Fat soluble vitamins

Food chemistry

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Introduction:

Vitamins are a group of organic compounds that are required in very small amounts, essential for the normal functioning of the human body. They have widely varying chemical and physiological functions and are broadly distributed in natural food sources. Thirteen vitamins are recognized in human nutrition and these may be conveniently classified into two groups according to their solubility. The fat-soluble vitamins are vitamins A, D, E, and K. The water-soluble vitamins comprise vitamin C and the members of the vitamin B group, namely thiamin (vitamin B_1), riboflavin (vitamin B_2), niacin, vitamin B_6, pantothenic acid, folate, and vitamin B_{12}. To learn more about vitamins, their absorption, transport and functions, the session is divided into 5 major topics namely:

1) Transport and Absorption of vitamins
2) Fat soluble vitamins, functions and their forms
3) Structure of fat soluble vitamins
4) Stability of fat soluble vitamins
5) Bioavailability of fat soluble vitamins

1) Transport and Absorption of vitamins:

Absorption is a complex process in which the nutrients pass through the intestinal mucosal cells into the bloodstream.Mammalian epithelia are enveloped by a plasma membrane composed of a phospholipid bilayer interspersed frequently with cholesterol molecules. Integral transmembrane proteins span the lipid bilayer in a weaving fashion and account for most membrane-associated receptors, transporters and certain enzymes. Tight junctions prevent the passage of water and molecular solutes between adjacent epithelial cells. The lipid bilayer along with membrane associated receptors is displayed on the screen (Figure 1). The plasma membrane constitutes a selective barrier to the transcellular movement of molecules and ions between the extracellular and intracellular fluid compartments. Fat-soluble substances, water, and small uncharged polar solutes can simply diffuse through the membrane, but ions and water-soluble molecules having five or more carbon atoms cannot do so. Most biologically important water-soluble substances such as glucose, amino acids, water-soluble vitamins, and certain inorganic ions are translocated across the plasma membrane by means of protein transporters, which exert their effect through a change in their three-dimensional shape. Specific transporters are responsible for the translocation of a specific molecule or a group of closely related molecules. Specificity is imparted by the tertiary and quaternary structures of the transporter molecule — only if a solute's spatial configuration fits into the protein, will the solute be transferred across the membrane. Transporters fall into two main classes: carriers and ion channels. Ion pumps are a type of carrier protein, which is also an enzyme. At physiological concentrations, the translocation of several watersoluble vitamins (thiamin, riboflavin, pantothenic acid, biotin, and vitamin C) across cell membranes is mediated by carrier proteins as displayed on the screen (Transporters-Figure 2). The term "transport" implies a carrier-mediated translocation. The downhill movement of a substance from a region of higher concentration to lower concentration is a passive process driven by the concentration gradient. There are two types of passive movement: facilitated diffusion, which is carrier mediated, and simple diffusion, which is not. The uphill movement of a substancei.e movement from lower to higher concentration gradient is referred to as active transport and requires the expenditure of metabolic energy. Primary active transport is driven directly by metabolic energy and is carried out exclusively by ion pumps, such as the calcium pumps, the sodium pump, and the proton pumps. Ion pumps are ATPases, which utilize the energy released by the hydrolysis of ATP. Secondary active transport is indirectly linked to metabolic energy through a coupling of the solute to the pump-driven movement of an inorganic ion (usually Na^+).

*Intestinal absorption:*The functional absorptive unit of the small intestine is the villus, a finger-like projection of the mucosa. The lamina propria core of each villus contains a capillary network with a supplying arteriole and draining venule. Each villus is covered by an epithelium composed of a single layer of columnar absorptive cells called enterocytes interspersed occasionally with mucus-secreting goblet cells. The enterocyte constitutes the only anatomical barrier of physiological significance controlling the absorption of nutrients.The apical membrane of the enterocyte that is the membrane facing the intestinal lumen is covered with microvilli, which are minute projections of the plasma membrane. Because of its brush-like appearance under the microscope, the apical membrane is also known as the brush-border membrane. The picture of villus is displayed on the screen (Figure 3 - villus)

Absorption of fat soluble vitamins: Absorption of the fat-soluble vitamins takes place mainly in the proximal jejunum and depends on the proper functioning of the digestion and absorption of dietary fat. The stomach is the major site for emulsification of fat. The coarse lipid emulsion, on entering the duodenum, is emulsified into smaller globules by the detergent action of bile. Pancreatic lipase hydrolyses triglycerides at the 1 and 3 positions, yielding 2-monoglycerides and free fatty acids. During their detergent action, bile salts exist as individual molecules. Above a critical concentration of bile salts, the bile constituents i.e., bile salts, phospholipids, and cholesterol form aggregates called micelles, in which the polar ends of the molecules are orientated toward the surface and the nonpolar portion forms the interior. The picture of micelles is given in (Figure 4). The 2-monoglycerides and free fatty acids are sufficiently polar to combine with the micelles to form mixed micelles. These are stable water-soluble structures, which can dissolve fat-soluble vitamins and other hydrophobic compounds in their oily interior. Mixed micelles do not cross the brush-border membrane of enterocytes as intact structures: the products of lipolysis must dissociate from these structures before they can be absorbed.

Individual lipids, including fat-soluble vitamins, can then be passively ~~be~~ absorbed across the brush-border membrane. After the lipolyticmicellar products enter the enterocytes, a cytosolic fatty acid-binding protein (FABP) facilitates intracellular transport of fatty acids by directing them from the cell membrane to the smooth endoplasmic reticulum, where triglyceride synthesis takes place. The triglycerides are packaged into chylomicrons, together with free and esterified cholesterol, phospholipids, apolipoproteins, fat-soluble vitamins, and carotenoids. After further processing, the chylomicrons are discharged from the enterocyte by exocytosis across the basolateral membrane and enter the central lacteal of the villus. From there, they pass into the larger lymphatic channels draining the intestine, into the thoracic duct, and ultimately into the systemic circulation.Associated with the endothelium of blood capillaries in most tissues is the enzyme lipoprotein lipase, which attacks circulating chylomicrons and converts them into much smaller triglyceride-depleted particles known as chylomicron remnants. These particles contain apolipoprotein E (apoE) acquired from other circulating lipoproteins. The released free fatty acids and diglycerides can then be absorbed by the tissue cells. The liver has the capacity to rapidly remove chylomicron remnants from the circulation.

2) Fat soluble vitamins, functions and their forms: Vitamin A, D, E and K are regarded as fat soluble vitamins. They are stored in the liver and require bile salts for absorption.

*Vitamin A:*Vitamin A-active compounds includeretinoids (designated as vitamin A) and their carotenoid precursors (provitaminA carotenoids). The retinoids comprise retinol, retinaldehyde, and retinoic acid, together with their naturally occurring and synthetic analogs. Retinal and retinoic acid are formed from retinol. Further retinal and retinol are inter-convertible.But retinoic acid cannot be converted to either retinal or retinol.In plant foods it is present in provitamin form which is known as carotenes. There are three types of carotenes present in plants. They are α-carotenes, β-carotenes and γ-carotenes.β-carotenes are most potent source of retinol because one molecule of β-carotene yields two molecules of Vitamin A *in vivo.* Generally speaking, dietary vitamin A is obtained from animal-derived foods, while plant foods provide carotenoid precursors such as β-carotenes, β-Cryptoxanthin, z(zeta)-carotene, zeinoxanthin, zeaxanthin, neoxanthin, and violaxanthin.

Vision is a non-hormonal, biochemical process involving a different vitamin A metabolite. Vitamin A is an essential dietary factor for normal embryogenesis, cell growth and differentiation, reproduction, maintenance of the immune system, and vision. Retinol is required for differentiation and function as steroid hormone. Retinol and retinoic acid are involved in regulation of gene expression. Vitamin A is required for maintenance of nervous tissue particularly myelin sheath formation.

*Vitamin D:*Vitamin D is represented by cholecalciferol (vitamin D_3) and ergocalciferol (vitamin D_2) which is structurally similar secosteroids derived from the UV irradiation of provitamin D sterols. Exposure of the skin to sunlight converts 7-dehydrocholesterol to vitamin D_3, which, on reaching the blood capillaries of the dermis, is conveyed to the liver on a specific plasma transport protein. Vitamin D_2 is produced in plants, fungi, and yeasts by the solar irradiation of ergosterol. On irradiation, the provitamins are initially converted to previtamin D, which undergoes thermal transformation to vitamin D.

Vitamin D in its active form1, 25-dihydroxy cholecalciferol orcalcitriol acts as a steroid hormone. It is synthesized from ergocalciferol and cholecalciferol. Vitamin D binds to chromatin of target tissue and expresses the genes for calcium binding protein and Ca^{2+}-ATPase (Calcium ion-ATPase) in the intestinal cells which increases calcium absorption by actively transporting Ca^{2+} across the plasma membrane. It is essential for mineralization of bones by stimulating the transcription of mRNA for calcium binding protein and alkaline phosphatase thus increasing the absorption calcium and phosphate ions in bone mineralization. Vitamin D decreases the pH of the lower gastrointestinal tract. It helps in the excretion of phosphate and citric acid.Calcitriol is an immuno regulatory hormone. It stimulates cell mediated immunity. It plays a vital role in monocyte/macrophage activation.

Vitamin E: The term vitamin E refers to group of four (often six) compounds that exhibit vitamin E activity. They are α-tocopherol, β-tocopherol, γ-tocopherol and δ-tocopherol.α-tocopherol present in cell membrane, membrane of subcellular organelle and in cytosol function as antioxidant or free radical scavenger. It is present in high concentration in tissues which are exposed to high O_2 pressure like erythrocytes, lungs, retina etc. It prevents peroxidation of membrane lipids particularly polyunsaturated fatty acid (PUFA) of membrane phospholipids. Vitamin E is required for fertility in animals. Vitamin E increases synthesis of hemeproteins by increasing synthesis of ALA synthase and ALA dehydratase. Vitamin E prevents dietary vitamin A and carotenes from oxidative damage.

*Vitamin K:*The term vitamin K refers to group of compounds that exhibits vitamin K activity. They are Vitamin K_1also called as phylloquinone is the major form of vitamin found in plants particularly in green leafy vegetables. Vitamin K_2 also known as menaquinone is the vitamin K present in animals and synthesized by intestinal flora. Menadione is a synthetic analog of vitamin K. It is also called as vitamin K_3. It lacks characteristic side chain present in vitamin K_1 and K_2. It is converted to vitamin K_2 by alkylation in the body.

Vitamin K is essential for the activation of specific proteins such as prothrombin involved in blood clotting and in bone mineralization through its role as a cofactor for γ-glutamylcarboxylase. This enzyme catalyzes a unique post-translational conversion of selected glutamate residues in the proteins to γ -carboxyglutamate residues, allowing the proteins to bind calcium and thus become activated.

3) Structure of fat soluble vitamins:

*Vitamin A:*The parent vitamin A compound, retinol, has the empirical formula $C_{20}H_{30}O$. The molecule comprises a β-ionone (cyclohexenyl) ring attached at the C-6 position and side chain containing two isoprene units with four conjugated double bonds which give rise to cis– trans (geometric) isomerism. Carotenoids can be considered chemically as derivatives of lycopene — a $C_{40}H_{56}$ polyene composed of eight isoprenoid units. Derivatives are formed by a variety of reactions that include cyclization, hydrogenation, dehydrogenation, and insertion of oxygen. Hydrocarbon carotenoids are known as carotenes, and the oxygenated derivatives are termed xanthophylls. In nature, carotenoids exist primarily in the all-trans configuration. The structure of Vitamin A is displayed on the screen figure 5.

Vitamin D: All forms of Vitamin D belong to a family of lipids called secosteroids. Secosteroids are very similar in structure to steroids except that two of the B-ring carbon atoms of the typical four steroid rings are not joined. The structural difference between vitamin D_2 and vitamin D_3 is the side chain of D_2 contains a double bond between carbons 22 and 23, and a methyl group on carbon 24.The structure of Vitamin D is displayed on the screen figure 6.

*Vitamin E:*Tocopherols are methyl-substituted derivatives of tocol, which comprises a chroman-6-ol ring attached at C-2 to a saturated isoprenoid side chain. Tocotrienols are analogous structures whose side chains contain three trans double bonds. In nature, there are four tocopherols and four corresponding tocotrienols; these are designated as alpha- (α), beta- (β), gamma- (γ) and delta- (δ) according to the number and position of the methyl substituents in the chromanol ring. They differ in methyl groups in positions 5, 7, and 8 of chromanol ring. α-tocopherol has three methyl groups in positions, 5, 7 and 8 of chromanol ring. The chromanol ring of β- and γ-tocopherols contains two methyl groups in 5, 8 and 7, 8 respectively. However δ-tocopherol has one methyl group in position 8 of chromanol ring. The structure of Vitamin E is displayed on the screen figure 7.

Vitamin K: They are derivatives of naphthoquinone and differ in side chain. Phylloquinone contain phytylside chain whereas menaquinone contains polyisoprenoid side chain made up of 7 isoprene units. Several variants of vitamin K_2 containing more than 7 isoprenoid units in the side chain are also identified.The structure of Vitamin K is displayed on the screen figure 8.

4) Stability of fat soluble vitamins:

*Vitamin A:*Retinol is readily oxidized by atmospheric oxygen, resulting in an almost complete loss of biological activity. The 5,6-epoxide and 5,8-furanoxide are among the oxidation products. Retinyl esters are more stable towards oxidation when compared to retinol. Retinol is extremely sensitive towards acids, which can cause rearrangement of the double bonds and dehydration. Solutions of all-trans-retinol or retinylpalmitate in hexane undergo slow isomerization to the lower potency cis-isomers when exposed to white light. The photoisomerization rate is greatly increased in the presence of chlorinated solvents. However, it is stable in the dark. Irradiation also rearranges double bonds to form inactive retro structures. The carotenoids are stable within their natural plant cell environment, but once isolated they are prone to molecular rearrangement, trans to cis isomerization, and degradation by heat, light, oxygen, trace amounts of acids, and active surfaces such as silica. They are sensitive to enzymatic and non-enzymatic oxidation. The enzyme lipoxygenase in plant tissues catalyzes lipid peroxidation, giving rise to hydroperoxides. The hydroperoxides decompose to form peroxyl and alkoxyl radicals which attack carotenoids. The cutting of fruits and vegetables into small pieces or maceration increases exposure to oxygen and brings the carotenoids and enzymes together. Moderate heat treatments such as blanching and cooking denature carotenoid binding proteins, thereby releasing the carotenoids so that they can be more readily extracted. Blanching of fruits and vegetables before processing inactivates lipoxygenase and other enzymes (e.g., peroxidase) that are involved in carotenoid destruction.

Vitamin D: It is sensitive to oxygen and light. In the presence of mild acid, vitamin D undergoes isomerization.

*Vitamin E:*Tocopherols are alkaline sensitive and their vitamin activity is destroyed by oxidation. Cooking and food processing may destroy vitamin E to some extent.Tocopherols and tocotrienols are destroyed fairly rapidly by sunlight and artificial light containing wavelengths in the UV region. The vitamers are slowly oxidized by atmospheric oxygen to form mainly biologically inactive quinones; the oxidation is accelerated by light, heat, alkalinity, and certain trace metals. The tocotrienols, by virtue of their unsaturated side chains, are more susceptible to destruction than the tocopherols.Vitamin E is the most radiation-sensitive of the fat-soluble vitamins. Presence of lipoxygenase destructs the vitamin.

Vitamin K: Compounds of vitamin K are decomposed by UV radiation, alkali, strong acids, and reducing agents, but are reasonably stable to oxidizing conditions and heat. Phylloquinone is sensitive to both fluorescent light and sunlight. However they are stable to cooking, γ-irradiation and freezing.

5) Bioavailability of fat soluble vitamins:

Bioaccessibility is defined as the fraction of vitamin transferred during digestion from the food matrix to mixed micelles and thus made accessible for absorption. Bioefficacy defines the percentage efficiency with which ingested vitamin is absorbed and converted to its active form in the body. When meals containing natural amounts of vitamin A and provitaminA carotenoids are consumed, vitamin A is absorbed with an efficiency of 70–90% compared with 20–50% for the provitamins. Bioavailability of carotenoids is frequently assessed by absorption efficiency, which is defined as the percentage of ingested carotenoid that is secreted into the general circulation and therefore made available for tissue uptake. Bioavailability also depends on certain nutrients. The serum level of vitamin A is lesser in subjects with severe protein malnutrition. Protein is necessary for the mobilization of vitamin A from the liver to the bloodstream. Dietary fat is also important for micelle formation thus facilitating the absorption of hydrophobic carotenes. Dietary fibre inhibits the absorption of lipids and therefore the absorption of fat soluble vitamins. Vitamin D given with milk has been reported to be 3–10 times more potent than that given with oil, the stimulatory factor being attributable to the lactalbumin fraction. Alcoholism and smoking reduces the serum level of vitamin D. Plant sterols and PUFAs decrease the absorption of vitamin E. The efficiency of vitamin K absorption varies widely, depending on the source of the vitamin and the amount of fat in the meal. Presence of fat enhances absorption. The tight binding of phylloquinone to the thylakoid membranes of chloroplasts explains the poor bioavailability of the vitamin in green plants. The free phylloquinone in vegetable oils, margarines, and dairy products is well absorbed, owing to the stimulating effect of fat.

Conclusion:

Translocation of nutrients occurs between membranes by different processes such as active transport and passive diffusion. The transport system varies according to the nature and solubility of nutrients. The transport of fat soluble vitamins mainly requires chylomicrons which carry them to the target tissue. Fat soluble vitamins are hydrophobic molecules and isoprene derivatives. The bioavailability of fat soluble vitamins is affected by high intake of fibre, smoking and alcoholism.