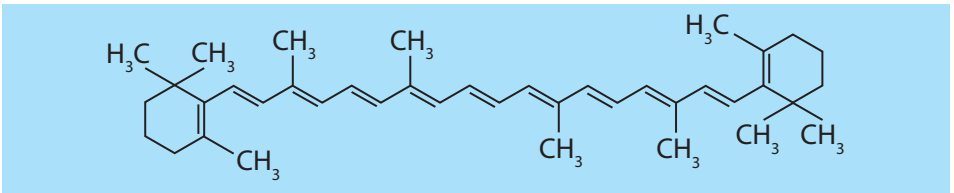
Beta-carotene

Beta-carotene crystals in polarised light

Chemistry

Beta-carotene is a terpene. It is made up of eight isoprene units, which are cyclised at each end. The long chain of conjugated double bonds is responsible for the orange colour of beta-carotene.



Molecular formula of beta-carotene

Introduction

Beta-carotene is one of more than 600 carotenoids known to exist in nature. Carotenoids are yellow, orange and red pigments that are widely distributed in plants. In 1831, beta-carotene was isolated by Wackenroder. Its structure was determined by Karrer in 1931, who received a Nobel prize for his work.
About 50 of the naturally occurring carotenoids can potentially yield vitamin A and are thus referred to as provitamin A carotenoids. Beta-carotene is the most abundant and most efficient provitamin A in our foods.
Currently available evidence suggests that in addition to being a source of vitamin A, beta-carotene plays many important biological roles that may be independent of its provitamin status.

Functions

Beta-carotene is the main safe dietary source of vitamin A. Vitamin A is essential for normal growth and development, immune system function, and vision.
Beta-carotene can quench singlet oxygen, a reactive molecule that is generated, for instance, in the skin by exposure to ultraviolet light, and which can induce precancerous changes in cells. Singlet oxygen is capable of triggering free radical chain reactions.

Beta-carotene has antioxidant properties that help neutralise free radicals – reactive and highly energised molecules which are formed through certain normal biochemical reactions (e.g. the immune response, prostaglandin synthesis), or through exogenous sources such as air pollution or cigarette smoke. Free radicals can damage lipids in cell membranes as well as the genetic material in cells, and the resulting damage may lead to the development of cancer.

Main functions in a nutshell:
- Provitamin A
- Antioxidant activity

Dietary sources

The best sources of beta-carotene are yellow/orange vegetables and fruits and dark green leafy vegetables:

- Yellow/orange vegetables – carrots, sweet potatoes, pumpkins, winter squash
- Yellow/orange fruits – apricots, cantaloupes, papayas, mangoes, carambolas, nectarines, peaches
- Dark green leafy vegetables – spinach, broccoli, endive, kale, chicory, escarole, watercress and beet leaves, turnips, mustard, dandelion
- Other good vegetable and fruit sources – summer squash, asparagus, peas, sour cherries, prune plums.

The beta-carotene content of fruits and vegetables can vary according to the season and degree of ripening.

Beta-carotene content of foods

Food	Beta-carotene (mg/100g)
Carrots	7.6
Kale	5.2
Spinach	4.8
Cantaloupes	4.7
Apricots	1.6
Mangoes	1.2
Broccoli	0.9
Pumpkins	0.6
Asparagus	0.5
Peaches	0.1

(Souci, Fachmann, Kraut)

Absorption and body stores

Bile salts and fat are needed for the absorption of beta-carotene in the upper small intestine. Many dietary factors, e.g. fat and protein, affect absorption. Approximately 10-50% of the total beta-carotene consumed is absorbed in the gastrointestinal tract. The proportion of carotenoids absorbed decreases as dietary intake increases. Within the intestinal wall (mucosa), beta-carotene is partially converted into vitamin A (retinol) by the enzyme dioxygenase. This mechanism is regulated by the individual's vitamin A status. If the body has enough vitamin A, the conversion of beta-carotene decreases. Therefore, beta-carotene is a very safe source of vitamin A and high intakes will not lead to hypervitaminosis A.
Excess beta-carotene is stored in the fat tissues of the body and the liver. The adult's fat stores are often yellow from accumulated carotene while the infant's fat stores are white.

Bioavailability of beta-carotene
Bioavailability refers to the proportion of beta-carotene that can be absorbed, transported and utilised by the body once it has been consumed. It is influenced by a number of factors:
- Beta-carotene from dietary supplements is better absorbed than beta-carotene from foods
- Food processing such as chopping, mechanical homogenisation and cooking enhances bioavailability of beta-carotene
- The presence of fat in the intestine affects absorption of beta-carotene. The amount of dietary fat required to ensure carotenoid absorption seems to be low (approximately 3-5g per meal)

Measurement

Plasma carotenoid concentration is determined by HPLC. It reflects the intake of carotenoids. Traditionally, vitamin A activity of beta-carotene has been expressed in International Units (IU; 1 IU = 0.60 µg of all-trans beta-carotene). However, this conversion factor does not take into account the poor bioavailability of carotenoids in humans. Thus, the FAO/WHO Expert Committee proposed that vitamin A activity be expressed as retinol equivalents (RE). 6 µg beta-carotene provide 1 µg retinol.
For labelling, official national directives should be followed.

1 RE = 1 µg retinol
= 6 µg beta-carotene
= 3.33 IU vitamin A activity from retinol
= 10 IU vitamin A activity from beta-carotene

Stability

Carotenoids can lose some of their activity in foods during storage due to the action of enzymes and exposure to light and oxygen. Dehydration of vegetables and fruits may greatly reduce the biological activity of carotenoids. On the other hand, carotenoid stability is retained in frozen foods.

Interactions

Negative interactions
Cholestyramine and colestipol (cholesterol-lowering agents), mineral oil, orlistat (a weight loss medication) and omeprazole (proton-pump inhibitor) can reduce absorption of carotenoids.

Deficiency

Although consumption of provitamin A carotenoids can prevent vitamin A deficiency, there are no known adverse clinical effects of a low carotenoid diet, provided vitamin A intake is adequate.

Disease prevention and therapeutic use

Immune system
In a number of animal and human studies beta-carotene supplementation was found to enhance certain immune responses. Early studies demonstrated the ability of beta-carotene and other carotenoids to prevent infections. Some clinical trials have found that beta-carotene supplementation improves several biomarkers of immune function. It can lead to an increase in the number of white blood cells and the activity of natural killer cells. Both of these are important in combating various diseases. It may be the case that beta-carotene stimulates the immune system once it has undergone conversion to vitamin A. Another explanation could be that the antioxidant actions of beta-carotene protect cells of the immune system from damage by reducing the toxic effects of reactive oxygen species.

Skin
Recent evidence points to a role of beta-carotene in protecting the skin from sun damage. Beta-carotene can be used as an oral sun protectant in combination with sunscreens for the prevention of sunburn. Its effectiveness has been proven both alone and in combination with other carotenoids or antioxidant vitamins.

Cancer and cardiovascular diseases
Epidemiological studies consistently indicate that as consumption of beta-carotene-rich fruits and vegetables increases, the risk of certain cancers (i.e. lung and stomach cancer) and cardiovascular diseases decreases.
Additionally, animal experiments have shown that beta-carotene acts as a cancer risk reduction agent.

This is further supported by studies of biomarkers for the development of certain cancers. There is no evidence that beta-carotene supplementation reduces the risk of cardiovascular diseases.

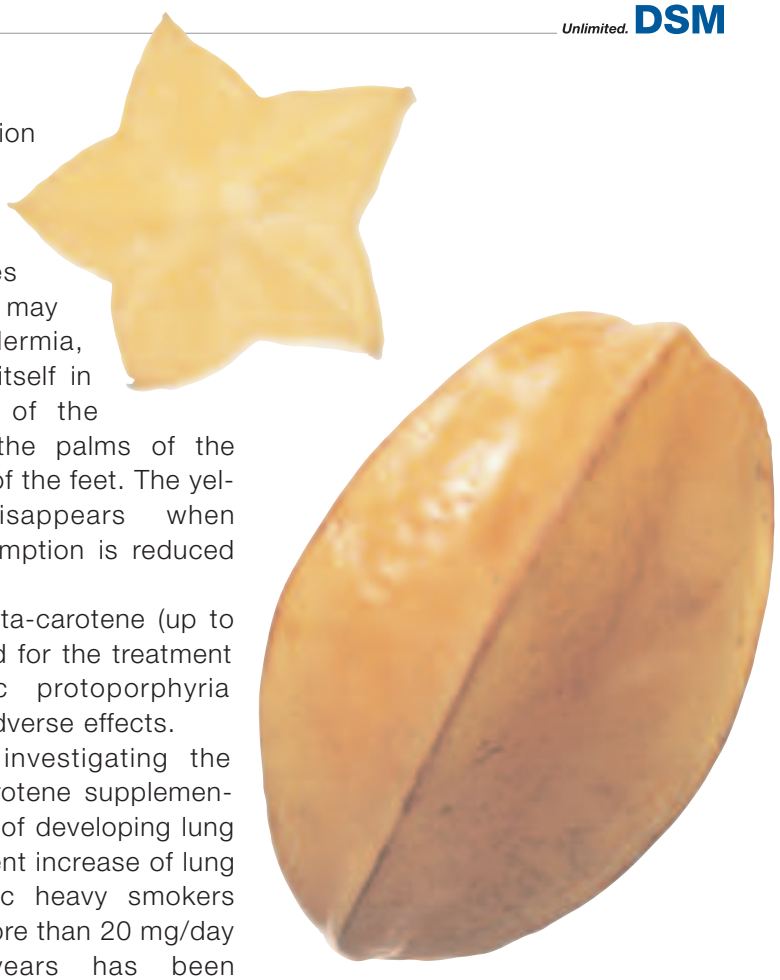
Erythropoietic protoporphyria
In patients with erythropoietic protoporphyria – a photosensitivity disorder leading to abnormal skin reactions to sunlight – beta-carotene in doses of up to 180 mg has been shown to exert a photoprotective effect.

Recommended Dietary Allowance (RDA)

Until now, dietary intake of beta-carotene has been expressed as part of the RDA for vitamin A. The daily vitamin A requirements for adult men and women are 900 µg and 700 µg of preformed vitamin A (retinol) respectively (FNB, 2001). Apart from its provitamin A function, data continue to accumulate supporting a role for beta-carotene as an important micronutrient in its own right. Consumption of foods rich in beta-carotene is being recommended by scientific and government organisations such as the US National Cancer Institute (NCI) and the US Department of Agriculture (USDA). If these dietary guidelines are followed, dietary intake of beta-carotene (about 6 mg) would be several times the average amount presently consumed in the US (about 1.5 mg daily).

Safety

Beta-carotene is a safe source of vitamin A. Due to the regulated conversion of beta-carotene into vitamin A, overconsumption does not produce hypervitaminosis A. Excessive intakes of beta-carotene may cause carotenodermia, which manifests itself in a yellowish tint of the skin, mainly in the palms of the hands and soles of the feet. The yellow colour disappears when carotenoid consumption is reduced or stopped.
High doses of beta-carotene (up to 180 mg/day) used for the treatment of erythropoietic protoporphyria have shown no adverse effects.
In two studies investigating the effect of beta-carotene supplementation on the risk of developing lung cancer, an apparent increase of lung cancer in chronic heavy smokers with intakes of more than 20 mg/day over several years has been observed.The reasons for these findings are not yet clear.
The British Expert Committee on Vitamins and Minerals (EVM) recommends a Safe Upper Level for supplementation of 7 mg/day over a lifetime period. Other agencies such as the European DACH Society (German Society of Nutrition, Austrian Society of Nutrition, Swiss Society of Nutrition Research) have concluded that a daily intake of up to 10 mg of beta-carotene is safe.



Supplements and food fortification

Beta-carotene is available in hard and soft gelatine capsules, in multivitamin tablets, and in antioxidant vitamin formulas and as food colour. Margarine and fruit drinks are often fortified with beta-carotene. In 1941, the US Food and Drug Administration (FDA) established a standard of identity for the addition of vitamin A to margarine; since then, however, vitamin A has been partly replaced by beta-carotene, which additionally imparts an attractive yellowish colour to this product. Due to its high safety margin, beta-carotene has been recognised as more suitable for fortification purposes than vitamin A.

Industrial production

Isler and coworkers developed a method to synthesise beta-carotene, and it has been commercially available in crystalline form since 1954.

History

1831 Wackenroder isolates the orange-yellow pigment in carrots and coins the term 'carotene'.

1847 Zeise provides a more detailed description of carotene.

1866 Carotene is classified as a hydrocarbon by Arnaud and co-workers.

1887 Arnaud describes the widespread presence of carotenes in plants.

1907 Willstatter and Mieg establish the molecular formula for carotene, a molecule consisting of 40 carbon and 56 hydrogen atoms.

1914 Palmer and Eckles discover the presence of carotene and xanthophylls in human blood plasma.

1919 Steenbock (University of Wisconsin) suggests a relationship between yellow plant pigments (beta-carotene) and vitamin A.

1929 Moore demonstrates that beta-carotene is converted into the colourless form of vitamin A in the liver.

1931 Karrer and collaborators (Switzerland) determine the structures of beta-carotene and vitamin A.

1939 Wagner and coworkers suggest that the conversion of beta-carotene into vitamin A occurs within the intestinal mucosa.

1950 Isler and colleagues develop a method for synthesising beta-carotene.

1966 Beta-carotene is found acceptable for use in foods by the Joint FAO/WHO Expert Committee on Food Additives.

1972 Specifications for beta-carotene use in foods is established by the U.S. Food Chemicals Codex.

1979 Carotene is established as 'GRAS', which means that the ingredient is 'Generally Recognised As Safe' and can be used as a dietary supplement or in food fortification.

1981-82 Beta-carotene/carotenoids are recognised as important factors (independent of their provitamin A activity) in potentially reducing the risk of certain cancers. R. Doll and R. Peto: “Can Dietary Beta-carotene Materially Reduce Human Cancer Rates?” (in: Nature, 1981; 290: 201-208) R. Shekelle et al: “Dietary Vitamin A and Risk of Cancer in the Western Electric Study” (in: Lancet, 1981: 1185-1190) “Diet, Nutrition and Cancer” (1982): Review of the U.S. National Academy of Sciences showing that intake of carotenoid-rich foods is associated with reduced risk of certain cancers.

1982 Krinsky and Deneke show the interaction between oxygen and oxyradicals using carotenoids.

1983-84 The US National Cancer Institute (NCI) launches large-scale clinical intervention trials using beta-carotene supplements alone and in combination with other nutrients.

1984 Beta-carotene is demonstrated to be an effective antioxidant in vitro.

1988 Due to the large number of epidemiological studies that demonstrate the potential reduction of cancer incidence with increased consumption of dietary beta-carotene, the US National Cancer Institute (NCI) issues dietary guidelines advising Americans to include a variety of vegetables and fruits in their daily diet.

1993-94 Availability of results from several large-scale clinical intervention trials using beta-carotene alone or in various other combinations.

1997 Evidence indicates that beta-carotene acts synergistically with vitamins C and E.

1999 The Women´s Health Study shows no increased risk of lung cancer for woman receiving 50 mg beta-carotene on alternate days.

2004 Results from the French SU.VI.MAX study indicate that a combination of antioxidant vitamins (C, E and beta-carotene) and minerals lowers total cancer incidence and all-cause mortality in men.

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Otto Isler