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"Vitamin A – how much vital and toxic to the body"

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I. Introduction:

We all know, bulk component – proteins, nucleic acids, carbohydrates and lipids are required for growth and development of living cells. Balanced diet is needed for disease free development some special foods were known for curing symptoms of disease since ambiguity. F.G. Hopkins in 1912 in England proved through experiment that animals requires more than proteins, fat and carbohydrates in the diet, for normal growth. He called them "Accessory factors." The findings were supported by Casimir Funk in the same year, who coined the term 'Vitamine' for these essential accessory factors. Later on, it was F.V. Mc Collum of united states, discovered the young rats requires both fat soluble and water soluble growth factors. In the mid 1930, various forms of Vitamins B were isolated and their functions become visible to us.

Table 1.1 Vitamins and their Co-enzyme forms-

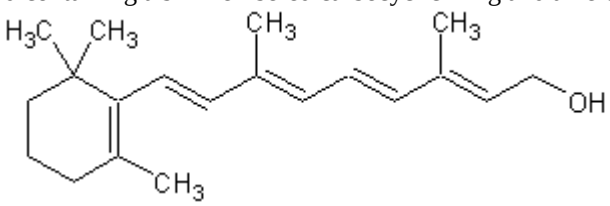
Type	Co-enzyme or active form	Function promoted
Water soluble		
Thiamin	Thiamin pyrophasphate (TPP)	Aldehyde–group transfer
Riboflavin	Flavin mononucleotide (FMN)	Hydrogen atom transfer
Nicotinic acid	Flavin adenine dinucleotide (FAD)	H atom (e-) transfer
Pantothenic acid	Nicotinamide adenine dineuclotide (NAD)	H atom (e-) transfer
Pyridoxine	Co-A (Co-enzyme –A)	phosphate (NADP)
Biotin	Pyridoxal phosphate	Acyl group transfer
	Biocytin	Carboxylgroup Transfer
Folic acid	Tetrayhydrofolic acid	one carbon group Transfer
Vitamin B_{12}	Co-enzyme B_{12}	1,2 shift of H-atom
Lipoic acid	Lipoyllysine	H-atom and acyl group transfer
Ascorbic acid	_	co-factor in hydroxylation
Fat soluble		
Vitamin A	11 – Cis Retinal	visual cycle
Vitamin D	1, 25 Dihydroxy Cholecalciferol	Calcium and Phosphate metabolism
Vitamin E	_	Antioxidant
Vitamin K	_	Prothrmbin biosynthesis

Chemical Nature of Vitamin A

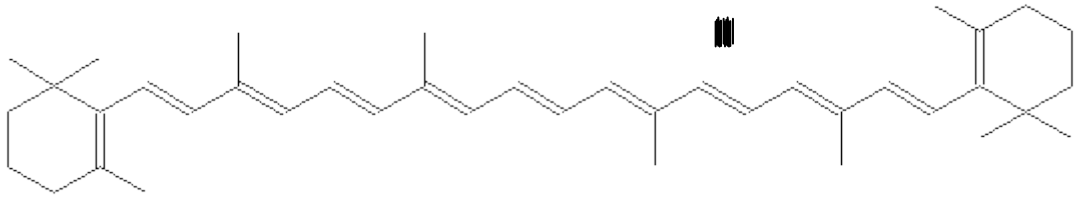
Dating back to 1906, vitamin A discovery was result of fact that factors other than carbohydrates, proteins and fats were necessary to keep cattle healthy. In 1917,Elmer McCollum at the university of Wisconsin – Medison and Lafayette Mendel and Thomas Burr Osborne at Yale university discovered 'Fat Soluble Factor A" independently. Now, it is well known that Vitamin A can be found in two principal forms in foods.

Retinol-

This form of Vitamin A is yellow fat soluble substance. Since Retinol is unstable, it is found in tissues in form of Retinyl ester. Commercially available as retinyl acetate or palmitate. Further, Retinol is isoprenoid compound containing a six membered carbocyclicr ring and an eleven carbon side chain (Fig 1)



Vitamin A (Retinol)



β-Carotenol

Fig 1: Vitamin A_1 (Retinol) and β-Carotenoid, its precursor, oxidative cleavage yield two molecules of Vitamin A. Vitamin A_2 has second double bond between Carbon Atoms 3 & 4 in the rings, otherwise it is identical with Vitamin A_1.

The carotene, α -Carotene, β- Carotene, γ-Carotene and the Xanthophyll beta-crypto xanthin (having β- ionone ring) function as Vitamin A in herbivores and omnivores animal which posses enzyme to convert in the retinol.

Food sources of Vitamin A-

Vitamin A is found naturally in many foods-

- Liver (beef, pork, chicken, turkey, fish) (6500 μg 722%)
- Carrot (835 μg 93%)
- Broccoli leaf (800 μg 89%)
- Sweet potato (709 μg, 79%)
- Butter (684 μg, 76%)
- Kale (681 μg, 76%)
- Spinach (469 μg, 52%)
- Pumpkin (400 μg, 41%)
- Collard Green (333 μg 37%)
- Cheddar Cheese (265 μg 29%)
- Cantaloupe Melan (169 μg 19%)
- Egg (140 μg 16%)
- Apricot (95 μg, 11%)
- Papaya (55 μg) 6%
- Mango (38μg 4%)
- Pea (38 μg) 4%
- Milk (28μg 3%)

Bracketed values are Retinol activity equivalences (RAES) and % of adult male RDA per food.

Even conversion of carotene to retinol varies from person to person and bioavailability of carotene in food varies also.

Vitamin A: How it functions in body ?

Vitamin A- Plays various functions in the body such as:
Maintaining vision
Regulating gene transcription
Skin and Cellular health

Helps in Vision

It is certainly a vision vitamin. Vitamin A deficiency effect vision, this was first recognized in rat, but now it is confirmed in all mammals, including man, with little variation in symptoms. The most studied deficiency symptoms is 'Xerophthalmia' (Dry eyes) in young children, which is early symptoms of deficiency, where as in adults 'Night blindness" is observed due to vitamin A deficiency. There are various things which are affected by vitamin A deficiency but its role in visual cycle is certain (Fig. 2) (usual cycle third cells)
In mammals, Retina have two types of Photo receptor cells
a) Rod cells
b) Cone cells
Rod cells are ment for sensing low light intensities, but not colors and thus help in Night vision.

Cone cells sense colors are adopted for high light intestines. Studies on Biochemical nature of Pigments related to vision by G. Wald of Harvard University helps us to substantiate the role of Vitamin A in visual cycle. Now going to deep retinal rod cells have many stalked, disc like membrane vesicles, parrell to light receiving surface of the retina, which acts as receptor surface of light. Half of membrane protein of these vesicles consist of conjugate protein called Rhodopsin with mol. Wt. 28,000. It is insoluble in water but extracted with detergens. It consist of protein "opsin" and tightly bound 11-cis retinal. The aldehyde of vitamin (A) which contain four carbon- Carbon double bond in its side chain. Three are in transform and forth at position 11,12 is cis (fig. 2).When rhodopsin is exposed to light, the bound 11-cis-retinal undergoes transformation in all trans retinal. This reaction is non –enzymatic and purely photo-chemical reaction which can take place at liquid nitrogen temperature. Cis to trans change also promote dissociation of the bleached rhodopsin to yield free ofsin and all trans retinal, which function as a trigger setting of the Nerve impulse. In order for regeneration of rhodopsin, all trans retinal get isomerizes to all 11-cis retinol. This process requires enzymatic actions.

$$\text{All} - \text{Trans} - \text{Retinal} + \text{NADH} + \text{H}^{+} \xrightarrow[\text{Reductase}]{\text{Retinal}} \text{all} - \text{Trans} - \text{Retinol} + \text{NAD}^{+}$$

$$\text{All} - \text{Trans} - \text{Retinal} \xrightarrow[\text{isomerase}]{\text{Retinol}} 11 - \text{cis-retinol}$$

$$11 - \text{Cis} - \text{Retinol} + \text{NAD}^{+} \xrightarrow[\text{Reductase}]{\text{Retinol}} 11\text{-Cis-Retinal} + \text{NADH} + \text{H}^{+}$$

The 11-cis-retinal so formed now combine with opsin to yield rodopsin, thus completing the visual cycle. But all of us know that visuality is related to nerves and brain. Recent Research have shown that absorption of light by disc like flattened membrane.Vesicles in the rod cells cause rodopsin molecule to undergoes changes of conformation accompanying the conversion of 11-Cis-retionl to all trans- retinal. This change alter the permeability of vesicle – membrane, across which there is normally a potential difference, so that Ca^{2+} ion are allowed to flow out of vesicle thus triggering the nerve impulse.Ca^{2+} serve as messanger or mediator for coupling the exciting stimulus to the function of receptor system.

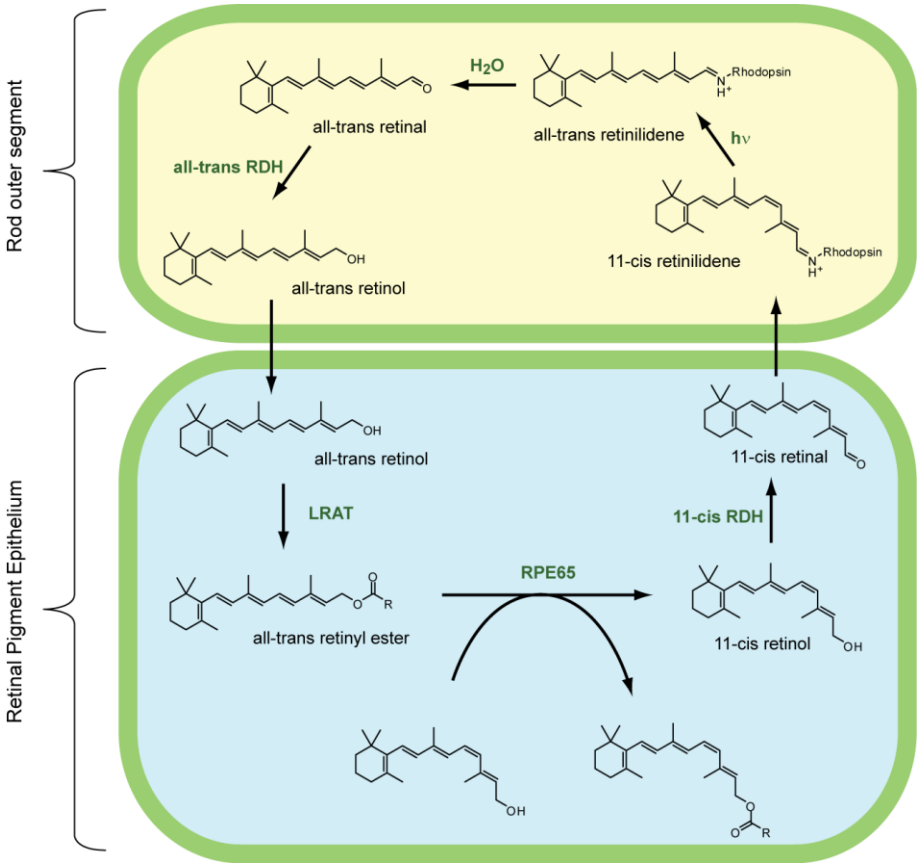


Fig.3 Photochemical isomerisations of 11-Cis-retinal.

Gene Transcription Regulations:

Vitamin A, in form of retinoic acid, plays important role in gene transcription. Retinol taken by cell is oxidized to retinal (aldehyde) by Retinol dehydrogenase and then retinaldehyde can be oxidized to retinoic acid by retinal dehydrogenase. This conversion is irreversible process, this process is highly regulated due to activity as ligand for nuclear. Receptors, which are known as RARS e.i. retinoic acid receptors. These RARS bind with retionoid (X) receptor (RXR) form the hetrodimers before attaching to DNA sites.

The RAR – RXR heterodimer recognised retinoic acid response element (RARES) to control various physiological process.

Dermatology:

Vitamin A and more specifically Retinoic acid appear to maintain normal skin health by switching on gene and differentiating Keratinocytes in to mature epidermal cells. Most prescribed retionoid drug is 13-Cis retinoic acid (isotretinoin). Potential to regenerate cell have been proved of this drug but it should be taken under medical supervision as it is tetragen with potential side effects.

In addition to above said role of vitamin A other roles have to confirmed but not well understood still. For example proper amount supply is needed for pregnant and breast feeding women for normal fetal development and breast milk. Moreover, it function upon all over body is still least understood because its excess can have ill effect on body and connective tissues.

Vitamin A – toxicity or Hypervitaminosis A

Vitamin A is fat soluble, since disposing of excess is difficult it shows toxicity when taken in excess in general acute toxicity occurs at dose of 25,000 I.U. / Kg of body weight. Toxicity leads to nusea, irratibility, anorexia (Reduce appetite), vomiting, blurry vision, headache, hair loss, muscle and abdominal pain, weakness,drowsiness, altered mental status. Chronic intake effect fetal developmentduring period of organogenesis. Hepatic injuries have been observed with alcoholism along with high vitamin A intake.

II. Conclusion:

So, vitamin A and its derivatives are remarkable biochemical compound whose function is understood and not understood equally. It is good in right amount and right timing but prolonged use in excess either as food or drug can be dangerous even. Retinoic acid based drugs have hope in solving big disease like cancer, HIV and dermatological disorders but only when we will solve the mysterial facts of Vitamin A toxicity.

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