calcitriol is depicted in Figs.4.2

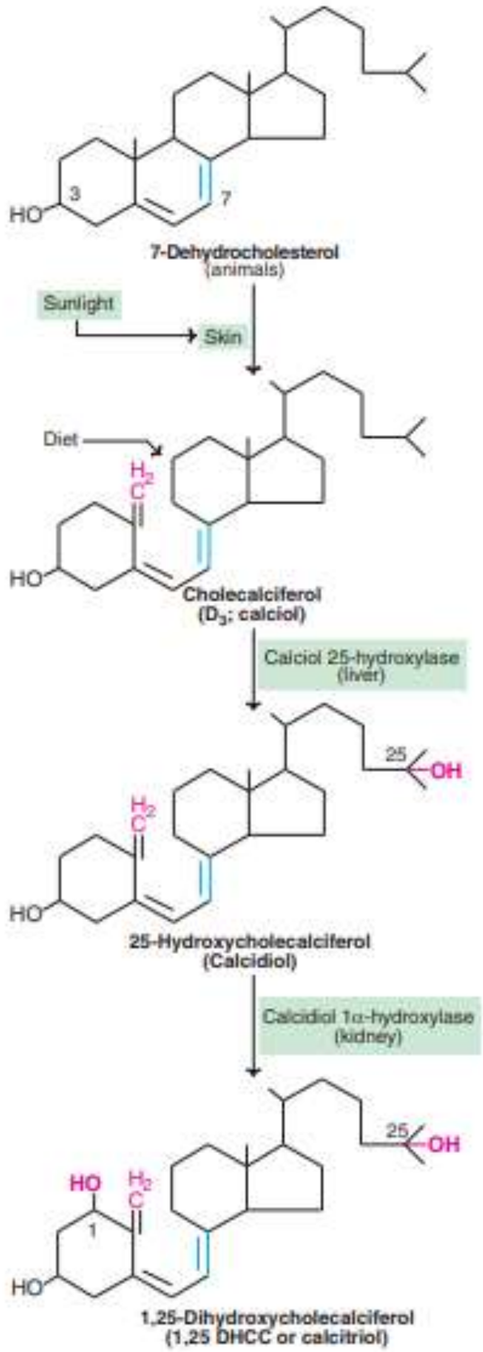


Figure 4.2: : Biosynthesis of active form of vitamin D-calcitriol (1,25 DHCC).

Biochemical functions

Calcitriol (1,25-DHCC) is the biologically active form of vitamin D. It regulates the plasma levels of calcium and phosphate. Calcitriol acts at 3 different levels (intestine, kidney and bone) to maintain plasma calcium (normal 9–11 mg/dl).

1-Action of calcitriol on the intestine :

Calcitriol increases the intestinal absorption of calcium and phosphate. In the intestinal cells, calcitriol binds with a cytosolic receptor to form a calcitriol-receptor complex. This complex then approaches the nucleus and interacts with a specific DNA leading to the synthesis of a specific calcium binding protein. This protein increases the calcium uptake by the intestine. The mechanism of action of calcitriol on the target tissue (intestine) is similar to the action of a steroid hormone.

2. Action of calcitriol on the bone :

In the osteoblasts of bone, calcitriol stimulates calcium uptake for deposition as calcium phosphate. Thus calcitriol is essential for bone formation. The bone is an important reservoir of calcium and phosphate. Calcitriol along with parathyroid hormone increases the mobilization of calcium and phosphate from the bone. This causes elevation in the plasma calcium and phosphate levels.

3. Action of calcitriol on the kidney :

Calcitriol is also involved in minimizing the excretion of calcium and phosphate through the kidney, by decreasing their excretion and enhancing reabsorption. The sequence of events that take place in response to low plasma calcium concentration and the action of calcitriol on intestine, kidney and bone, ultimately leading to the increase in plasma calcium. In this way, to maintain the homeostasis of calcium is important.

Deficiency symptoms

Vitamin D deficiency is relatively less common, since this vitamin can be synthesized in the body. However, insufficient exposure to sunlight and consumption of diet lacking vitamin D results in its deficiency. Vitamin D deficiency occurs in strict vegetarians, chronic alcoholics, individuals with liver and kidney diseases or fat malabsorption syndromes. vitamin D deficiency is also observed, if the requirement is not met through diet. Deficiency of vitamin D causes rickets in children and osteomalacia in adults. Osteomalacia is derived from Greek (osteon-bone; malakia-softness). Vitamin D is often called as antirachitic vitamin. Rickets in children is characterized by bone deformities due to incomplete

mineralization, resulting in soft and pliable bones and delay in teeth formation. In rickets, the plasma level of calcitriol is decreased and alkaline phosphatase activity is elevated. Alkaline phosphatase is concerned with the process of bone formation. There is an overproduction of alkaline phosphatase related to more cellular activity of the bone. In case of osteomalacia (adult rickets) demineralization of the bones occurs (bones become softer), increasing their susceptibility to fractures.

Hypervitaminosis D

Vitamin D is stored mostly in liver and slowly metabolised. Among the vitamins, vitamin D is the most toxic in overdoses (10-100 times RDA). Toxic effects of hypervitaminosis D include mineralization of bone (resorption) and increased calcium absorption from the intestine, leading to elevated calcium in plasma (hypercalcemia). Prolonged hypercalcemia is associated with deposition of calcium in many soft tissues such as kidney and arteries. Hypervitaminosis D may lead to formation of stones in kidneys (renal calculi). High consumption of vitamin D is associated with loss of appetite, nausea, increased thirst, loss of weight etc.