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Vitamin A and Provitamin A

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Abstract

Vitamin A is a fat-soluble vitamin obtained from two classes of compounds: preformed natural vitamin A: retinol and its compounds; and precursors of vitamin A (provitamin A): beta carotene and related compounds or vitamin A (retinol, retinyl esters), and provitamin A carotenoids such as alpha-carotene and beta-carotene that are converted to retinol. Food sources of vitamin A are represented by: liver (in high concentration in fish and polar bear), dairy products, egg yolk - for retinol; green, yellow, orange fruits and vegetables (broccoli, melon, potatoes, carrots, tomatoes, spinach) – for beta carotene. Retinol is indispensable for vision (especially twilight vision); it is also necessary for tissue growth and differentiation, bone growth, reproductive process, embryonic development, glycoprotein synthesis, prevention of cancer and cardiovascular diseases. Together with certain carotenoids, vitamin A increases immunity, reducing the risk of infections.

Keywords: Vitamin A; Provitamin A; Carotenoids; Fat-Soluble Vitamin; Nutritional Status

Abbreviations: IU: International Units; ATRA: All-Trans Retinoic Acid; RAR: Retinoic Acid Receptor; USP: United States Pharmacopeia; RE: Retinol Equivalents.

Introduction

Vitamins represent organic compounds that the body needs in varying quantities and that it cannot synthesize in sufficient quantities or some at all. Therefore, the need for vitamins can be supplemented from food or by administering food supplements. In general, food supplements that have vitamin A in their composition are not administered after assessing the nutritional status of the body in vitamin A, precautions are required to avoid excessive intake of this micronutrient.

The registration and marketing of food supplements is not subject to the same regulations as in the case of medicines and therefore, in the case of vitamin A, a micronutrient where the deficit/excess balance is within very narrow limits, it is necessary to observe the concentration of the micronutrient per unit dose administered. Ensuring the optimal intake of fat-soluble vitamins is a necessity in ensuring a balanced diet. Dietary sources of fat-soluble vitamins are not always sufficient to ensure this intake. Nutritional supplements with vitamins can supplement this intake. The advantage of resorting to supplements is that of estimating the daily intake, but it is countered by the insufficient knowledge of the bioavailability of each component of the administered product, given that the standardization of different nutritional principles in the form of "nutritional supplement" is not strictly controlled. Vitamin A is found naturally in many food products, of plant and animal origin. Some foods (margarine) are fortified with vitamin A to improve their quality. Margarine is a food of vegetable origin, widely used in the diet due to the increased intake of vegetable fats, vitamin A and vitamin D [1].

The health legislation in force provides for vitamin A and its esters in margarine, a minimum of 25.0 I.I/kg, in depending on its fate.

The chemical complexity of the studied food product, but especially the extremely low chemical stability of vitamin A, makes its determination in margarine rather difficult. Pharmacokinetics studies of fat-soluble vitamins from nutritional supplements authorized can contribute to the optimization of formulation (concentrations, possible associations, incompatibilities), administration and bioavailability of nutritional principles.

Retinol, the dietary form of vitamin A, is a fat-soluble, antioxidant vitamin important for vision and bone growth. It belongs to the family of chemical compounds called retinoids. Retinol is ingested in a precursor form; animal sources (milk and eggs) contain retinyl esters, while plants (carrots, spinach) contain provitamin A carotenoids. Hydrolysis of retinyl esters results in retinol, and pro-vitamin A can be broken down to produce retinal. Retinal, also called retinaldehyde, can be reversibly reduced to retinol or irreversibly oxidized to retinoic acid. The most active retinoid metabolizers are 11-cis-retinal and all-trans and 9-cis-isomers of retinoic acid [2].

The Spread of Vitamin A in Nature

Vitamin A is also called the "anti-infection" vitamin due to its role in supporting the immune system. Vitamin A is the first soluble vitamin discovered. Vitamin A was identified in 1913 and is a compound also known as retinol.

Vitamin A is essential for reproduction, for maintaining and rejuvenating the epithelial tissues of the skin (dermis and epidermis), lungs, gastrointestinal tract, uterus and others. Vitamin A is found in two forms:

- The form of animal origin, retinol, which is stored in the body;
- The form of vegetable origin, beta-carotene, which is converted into retinol if the level in the body is not sufficient [3].

Thus, it can be said that beta-carotene is not toxic, except for the case where excessive intake can cause a reversible yellowing of the skin. Beta-carotene can increase the incidence of lung and colon cancer if it is offered alone to smokers. The name retinol was given as a reference to the participation of this compound in the functions of the retina of the eye. Retinol (or vitamin A) is found in foods of animal origin, fruits and vegetables that contain carotenoids [4].

Carotenoids are pigments that determine the red, orange and yellow colors of plants, fruits and vegetables. The body can convert certain members of the carotenoid family into vitamin A - such as beta-carotene, alpha-carotene and gamma-carotene. These carotenoids are also called "provitamin A". Beta-carotene is the most active precursor of vitamin A and in large doses is not toxic, unlike vitamin A. Vitamin A is best known for its essential role for vision, but it is good to know that this vitamin also participates in the activities physiological related to the immune system, the maintenance of epithelial tissues and mucous membranes, growth, reproduction and bone development [5].

Vitamin A usually occurs in foods as a fatty compound called retinyl palmitate. The body transforms retinyl palmitate into three metabolically active forms of the vitamin: retinol, retinal and retinoic acid.

Chemical Structure and Functions

Many different geometric isomers of retinol, retinal, and retinoic acid can occur as a result of the trans or cis configuration of the four double bonds found in the side chain. The cis isomers are less stable and can easily convert to the all-trans configuration (as seen in the all-trans retinol structure next door). However, some cis isomers are found in the natural state and have essential functions.

For example, the 11-cis-retinal isomer is the chromophore of rhodopsin, the vertebrate photoreceptor molecule. Rhodopsin is formed by the covalent binding through a Schiff base of 11-cis-retinal to the protein opsin (either rod opsin or blue, red, or green cone opsin). The vision process is based on the light-induced isomerization of the chromophore from 11-cis to all-trans, resulting in a change in the photoreceptor molecule. One of the first signs of vitamin A deficiency is night blindness, followed by decreased visual acuity. Many of the non-visual functions of vitamin A are mediated by retinoic acid, which regulates gene expression by activating intracellular retinoic acid receptors [6].

The non-visual functions of vitamin A are essential in the immunological, reproductive and embryonic development functions of vertebrates, as shown by the insufficient growth, susceptibility to infection and birth defects observed in populations receiving less than optimal amounts of dietary vitamin A. Retinol can also be used as an acne treatment in creams. One form of retinoic acid, all-trans retinoic acid (ATRA), is currently used as chemotherapy for acute promyelocytic leukemia, a subtype of acute myelogenous leukemia. This happens because these transformed cells of this subtype mostly respond to the retinoic acid receptor (RAR) [7].

It increases visual acuity at night, improves vision and helps in the treatment of many eye diseases by allowing the

formation of purpura. Increases resistance to respiratory infections. It helps the normal functioning of the immune system. It shortens the duration of illness. It maintains the health of the superficial layers of tissues and internal organs. Contributes to the removal of age-related pigmentation spots. It maintains the growth and strengthening of bones and the health of the skin, hair, teeth and gums. It helps in the treatment of acne, superficial wrinkles and conditions such as impetigo, furunculosis, burns and open ulcers (when used externally). It is adjuvant in the treatment of emphysema and hyperthyroidism [8].

The view

Vitamin A is used in the production of rhodopsin, the visual pigment used in low light. Epithelial cells Vitamin A is essential for the proper functioning of epithelial cells. In vitamin A deficiency, mucus-secreting cells are replaced by keratin-producing cells, which lead to xerosis. Glycoprotein synthesis Vitamin A is required for glycoprotein synthesis. In severe vitamin A deficiencies, the lack of glycoprotein can lead to corneal ulcers or liquefaction. Immune System Vitamin A is essential for keeping epithelial tissue intact as a physical barrier against infection; it is also involved in maintaining healthy lymphocytes and T cells. Formation of red blood cells (hematopoiesis) Vitamin A may be required for normal hematopoiesis; deficiency causes abnormalities in iron metabolism [9].

The Increase

Vitamin A is necessary for normal growth and development of cells. Although the mechanisms by which vitamin A promotes cell growth and development are not yet fully understood, it is known that retinoic acid is necessary for the synthesis of many glycoproteins, which control cell adhesion (the ability of cells to attach to each other), growth and cell differentiation. Food intake during the absorption process from the intestines, retinol is retained by chylomicrons in the form of esters and these particles mediate the transport to the liver. Hepatocytes store vitamin A as an ester, and when retinol is needed in other tissues, it is de-esterified and released into the blood as alcohol. The retinol then attaches to a transport molecule, retinol binding protein, for its journey to the target tissue. A binding protein within cells, intracellular retinoic acid binding protein, serves as a storage and transporter of retinoic acid within the cell [10].

The bioavailability of carotenoids ranges from 1/5 to 1/10 that of retinol. Carotenoids are better absorbed when ingested with a high-fat meal. In order to be effectively absorbed in the digestive tract, it also requires the presence of minerals. It works better in the presence of the following minerals: calcium, magnesium, phosphorus, selenium and zinc. Surface use all forms of vitamin A are used in cosmetics and medicine, being applied to the skin. Retinoic acid, retinyl palmitate, isotretinoin, tretinoin, and retinol are used medicinally as a topical treatment for acne and keratosis pilaris [11].

In cosmetics, vitamin A derivatives are used as so-called anti-aging chemicals - vitamin A is absorbed through the skin and increases the skin's receptivity rate and gives a temporary increase in collagen, thus causing a younger appearance. Other roles of vitamin A it is known that vitamin A is essential for reproductive processes in both men and women and plays an important role in the normal metabolism of bones. In addition, some of the latest cutting-edge research in the field of genetics shows the role given by vitamin A (in the form of retinoic acid) in making genetic links. Vitamin A deficiency is common in developing countries but rarely seen in developed countries. An estimated 250,000 to 500,000 malnourished children in developing countries go blind each year due to vitamin A deficiency.

Night blindness is one of the first signs of deficiency. Xerophthalmia and weakening of night vision. The conditions can be caused by chronic fat absorption deficiencies and are most often encountered in children under the age of five, due to the insufficient amount of vitamin A ingested. It contributes to blindness by drying out the cornea and destroying the retina and cornea.

Vitamin A deficiency impairs the ability to fight infections. In countries where children are not immunized, infectious diseases such as measles have higher mortality rates. Deficiency can also be a problem because it can increase children's risk of developing respiratory and diarrheal infections, stunted growth, stunted bone development and reduced chances of survival from serious illness. Iron deficiency can affect vitamin A intake [12].

Excessive alcohol consumption destroys vitamin A, although a stressed liver may be more susceptible to vitamin A toxicity. People who consume large amounts of alcohol should consult a doctor before taking vitamin A supplements. The units of measurement for vitamin A are: UI (International Units), USP (United States Pharmacopeia) and more recently RE (Retinol Equivalents). Required daily dose:

- Refers to the minimum vitamin requirement for a normal person, under normal living conditions;
- Vitamin deficiency can occur due to insufficient intake: harmful eating habits, prohibitions or religious practices, lack of necessary food, etc.
- Exocarience; or due to absorption disorders;
- Enterocariency: pathogenic intestinal flora, metabolic disorders, imbalanced vitamin excess, genetic factors; in cases of hypovitaminosis;
- Mild deficiency, or avitaminosis;

- Serious vitamin deficiency, the recommended compensation doses can be very high [13].

For preventive purposes, for adults it is 5,000 IU (1,000 RE) for men and 4,000 IU (800 RE) for women. For nursing mothers, the daily dose can be increased by 2,500 IU for the first six months and by 2,000 IU for the next six months [14].

Vitamin A Overdose

Exceeding a daily dose of 50,000 for months can cause toxic effects in adults. More than 18,500 IU daily risks producing negative effects in children. Symptoms of vitamin A poisoning are: hair loss, nausea, vomiting, thickening of the skin, blurred vision, skin rashes, osteoporosis, irregular periods, fatigue, headaches, and enlarged liver. Too much vitamin A can be harmful or even fatal. The body converts the dimerized form, carotene, to vitamin A as needed, so high levels of carotene are not toxic compared to the ester forms. The livers of certain animals, especially those adapted to polar environments, usually contain amounts of vitamin A that would be toxic to humans. The first documented death from vitamin A poisoning is that of Xavier Mertz, a Swiss scientist, who died in January 1913 on an expedition to Antarctica when food supplies were lost and dogs were slaughtered and eaten who pulled the sleds. Mertz consumed lethal amounts of vitamin A by ingesting dog liver. Polar bear liver also has enough vitamin A to kill a human, or make sled dogs seriously ill [15].

Excess vitamin A has been suspected as a contributing factor to osteoporosis. The carotenoid beta-carotene was associated with an increased risk of lung cancer when studied in a lung cancer prevention trial in male smokers.

Although cases of vitamin A toxicity have been reported in arctic explorers and some long-term megadoses of vitamin A, pregnant women need large amounts of vitamin A, preferably from natural animal sources such as liver, butter unpasteurized and cod liver oil. Enemies of vitamin A Carotene polyunsaturated fatty acids can destroy vitamin A in the absence of antioxidants.

Measurement Units

When referring to food doses or nutritional science, retinol is usually measured in International Units (IU). IU refers to biological activity and is therefore unique to each compound, with 1 IU of retinol being equivalent to approximately 0.3 μg (300nanograms) [16].

Retinol is the best-known derivative of vitamin A and is involved in the development of the bone system and dentition, the reproductive system, the skin and mucous membranes, as well as the vision. Vitamin A also has an important antioxidant role in the human body. Although it has many functions in the body, vitamin A is known for its beneficial effects on the skin and is considered the most powerful anti-aging agent that we can add to skin care products. It helps to reduce fine wrinkles; pigment spots and also stimulates collagen synthesis. Vitamin A is therefore a basic ingredient in rejuvenating mature skin.

Sources of Vitamin A

Vitamin A is found in many foods rich in beta-carotene, such as: egg yolks, beef liver, butter, cod liver oil, chicken liver, salmon, Cheddar cheese, mackerel, trout, sweet potatoes, pumpkin, carrots, spinach, cabbage, pumpkin pie, melon, papaya, red peppers. And the human body transforms beta-carotene into vitamin A, so useful for physiological processes. Oral vitamin A supplementation is a viable alternative mainly for people whose diet is poor or limited or who have a condition that requires increased vitamin A intake, such as pancreatic disease, eye disease or measles [17].

Conclusions

Although vitamin A is often considered a single nutrient, in fact it is a group of fat-soluble compounds that includes retinol, retinal, retinoic acid, retinoids and carotenoids. Vitamin A is found in many foods rich in beta-carotene, such as: egg yolks, beef liver, butter, cod liver oil, chicken liver, salmon, Cheddar cheese, mackerel, trout, sweet potatoes, pumpkin, carrots, spinach, cabbage, pumpkin pie, melon, papaya, red peppers. And the metabolic reactions in the body transform beta-carotene into vitamin A, so useful for physiological processes. Oral vitamin A supplementation is a viable alternative mainly for people whose diet is poor or limited or who have a condition that requires increased vitamin A intake, such as pancreatic disease, eye disease or measles. Vitamin A is stored in the liver. The vitamin A deposits in the liver of a healthy fed adult can provide the body's needs for several months. The administration of too large amounts of vitamin A can exceed the storage capacity of the liver, causing unfavorable effects in the body. However, it is unlikely that a person through a normal diet will reach an excess of vitamin A. When vitamin A is obtained from beta-carotene, there is no risk, because it is converted in the body when it needs it she.

References

1. Patil S, Zamwar UM, Mudey A (2023) Etiology, Epidemiology, Pathophysiology, Signs and Symptoms, Evaluation, and Treatment of Vitamin A (Retinol) Deficiency. Cureus 15(11): e49011.

2. Ablonczy Z, Crouch RK, Goletz PW, Redmond TM, Knapp DR, et al. (2002) 11-cis-retinal reduces constitutive

opsin phosphorylation and improves quantum catch in retinoid-deficient mouse rod photoreceptors. The Journal of biological chemistry 277(43): 40491-40498.

3. Ford JL, Green MH, Brownell JN, Green JB, Oxley A, et al. (2023) Use of Compartmental Modelling and Retinol Isotope Dilution to Determine Vitamin A Stores in Young People with Sickle Cell Disease Before and After Vitamin A Supplementation. The Journal of nutrition 153(9): 2762-2771.

4. Habre RE, Aoun R, Tahtouh R, Hilal G (2024) All-trans-retinoic acid modulates glycolysis via H19 and telomerase: the role of mir-let-7a in estrogen receptor-positive breast cancer cells. BMC cancer 24(1): 615.

5. Wu S, Wang L, Cui B, Wen X, Jiang Z, et al. (2023) Effects of Vitamin A on Growth Performance, Antioxidants, Gut Inflammation, and Microbes in Weaned Piglets. Antioxidants (Basel, Switzerland) 12(12): 2049.

6. Su X, Patel N, Zhu S, Zhou X, Chen Y, et al. (2024) Association between serum vitamin A and body mass index in adolescents from NHANES 1999 to 2006. Scientific reports 14(1): 10859.

7. Cheng X, Li D, Yang C, Chen B, Xu P, et al. (2024) Oral vitamin A supplements to prevent acute upper respiratory tract infections in children up to seven years of age. The Cochrane database of systematic reviews 5(5): CD015306.

8. Lerner UH (2024) Vitamin A - discovery, metabolism, receptor signaling and effects on bone mass and fracture susceptibility. Frontiers in endocrinology 15: 1298851.

9. Saari JC (2016) Vitamin A and Vision. Sub-cellular biochemistry 81: 231-259.

10. Patel R, Nair S, Choudhry H, Jaffry M, Dastjerdi M (2024) Ocular manifestations of liver disease: an important diagnostic aid. International ophthalmology 44(1): 177.

11. Miller AP, Hornero MD, Bandara S, Parra RO, Limon MC, et al. (2023) Bioavailability and provitamin A activity of neurosporaxanthin in mice. Communications biology 6(1): 1068.

12. Dewett D, Lam KK, Poupault C, Khurana H, Rister J (2021) Mechanisms of vitamin A metabolism and deficiency in the mammalian and fly visual system. Developmental biology 476: 68-78.

13. Li B, Vachali PP, Shen Z, Gorusupudi A, Nelson K, et al. (2017) Retinal accumulation of zeaxanthin, lutein, and β-carotene in mice deficient in carotenoid cleavage enzymes. Experimental eye research 159: 123-131.

14. Broulik PD, Raska I, Broulikova K (2013) Prolonged overdose of all-trans retinoic acid enhances bone sensitivity in castrated mice. Nutrition 29(9): 1166-1169.

15. Ross AC, Russell RM, Miller SA, Munro IC, Rodricks JV, et al. (2009) Application of a key events dose-response analysis to nutrients: a case study with vitamin A (retinol). Critical reviews in food science and nutrition 49(8): 708-717.

16. Leithead JA, Simpson KJ, MacGilchrist AJ (2009) Fulminant hepatic failure following overdose of the vitamin A metabolite acitretin. European journal of gastroenterology & hepatology 21(2): 230-232.

17. Saxe CA, LaChance J, Kerver JM (2024) A Fresh Fruit and Vegetable Prescription Program for Prenatal Patients in Flint, Michigan: Baseline Food Security and Dietary Intake. Nutrients 16(8): 1234.