A COMPREHENSIVE REVIEW: THE ROLE OF VITAMINS IN HUMAN DIET I. VITAMIN A-NUTRITION

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SUMMARY: From this review, it is very clear that vitamin A ingested as a provitamin (carotenoid) from vegetable food or as retinol palmitate from animal sources, can play a vital role in human nutriture. It is important for cell growth and cell differentiation, its deficiency leads to metaplasia of the respiratory, gastrointestinal and genitourinary tracts. An appreciable quantity of this vitamin in the diet is essential. It was observed that vitamin A in dehydrated foods is readily destroyed in the presence of oxygen, moisture, sunlight, mineral matter and temperature which lead to deficiency of vitamin A in the diet of most of the Asian populations. Therefore, an appropriate amount of vitamin A must be fortified to the staple diet according to the RDA level in order to avoid various serious complications in man, particularly among preschool children and pregnant women.

Key Words: Vitamin A, metabolism, physiological functions.

INTRODUCTION

Vitamins have been defined as a group of naturally occurring organic substances present in small quantities in foodstuffs. These nutrients are essentials for the normal metabolism and well being of animals and man (1). A lack of vitamins in the diet causes deficiency diseases. Many of these deficiency diseases such as xerophthalmia, scurvy, beri-beri and pellagra are the most common all over the world particularly in the developing countries. The dietary vitamins requirement are necessary to prevent deficiency disorders (2).

The stability of vitamin A is effected by oxygen, moisture content, temperature, sunlight, mineral matter and solvents (3). The diet most of the developing countries are deficient in vitamin A, therefore, the addition of an essential nutrient (i.e., vitamin A) to consumable foodstuffs is vital important. In fact, it may be the most suitable way to prevent certain nutritional problems associated with vitamin A deficiency, particularly in vulnerable populations where the problems are most commonly observed. This simple and impressive way of preventing a nutritional disease is still successfully practiced today in many developed countries.

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In the developed countries like UK (4), fortification of margarine with vitamin A has been carried out for many years and is practiced in some other developed countries as well. Fortification of vitamin A can be used to provide security against the occurrence of nutritional problems in areas where dietary vitamin A intake is inadequate. The increasing use of highly refined foods, and foods prepared from highly purified ingredients, may contribute to dietary vitamin A inadequacies in certain populations.

Since, vitamin A fortification is very important but the successful fortification programme needs knowledge of the nutritional status of a particular area and food habit of that particularly population. This paper will review and update the current state of scientific knowledge of vitamin A concerning the historical perspective, overview, biochemistry, metabolism, fortification, method of determination, degradative reaction, stability, and physiological functions.

HISTORICAL PERSPECTIVE

The first recognition of the existence of vitamin A was made in the papyrus Ebers, an ancient Egyptian pharmaceutical medical treatise written about 1500

B.C. (5). He recommended roast ox liver or the liver of a black cock as curative agents for night blindness. The first awareness of the chemical nature of vitamin A was the result investigations on the value of fats in animal nutrition. The well known work of Osborne and Mendel (6,7) and McCollum and Davis (8,9) at Yale led to the initial postulation of a 'fat-soluble-factor A' in butterfat, egg yolk and cod liver oil. After subsequent experiments, they restored the normal growth of deficient rats. Vitamin A was then shown to maintain growth as well as prevent xerophthalmia and night blindness (10,11). Moore (12) recognized early in 19th century that drying of the corneal pigment epithelium caused by severe lack of vitamin A in the diet, termed xerophthalmia, was a dietary deficiency disease. Lunin (13) found that mice were unable to survive on the diet of pure casein, fats, sucrose and water, even when the diet was supplemented with minerals. The growth rate of mice was normal when fed a diet of dried milk and water, therefore, he concluded that dried milk contained as essential nutrient 'fat soluble A'.

Steenbock (14) found a color pigment in animal and vegetable fats, called 'β-carotene' which could be converted to vitamin A in animals. He also demonstrated a compound in plants called 'provitamin A'. These compounds restored growth when added to the basal diet of the rat. Karrer *et. al.* (15,16) determined the chemical structure of β-carotene and vitamin A alcohol and found β-carotene, the precursor of vitamin A alcohol. Holms and Corbet (17) crystallized vitamin A from fish liver for the first time and Baxter and Robesen (18) were able to prepare several esters of pure crystalline vitamin A. Arens and VanDorp (19) and Isler *et. al.* (20) achieved the synthesis of vitamin A alcohol and the crystallization of the 13-cis isomer of vitamin A alcohol (21).

OVERVIEW

Nutrient survey of various countries have shown in the last few years that even in the most developed industrialized countries major portions of the populations are not obtaining their Recommended Dietary Allowances (RDA) of many nutrients (i.e., vitamin A) from the foods they are consuming. It has been reported that there are at least 190 million children living in the areas where food is deficient in vitamin A, out of which 40 million children are physiological deficient and 13 million have various degree of clinical aye signs or xerophthalmia (22). Because of vitamin A deficiency, 250.000-50.000 children become blind partially or totally around the world. Two-thirds of these children die within a few months of going blind. Vitamin A deficient children (11.4 million) are at risk around South and Southeast Asia (2). Xerophthalmia is prevalent in some developed countries and in Asia alone an estimated 500.000 are affected each year (2).

(i) Pakistan

In the region of Karachi, a study was conducted in 1987 and was found that 47% of children had low level of vitamin A in the blood serum. In another survey, conducted during 1965-66 in Pakistan, revealed that 24% of the rural and 13% of the urban population had deficient or low plasma vitamin A levels (23). According to UNICEF about 600.000 infants and children die every year from preventable diseases and an equal number are permanently handicapped.

It has also been reported that in Pakistan about 60% of the males, 71% of the non-pregnant/lactating females and 78% of pregnant women consume less than 70% of the RDA for vitamin A (24). It has also been reported that there is a serious underlying, undetermined degree of vitamin A deficiency in Pakistan (25). In Pakistan 60% of the child death under five are due to diarrhea and respiratory infections that are highly associated with vitamin A deficiency (26).

(ii) Türkiye

Report of survey conducted in 1987 and a paper presented in an international conference on Nutrition held in 1993, indicated that school children in different regions of the country showed clinical signs of vitamins deficiencies (27).

(iii) Iran

In Iran, no national programme or efforts in this regards have been made. It is clear from the existed published data that vitamin A deficiency is not a major public health problem (27).

(iv) Thailand

A survey conducted by Dhanamitta *et. al.* (28) found that the prevalence of sub-clinical vitamin A deficiency in various parts of Thailand. Bloem *et. al.* (29) reported that 13% of the school children in Northeast areas of Thailand had serum vitamin A level less than 0.35 μmol/L. In the same Udomkesmalee *et. al.* (30) reported 27% of the children had serum vitamin A level

less than 0.87 μmol/L may at risk for vitamin A deficiency. An another survey conducted in 1990 by the Ministry of Public Health, Government of Thailand (31) on the prevalence of vitamin A. It indicated that 20% of preschool children in certain Northern and Northeastern areas are at risk of vitamin A deficiency.

(v) India, Africa, Nepal and Indonesia

During the past years, various nutritionists/scientists have reported the traumatic consequences of vitamin A deficiency on child survival in India (32), Africa (33-35), Nepal (36) and Indonesia (37,38). In India, it has been estimated that vitamin A deficiency contributes to about 20% of all cases of blindness (39). The association between vitamin A deficiency and morbidity in children is clear, but may be altered by protein-caloric malnutrition, socioeconomic factors and other dietary inadequacies (40,41).

(vi) USA

A comparative analysis of the US Department of Agriculture's Nationwide Food Consumption Surveys (NFCS) of 1955, 1965 and 1977 reveals that the percentage of diets providing less than 100% of the RDA for vitamin A. The reason for this is the increased consumption of 'snacks' and 'fast food' (42). The first health and Nutrition Examination Survey in the US (43) indicated that a large group of the population examined had intakes falling considerably below RDA. About half of both black and white children had inadequate intakes of vitamin A. The same observations were made for adult men. It was also mentioned that a large proportion of school children did not consume the RDA amount of vitamin A.

(vii) France

A survey report on Vitamin Status, which was published in 1986 has shown that up to 30% of the population had borderline deficiency of vitamin A. The report also shows that in the region of Burgundy, it has been indicated that up to 86% of the adult population had only 50-80% of the French RDA for vitamin A and other nutrients (44).

(viii) Canada

The prevalence of vitamin A deficiency in Canada is very low, it may possibly be due to the addition of vitamin A to foods, particularly margarine and has contributed a better vitamin A nutrition status in Canada. In a study conducted in Canada, a sub-clinical deficiency of certain vitamins have been found (45).

(ix) Germany

A very comprehensive survey on food and nutrition situation published in the Federal Republic of Germany (46) provides evidence that quantitative nutritional deficiencies, including vitamin deficiencies, also occur in certain population groups. On the basic biochemical assessment of vitamin status, these age groups show inadequate levels of vitamin A and other vitamins particularly thiamin, riboflavin, pyridoxine and especially folic acid. In adults aged 20-50 years, the most frequent inadequacies were found for vitamin A and pyridoxine, followed by thiamin and folic acid. The report on the Food and Nutrition Status in German population (46) has shown that on the basis of the biochemical assessment of the vitamin nutrition status, the inadequate intake of vitamin A was quite common in the third trimester of pregnancy.

(x) Switzerland

A survey on food and nutrition in Swiss population have shown that despite the adequate average supplies of most of the vitamins, the intake of vitamin A, may still represent a problem in some population or age groups. It also report that even in some adults, inadequate levels of vitamin A can be found. In a study on the Food and Nutrition situation in the Swiss population (47), it was reported that in a sample of pregnant women about 78% had inadequate of vitamin A intake.

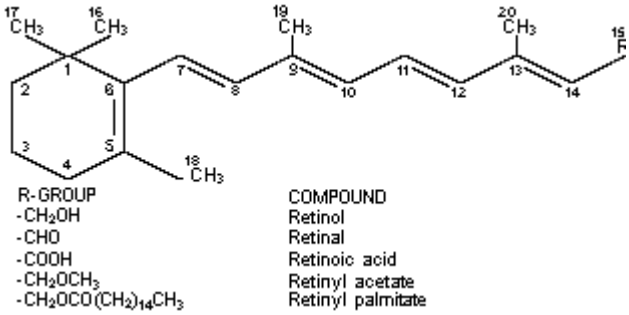
(xi) Australia, Italy, Sweden and UK

The population group that might particularly be affected is that of elderly people, since in this population a number of factors may contribute to the reduction of intake and utilization of dietary nutrients. Studies on the community-based people in Australia (48), Italy (49), Sweden (50) and UK (51) have shown the inadequate intake of vitamin A in some of the studied populations.

BIOLOGICAL AND CHEMICAL DATA

Vitamin A alcohol (retinol) is an unsaturated monohydric alcohol with the empirical formula $C_{20}H_{30}O$ (molecular weight=286.48). The structure of vitamin A alcohol (Figure 1) consists of cyclohexane ring linked to a polyunsaturated chain which terminates in an alcoholic group. The five conjugated double bonds (52) in

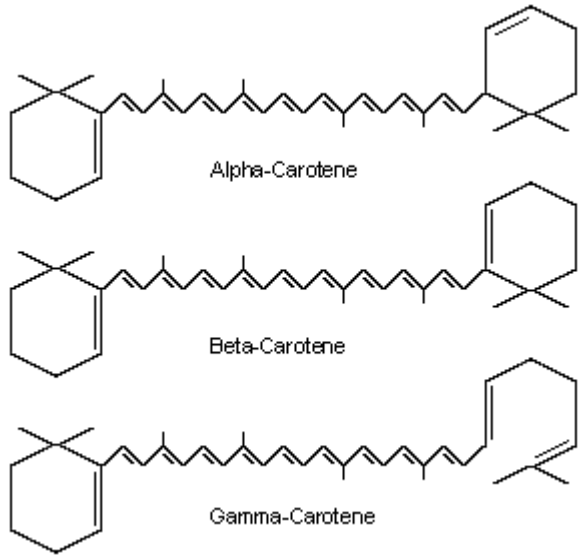
Figure 1: Nomenclature of vitamin A compounds.



R-GROUP	COMPOUND
-CH_2OH	Retinol
-CHO	Retinal
-COOH	Retinoic acid
-CH_2OCH_3	Retinyl acetate
-$CH_2OCO(CH_2)_{14}CH_3$	Retinyl palmitate

the configuration of retinol are an easy points of attack for oxygen. Vitamin A can exist in different isomeric forms with different biological activities (53). Vitamin A compounds are numbered according to an Official System adopted by the International Union of Pure and Applied Chemistry (54). Other biological active retinoid compounds are vitamin A aldehyde (retinal), retinyl acid (retinoic acid) and naturally occurring retinyl esters. Vitamin A_2 (3,4-dehydroretinol) has the same structure as retinol, with an additional double bond in the b-ionone ring. The provitamin naturally occurring in plants include α, β and T-carotene (Figure 2). The biological activity of the carotenoids varies considerably and these containing at least one unsubstantiated conjugated trimethyl cyclohexane ring (ß-ionone) are the most active. Oxygenated carotenoid pigments are less active.

Figure 2: Common carotenoid compounds exhibiting provitamin A activity.



The four double bonds present in the side chain of retinol may give rise to cis-trans isomerism, with 16th isomers theoretically possible (55). Pauling (56) found that substitutes other than hydrogen (e.g., methyl group) in the 1,4 position of a double bond result in steric hindrance in the cis-isomer and tend to favor the isomerization of retinol to the all-trans retinol configuration. Four non-hindered isomers (Figure 3), all-trans retinol, 13-cis, 9-cis and 9,13-dicis are believed to be formed in food products. The 11-cis isomer of retinol, important in vision, in considered a 'hindered' isomer due to spatial crowding between the C-10 and hydrogen and C-20 methyl group in the molecule (57). Improvements in the analytical techniques, Deny *et. al.* (58) have identified thirteen of the sixteen possible isomers of retinal, including two tri-cis isomers.

Some physical properties of vitamin A compounds are shown in Table 1. The chemistry and synthesis of vitamin and the provitamin A has been delt within sev-

Figure 3: Structural formulae of the non-hindered geometric isomers of vitamin A alcohol.

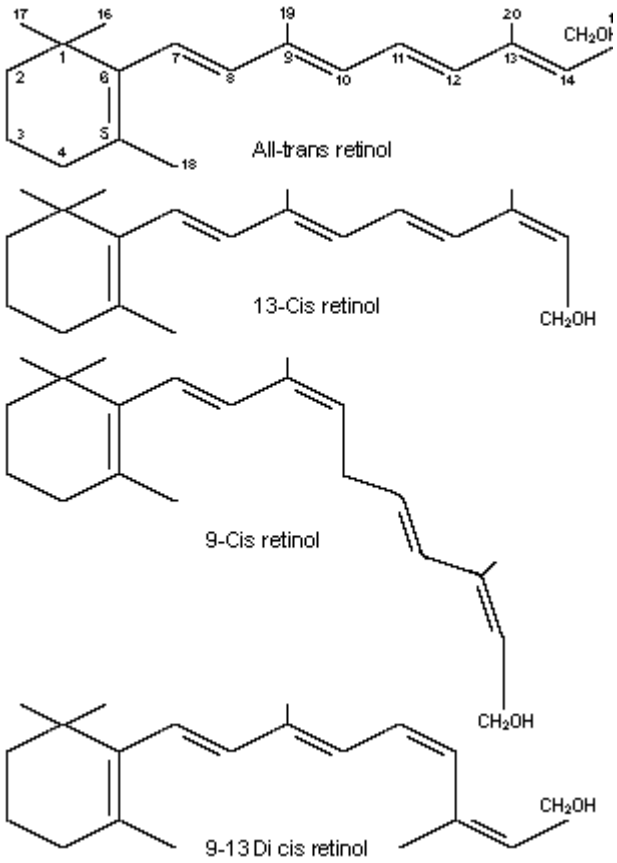


Table 1: Physical properties of all-trans vitamin A compounds*.

Compound	Molecular Formula	Molecular Weight	Melting Point °C	Absorbance in Maximum (Wavelength)	$E^{1\%}_{1cm}$
Vitamin A Alcohol	$C_{20}H_{30}O$	286.4	62-64	325	1832
Vitamin A Acetate	$C_{22}H_{32}O$	328.5	57-58	328	1550
Vitamin A Palmitate	$C_{36}H_{60}O_2$	468.8	28-29	328	975
Vitamin A Aldehyde	$C_{20}H_{28}O$	284.4	61-62	381	1530
Vitamin A Acid	$C_{20}H_{28}O_2$	300.5	179-180	350	1510

*Obtained from Kirk, R.E. and Othmer, D.F. (1984).In: Kirk Othmer Encylopaedia of Chemical Technology, 3rd Ed, Vol. 24, John Wiley and Sons, New York, USA.

eral review (59,60). Manan (61) and Manan *et. al.* (3) found that retinol is unstable in the presence of oxygen and is converted to 13-cis with the use of a copper catalyst in dehydrated food system. In the absence of oxygen, retinol is stable to alkali, but is unstable to acidic environments, resulting in dehydration and formation of rearrangement products. Retinyl esters are more stable to oxidation as compared to retinol. Ultraviolet light causes isomerization and degradation of retinoid compounds. Under more intense light, dimerization of retinyl esters (62) take place.

The effect of chemical changes on the biological activity of vitamin A (Table 2) result in a severe decrease in biological activity (63). The problems associated with the vitamin A activity if cis-isomers are present are summarized (Table 3) by Ames (57). The natural preformed vitamin A occurs only in animal food products mainly liver, eggs, butter and milk. The principal source of provitamin A carotenoids (α, β and T-carotenes and cryptoxanthine) are plant food products (green, yellow vegetables and fruits). Palm oil concentrate has been used in the past to prevent vitamin A deficiency in man. The vitamin A_2 (3,4-dehydroretinol) has vitamin A activity and is present in fresh water fish oil and fish liver. Table 4 showed vitamin A active compounds in foods.

The Recommended Dietary Allowances (RDA) for vitamin A, representing the average requirements for almost every healthy person, are age and sex related. The exact requirement for small, premature infants is unknown. Vitamin A supplements are available as the retinyl esters. Retinyl acetate or palmitate is more properly referred as it is more stable as compared to vitamin A alcohol in presence of oxygen. The RDA for vitamin A for Pakistani population is shown in Table 5 (64).

Table 2: Effect of various chemical changes on the biological activity of vitamin A*.

Process	Product	Biological Activity
Oxidation	Aldehyde	91-100
Oxidation	Epoxide	0
Cis-Isomerism	Cis-Isomers	15-75
Dchydrogenation	Vitamin A_2	30
Demethylation	Norvitamin A	3
Ether formation	Phenyl or methyl ethers	10-100
less of oxygen	Axerophthene	10
Ketone formation	C_{21}-ketone	10
Dehydration	Anhydrovitamin A	0.4
Additon of CH_2	Homovitamin A	1.5
Condensation	Kitol	0
Hydrnogenation	Dihydrovitamin A	0

*= Approximate activity of all-trans retinyl acetate = 100 Obtained from Ames (71)

Table 3: Bio-potencies of vitamin A acetate isomers*.

Isomers	Biopotency (RE/g)	% Relative activities
all-trans	872.000	100
13-cis	657.000	75
9-cis	529.000	21
9, 13 di-cis	206.000	24
11-cis	175.000	24
11, 13 di-cis	129.000	15

*Obtained from Ames (57)

Table 4: Moan of vitamin A active compound in foods por 100g edible matter.

Food	All-t-retinol (ug)	13-c-retinol (ug)	B-Carotene (ug)
Diary products			
Milk	36	2	12
Cream, double	431	32	238
Cheese, cheddar	300	56	126
Margarine			
Polyunsaturated	774	3	143
Margarine			
Hard	631	44	322
Meat and meat products			
Chicken breast	35	32	0
(Raw, flesh only)			
Kidney lamb, raw	92	14	0
Liver sausage	2500	620	0
Liver påte, coarse	5640	1260	260
Liver påte, fine	6200	2500	0
Fish and fish products			
Herring, raw	33	14	0
(flesh only)			
Mackerel, raw	37	10	0
(flesh only)			
Trout, raw	28	11	0
(flesh only)			

*Obtained from Sebrell, W.H. and Harris, R.S. (1967). The Vitamins, Chemistry and Physics, Pathology, Methods, Vol. 1, 2nd ed., Acad. Press. London.

METABOLISM

There are various factors that effect the absorption of vitamin A i.e., type and amount of fat in the diet, interfering substances in diet such as nitrites, amount of zinc, protein, vitamin E and drugs (65). Other factors include respiratory, renal and intestinal disease of man.

Vitamin A esters, after hydrolysis in small intestine (lumen) are converted into retinol. It is again esterified after passes through the mucosal cell wall and is stored in the liver as retinyl esters. β-Carotene is converted into retinyl esters after absorption, other carotenoids are only partially absorbed. Such absorption is effected by the presence of bile salt and lipases. It may be due to that vitamin A is a fat soluble vitamin, bile salt and lipases also effecting the absorption of fat. The absorption of retinoic acid is different than the absorption of retinyl esters. It is bound to serum albumin. The retinyl esters enters the circulation via lymphatic system rather than portal system.

Vitamin A as fat soluble vitamin, is carried to the liver with lipids as lipoproteins and chylomicrons in the lymph. Retinol leaves the liver in the form of retinol binding protein (RBP) and RBP complexes with serum pre-albumin. It is then circulated in the blood and may be removed from circulation by the kidney. Sufficient amount of zinc and dietary protein are essential for proper mobilization of retinal. Figure 4 shows the pathway by which dietary vitamin A reaches target cells of an organ (66).

Table 5: Recommended daily allowances of vitamin A of Pakistani population.

Age group (Months and years)	Vitamin A (ug)
Less than 6 months	-
6 months to 2 years	300
3 years	350
4 years	400
5 to 7 years	450
8 to 9 years	500
10 to 12 years	575
13 to 15 years	725
16 to 19 years	750
Reference man/woman with moderate activtiy (Average 25 years)	750
Pregnancy	750
Lactation	1200

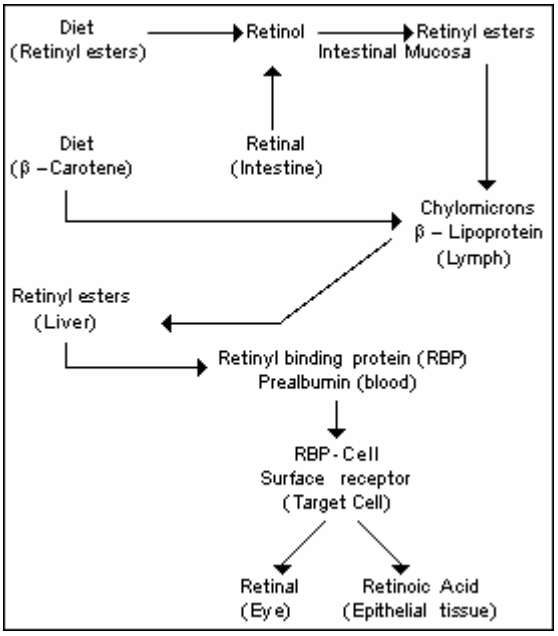
Data obtained from the food Composition Table for Pakistan (64)

The liver and kidney have the enzyme system to convert retinol to retinoic acid. The liver might store about 90% of the vitamin A and small amount are in lungs, kidney and fat depots.

UNITS AND ACTIVITY

Now-a-days, the activity of vitamin A is expressed as the equivalent weight of retinol or retinol equivalent (RE). One RE is equal to 1 μg retinol, 12 μg provitamin A carotenoids or 6 μg β-carotene. The vitamin A activity in foods is also expressed as International Units (I.U). One I.U is equivalent to 0.3 μg retinol, 0.344 μg retinyl acetate, 0.550 μg retinyl palmitate or 0.6 μg β-carotene. These equivalents were derived from studies using rats and are assume to be the same for human.

Figure 4: Absorption pathway of dietary vitamin A in the body. [Obtained from Krause and Manan (66).]



FORTIFICATION

In tropical and sub-tropical countries, vitamin A deficiency and xerophthalmia are the most widespread nutritional health problems and result in blindness in man. One of the remedies is the fortification of staple foods with vitamin A. In developing countries including Pakistan, tea can be used as the vehicle for enrichment because this drink is consumed universally by all age groups (67). It has been generally observed that in Pakistan, more than 80% young children are given one to two cups of tea each day. Thus, it appears that tea comes dose to being an ideal vehicle for conveying vitamin A to millions of Pakistani of all ages who diet is seriously deficient in vitamin A. Tea fortunately, contains many natural antioxidants such as catechol, epicatechol and gallic acid which aid the stability of added vitamin A.

In the Philippines, (68) the staple used is monosodium glutamate followed by Indonesia (69) and rice and table sugar in Guatemala (70). The best example is the addition of vitamin A esters to margarine, which was used as a staple at the start of World War II. In UK, margarine must contain be law 804 μg/100g to give a nutritive value similar to that of butter (4).

MATERIALS AND METHODS

The methods of assay for vitamin A activity in pharmaceutical products and foods can be divided into major classes (i) biological methods (ii) physicochemical methods.

(i) Biological Methods

The principle of biological methods for determination of vitamin A is based on its biological activity (71). Biological assays are especially useful when evaluating the effect of diet composition and the variation within animal species with regard to vitamin utilization (72). Three biological methods are still in use, based on the reversal of deficiency symptoms in vitamin A depleted animals, the measurement of vitamin A tissue level in vivo or miscellaneous responses to vitamin A administration such as inducing hyper-vitaminosis A or the in vitro opsin assay. Any example of an assay based on the reversal of deficiency symptoms is the rat growth curative bioassay. Experimental animals are fed a vitamin A deficient diet until growth ceases. Graded levels of a vitamin A reference standard and the test compound are then fed and growth response is recorded. Growth response is plotted versus the logarithm of the dose and the slope of the lines for different test compounds are compared to determine bio-potency of the test material. Measurement of the tissues levels in vivo usually involves determination of the concentration of vitamin A in the liver, which is the principal organ.

In biological assays, vitamin A acetate is considered the parent compound and other compounds are evaluated for bio-potency relative to the response elicited by retinyl acetate. The effect of chemical changes on the biological activity of vitamin A result in a severe decrease in biological activity (73). The problems associated with vitamin A activity of cis-isomers are summarized in Table 3 by Ames (57). The 13-cis retinyl acetate has a relative bio-potency of 75% of the all-trans;

introduction of a cis-double bond at the β- or 11-position decreases the potency to 24% or less.

(ii) Physicochemical Methods

Biological assay in foods is an expensive, imprecise, time consuming and impractical (74). Determination of vitamin A by physicochemical procedures is more rapid and precise. Colorimetric (75,76,77), spectrophotometric (75,78-80) and fluorimetric procedures (81-87) are the usual methods for determining vitamin A in foods and pharmaceutical products. The most common analytical procedures for vitamin A analysis have been reviewed by Hubbard *et. al.* (88), Hashmi (89), Parrish (80), Knobloch and Cerna-Heyrovska (90) and Manan (61). Other methods includes thin layer chromatography (TLC) (61,80,91), column chromatography (75,92-94), gas liquid chromatography (GLC) (95,96), nuclear magnetic resonance (NMR) (97,98), mass spectrometry (99-101), infrared spectroscopy (102) and electrochemical methods (103).

High performance liquid chromatography (HPLC) assay for vitamin A determination in foods and pharmaceutical products is very widely used by researches/scientists (104-150).

DEGRADATIVE REACTION

The main problem associated with work on vitamin A compounds arises from the inherent instability during the manufacture, storage and preparation of foodstuffs, vitamins are exposed to a wide range of physical and chemical factors as shown in Figure 5. Isomerization of vitamin A compounds occurs in the presence of heat, light, oxygen, acid, iodine and copper (151-153). Isomerization of retinoid compounds is most often caused by exposure to light with or without the addition of any catalyst.

Retinol is known to be unstable because of the conjugated double bond system in its structure (12, 52) and undergoes oxidation in unsaturated fatty acids (154). The oxidation of retinol may involve a free redical mechanism resulting in peroxy compounds (155). The free redical chain reaction of retinol involving oxygen uptake may have similarities with the oxidation of conjugated polyunsaturated fatty compounds (156). Direct oxidation of retinol might take place by attack upon the terminal alcoholic group, leading to the production of retinal (157) and upon the conjugated double bonds.

Any failure in handling in the laboratory results in a low overall quantitative recovery and the appearance of cis-isomers. The procedures which involve the concentration of solution by unnecessarily excessive heating, the use of unprotected columns or thin layer plates or even leaving a solution on the laboratory bench in the presence of air and light may result in the degradation of vitamin A. It is impossible in practice and often in the cause of convenience, to avoid all the dangers all the time, but recognition of the danger and an adherence to certain general precautions serve to minimize the risk of erroneous results. Factors which effect the stability of vitamin A are; light (158-160), solvents (161-162), oxygen (163-167), temperature (168-175), moisture (176-179), food composition (180), mineral content (181), acids (182) and enzymes (183,184).

STABILITY

Few literature reports are available on the stability of vitamin A in foods. The stability of vitamin A in foods is difficult to predict since it may be affected by moisture content, water activity, storage conditions, pH and product composition (3,61,185). Vitamin A is used in a number of forms for fortification or pharmaceutical use (186). Dry products includes powders, granules, microsphere and beadlets processed by methods involving absorption, granulation, spray congealing, chemical complexation and encapsulation in gelatin. Lipid forms are usually dissolved in a vegetable oil or specificity prepared emulsions. Both dry and liquid products made to be water or oil-dispersible.

The compilation of the available vitamin A stability data for many food products may be found in several excellent review (53,187-189). Manan (61) reported the stability of retinol in dehydrated food systems (Table 6)

Figure 5: Factors influencing the stability of vitamins in foods.

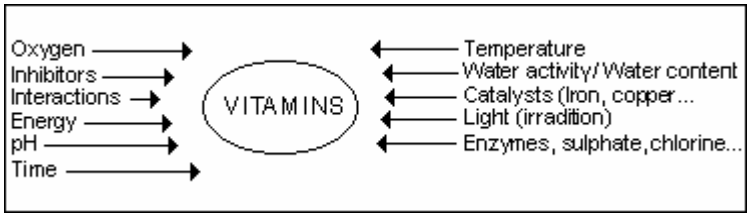


Table 6: Half life ($t^{1/2}$) of all-trans vitamin A alcohol as a function of temperature and water activity *.

$t^{1/2}$			
a_w	30 °C	40 °C	50 °C
0.11	346	226	169
0.23	277	181	129
0.32	215	159	101
0.42	120	69	49
0.52	105	65	35
0.57	86	38	30
0.66	37	21	11
0.69	28	13	9
0.75	17	9	6

$t^{1/2}$ half life hr
* Obtained from Manan (61)

and found that half of the retinol is destroyed in 346, 226 and 169 hr when stored at 30, 40 and 50°C, respectively at water activity (a_w) 0.11. These values dropped to 17,9 and 6 hr when stored at a_w 0.75 under the same temperature studied. Similarly, mineral contents such as iron, copper, zinc and calcium added to food system (Table 7) had a significant effect on the stability of retinol.

Table 7: Half life ($t^{1/2}$) of all-trans vitamin A alcohol as a function of temperature. Water activity and mineral fortification*.

$t^{1/2}$			
a_w/mineral	30 °C	40 °C	50 °C
0.11/Control	346	226	169
0.11/$FeSO_4.7H_2O$	55	44	29
0.11/$CuSO_4$(anhydrous)	41	36	24
0.11/ZnO	200	169	96
0.11/$CaCO_3$	137	86	61
0.42/Control	120	69	49
0.42/$FeSO_4.7H_2O$	44	37	23
0.42/$CuSO_4$.(anhydrous)	30	25	18
0.42/ZnO	92	65	38
0.42/$CaCO_3$	84	54	35

$t^{1/2}$ half life hr
* Obtained from Manan (61)

The degradation of vitamin A in fortified foods was reported by Liu and Parrish (190). They found little decrease in bio-potency of vitamin A in fortified flour after storage at elevated temperatures. Egberg *et. al.* (136) reported 11.4% to 34.8% of the total vitamin A in the food products analyzed as the 13-cis isomer. Thompson *et. al.* (191) have separated the 13-cis isomer from all-trans in fortified milk products. Formation of 13-cis, 9-cis and 9,13-dicis isomers in pharmaceutical preparation has been confirmed by several studies (192). Vitamin A is readily destroyed by sunlight and irradiation (3). The losses of retinol can be reduced by storage at very low temperature, exclusion of air or complexation of the retinol with starch, sugars and albumin.

PHYSIOLOGICAL FUNCTIONS

The physiological functions of vitamin A is divided into five major classes; (i) overall growth, (ii) vision, (iii) bone growth, (iv) epithelial growth and (v) reproduction (193).

Vitamin A deficiency causes abnormalities in tissue and bone growth. In animals, the first sign of vitamin A deficiency is cessation of growth. The vision is particularly sensitive to vitamin A deficiency which causes night blindness. Diminished reproductive capacity in both male and female is one of the earliest symptom of vitamin A deficiency. Vitamin A deficiency produces changes in epithelial growth and differentiation by an increase in aqueous keratinising cells and a decrease in mucous secreting cells in the animal body.

High dose of vitamin A may be toxic and hypercalcaemia (194-198) has been reported. Hypervitaminosis may results in cartilage destruction, bone lesions, hemorrhages in the spleen, bladder and pectoral muscles and congenital malformation (199-203). In 16th century it was recognized that eating polar bear liver (3,900-5,400 RE/g) is toxic and causes irritability, headaches, vomiting and drowsiness (193). The adverse effect of high dose of vitamin A are usually related with total serum vitamin A levels that exceed 1500 μg/g tissue and liver storage of retinol or its esters at levels which exceed 3000 μg/g tissue, a value that is some ten times the normal concentration (204).

The adverse report of high dose of vitamin A has been reported by Korner and Vollm (205) and Bauernfeind (206). They found between 500 and 600 reported cases of vitamin A adverse effects. The usual signs are peeling and redness of the skin, disturbed hair growth, loss of appetite and sickness (207). Cases of liver injury have been reported in adults (208). The amount of 9000 μg RE (130.000 I.U) daily in adults as no toxic

effect on health (206) and even in adults up to about 15,000 μg RE (50.000 I.U) would appear to be safe (205). It has also been reported that in early pregnancy, vitamin A dosage should not exceed 2400-3000 μ g RE (8,000-10,000 I.U) daily (209, 210).

Various researchers (211-213) have demonstrated the relationship of vitamin A with cancer. They reported that the manifestation of tumors of viral, chemically or physiologically induced cancer of the bladder or lungs, transplant or spontaneous origin can be delayed to some extent by the treatment of vitamin A. Hartmann (214) observed that unlike most transplanted tumors, the growth of a transplanted chondrosarcoma in rats was also inhibited. A number of published literature regarding the relationship of vitamin A with cancer are available (215-237).

CONCLUSION

Vitamin A alcohol (retinol) is mainly stored in the liver. If the amount of beta-carotene (as the precursor of retinol) in the diet is high, the deficiency of retinol will be very rarely present. This essential nutrient must be present in adequate amount for normal health and nutrition. From the above discussion, it is clear that high dose of vitamin A is also very toxic and led to cutaneous and mucosal changes, hair loss, headache, confusion, nausea, vomiting and osteomalacia (238,239). High dose of retinol is more toxic as compared to retinoids. The later is pharmacologically more active. It is therefore concluded that an appropriate dose of this vitamin is essential for normal growth and other body functions.

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