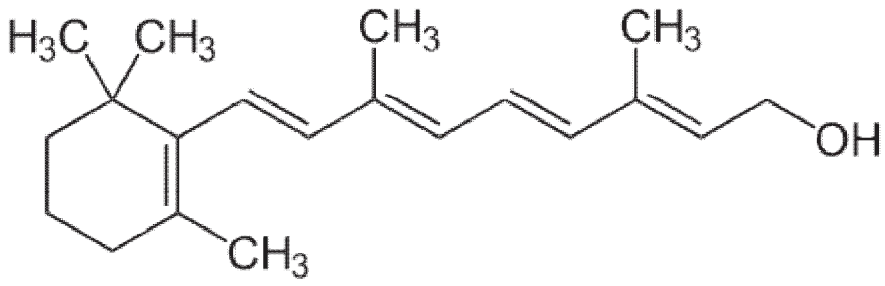
**Sultan Qaboos Univeristy**

**College of Agricultural & Marine Sciences**

**Vitamins & Human Metabolism**

**FSHN6026 with Dr. Amanat Ali**

# Lecture No. (1): Vitamin (A): Summary

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## ➢ Introduction:

### o History:

Vitamin A (retinol) is fat soluble and is primarily store in liver where retinol binding protein (RBP) is synthesized. In a well-nourished person, it last for many months on a vitamin deficient diet before the signs of deficiency appears. [(1)] The first observation of vitamin A activity in carotene was made in 1920. In 1929 it was discovered that β-carotene is converted into vitamin A in rats. Carotene was isolated in crystalline form from carrots in 1831 (H.F.W. Wacken-roder). The structural determination of β-carotene and vitamin A by P.Karrer, 1930-1932. [(2)]

### o Vitamin A:

Vitamin A (retinol, retinal, and four carotenoids including β-carotene) is a vitamin that is needed by the retina of the eye in the form of a specific metabolite, the light-absorbing molecule retinal, that is necessary for both low-light (scotopic vision) and color vision. Vitamin A also functions in a very different role as an irreversibly oxidized form of retinol known as retinoic acid, which is an important hormone-like growth factor for epithelial and other cells. Immune system function has also been depended on vitamin A level (Moriguchi et al., 1985). In addition it may also directly influence gene expression in the cells. (1) The effect of vitamin A was promotion of growth and cell differentiation. (2) Retinoic acid appears to maintain normal skin health by switching on genes and differentiating keratinocytes (immature skin cells) into mature epidermal cells. [(4)]

### o Stability & Physical Properties:

It's sensitive to oxygen in the air in the presence of light and heat. Esters farms are more stable to O2 than the alcohol. The α-Tocopherol protects the vitamin from oxidation. It's more stable in basic solution. Also more sensitive to acids. Vitamin A added to food for enrichment is more stable. Most farms are crystallizable compounds with low melting points. Retinol crystals are colorless. Retinoids have strong absorption spectra.

### o Requirements & Sources:

The US Recommended Daily Allowance (RDA) of vitamin A for adult is 5000 IU (1000 retinol equivalent). It's found in dairy products, eggs, and orange meats. Carotenoid which is found in dark green vegetables can be converted into vitamin A during digestion. (1) In foods of animal origin, the major form of vitamin A is an ester, primarily retinyl palmitate, which is converted to the retinol in the small intestine. The retinol form functions as storage form of the vitamin, and can be converted to its visually active aldehyde form, retinal. The associated acid (retinoic acid), a metabolite that can be irreversibly synthesized from vitamin A, has only partial vitamin A activity, and does not function in the retina for the visual cycle.

- **Deficiency:**

Vitamin A deficiency is estimated to affect approximately one third of children under the age of five around the world. It is estimated to claim the lives of 670,000 children under five annually. Approximately 250,000–500,000 children in developing countries become blind each year owing to vitamin A deficiency, with the highest prevalence in Southeast Asia and Africa.

Vitamin A deficiency can occur as either a primary or a secondary deficiency. A primary vitamin A deficiency occurs among children and adults who do not consume an adequate intake of provitamin A carotenoids from fruits and vegetables or preformed vitamin A from animal and dairy products. Early weaning from breast milk can also increase the risk of vitamin A deficiency.

Secondary vitamin A deficiency is associated with chronic malabsorption of lipids, impaired bile production and release, and chronic exposure to oxidants, such as cigarette smoke, and chronic alcoholism. Vitamin A is a fat soluble vitamin and depends on micellar solubilization for dispersion into the small intestine, which results in poor use of vitamin A from low-fat diets. **Zinc deficiency** can also impair absorption, transport, and metabolism of vitamin A because it is essential for the synthesis of the vitamin A transport proteins and as the cofactor in conversion of retinol to retinal. In malnourished populations, common low intakes of vitamin A and zinc increase the severity of vitamin A deficiency and lead physiological signs and symptoms of deficiency.

Symptoms of vitamin A deficiency are night blindness, keratinization of hair follicles, damage to eye tissue and sometimes to irreversible blindness. In epidemiological studies, a low intake of vitamin A has been associated with increased risk of developing certain cancers (Kummet *et al.*1983). It's required to maintain many epithelial cells, where many cancers are seen. [(1)]

Xerophthalmia associated with clouding and cornification of the cornea. In 1944 R. A. Morton renamed aldehyde form of vitamin A to retinaldehayde. [(2)]

- **Toxicity:**

Adequate supply, but not excess vitamin A, is especially important for pregnant and breastfeeding women for normal fetal development. Deficiencies cannot be compensated by postnatal supplementation. Excess vitamin A, which is most common with high dose vitamin supplements, can cause birth defects and therefore should not exceed recommended daily values.

In general, acute toxicity occurs at doses of 25,000 IU/kg of body weight, with chronic toxicity occurring at 4,000 IU/kg of body weight daily for 6–15 months. However, liver toxicities can occur at levels as low as 15,000 IU per day to 1.4 million IU per day, with an average daily toxic dose of 120,000 IU per day, particularly with excessive consumption of alcohol. In people with renal failure, 4000 IU can cause substantial damage. In addition, excessive alcohol intake can increase toxicity. Children can reach toxic levels at 1,500 IU/kg of body weight.

Excessive vitamin A consumption can lead to nausea, irritability, anorexia, vomiting, blurry vision, headaches, hair loss, muscle and abdominal pain and weakness, drowsiness, and altered mental status.

In chronic cases, hair loss, dry skin, drying of the mucous membranes, fever, insomnia, fatigue, weight loss, bone fractures, anemia, and diarrhea can all be evident on top of the symptoms associated with less serious toxicity.

High vitamin A intake has been associated with spontaneous bone fractures in animals. Cell culture studies have linked increased bone resorption and decreased bone formation with high intakes. This interaction may occur because vitamins A and D may compete for the same receptor and then interact with parathyroid hormone, which regulates calcium. Indeed, a study by Forsmo *et al.* shows a correlation between low bone mineral density and too high intake of vitamin A.

Researchers have succeeded in creating water-soluble forms of vitamin A, which they believed could reduce the potential for toxicity. However, a 2003 study found water-soluble vitamin A was approximately 10 times as toxic as fat-soluble vitamin. A 2006 study found children given water-soluble vitamin A and D, which are typically fat-soluble; suffer from asthma twice as much as a control group supplemented with the fat-soluble vitamins

- **Active Vitamin A farm:**

All forms of vitamin A have a β-ionone ring to which an isoprenoid chain is attached, called a **retinyl group**. Both structural features are essential for vitamin activity. The orange pigment of carrots – β-carotene – can be represented as two connected retinyl groups, which are used in the body to contribute to vitamin A levels. The α-carotene and γ-carotene also have a single retinyl group, which give them some vitamin activity. None of the other carotenes have vitamin activity. The carotenoid β-cryptoxanthin possesses an ionone group and has vitamin activity in humans. [3]

Vitamin A displays the usual reactions of a compound with a conjugated double bound system, and in addition, the group at position 15 undergoes specific reactions (as alcohol, aldehyde or carboxyl group). [2]

- **Metabolism and Excretion:**

Carotenoid absorbed and not stored or converted to retinol or retinal may be metabolized into other different compounds depending on the individual carotenoids. Retinol is conjugated with glucuronic acid thus excreted into feces through bile pathway. Retinol however; can be converted reversibly into retinal farm then into retinoic acid that been oxidize to be excrete as water soluble waste into urine. [4]

## ➢ Vitamin A

Dietary Reference Intake:

| Life stage group | RDA<br>Adequate intakes µg/day | Upper limit<br>µg/day |
|---|---|---|
| **Infants** | | |
| **0–6 months** | 400* | 600 |
| **7–12 months** | 500* | 600 |
| **Children** | | |
| **1–3 years** | 300 | 600 |
| **4–8 years** | 400 | 900 |
| **Males** | | |
| **9–13 years** | 600 | 1700 |
| **14–18 years** | 900 | 2800 |
| **19 – >70 years** | 900 | 3000 |
| **Females** | | |
| **9–13 years** | 600 | 1700 |
| **14–18 years** | 700 | 2800 |
| **19 – >70 years** | 700 | 3000 |
| **Pregnancy** | | |
| **<19 years** | 750 | 2800 |
| **19 – >50 years** | 770 | 3000 |
| **Lactation** | | |
| **<19 years** | 1200 | 2800 |
| **19 – >50 years** | 1300 | 3000 |

## ➢ References:


1. Suzanne K. Gaby, *et al.,* Vitamin Intake and Health-Scientific Review, 1st ed.270 Madison Avenue, New York: Marcel Dekker, Inc. USA; 1991.

2. Wilhelm Friedrich. Vitamins, 1st ed. Berlin. New York: Walter de Gruyter. 1988.

3. John Marks. The vitamins – their role in medical practice. 1st ed. Lancaster, England-Falcon House. MTP press limited. UK. 1985.

4. Sareen S. Gropper, *et al.,* Advance Nutrition and Human Metabolism. 4th ed. 10 Davis Drive Belmont, CA 94002-3098, Thomson-Wadsworth.USA. 2005.

5. Maurice E. Shils, *et al.,* Modern Nutrition in Health and Disease. 10th ed. 530 Walnut Street, Philadelphia, PA 19106. Lippincott Williams & Wilkins.USA. 2006.

6. http://en.wikipedia.org/wiki/Vitamin_A#Recommended_daily_intake