The Bioavailability of Dietary Carotenoids: Current Concepts

A Report of the International Vitamin A Consultative Group (IVACG)

Summary

- Carotenoids are a major source of vitamin A in the diets of a large proportion of the world's population. ß-Carotene, found primarily in fruits and vegetables, is the most common provitamin A carotenoid in most diets.
- In most world populations, the amount and bioavailability of ingested provitamin A carotenoids determine the adequacy of vitamin A intake.
- Bioavailability is defined as the efficiency with which ingested provitamin A carotenoids are absorbed and converted into vitamin A in the body.
- The reported relative amounts of ingested ß-carotene that are nutritionally equivalent to vitamin A in the body range from 26:1 to 2:1 (μg/μg). Thus, the widely quoted average equivalency ratio of 6:1 (6 μg ß-carotene = 1 μg retinol), devised by the World Health Organization, is a rough estimate that is not applicable to all diets.
- Provitamin A–containing foods, commonly available and eaten in almost all societies of the world, generally meet the minimum vitamin A requirements of humans. To maximize their benefits, strategies to increase the dietary intake of carotenoid-containing foods should also include measures to enhance carotenoid bioavailability.
- In a broader context, the inclusion of sizable amounts of fruits and vegetables in the diet is beneficial to health, independent of the conversion of carotenoids to vitamin A.

Background

The major sources of vitamin A in the diet are preformed vitamin A, commonly found in animal products, and provitamin A carotenoids, primarily derived from colored fruits and orange or green-colored vegetables.[1-3] In dark green leafy vegetables, the carotenoid color is masked by the presence of chlorophyll. Because many populations, particularly those in Asia and Africa, depend mainly on dietary carotenoids to satisfy their needs for vitamin A, the nutritional equivalency of carotenoids and preformed vitamin A in the diet becomes an important consideration.

> The yellow hue of carotenoids in many leafy vegetables is masked by the dark green color of chlorophyll

Of approximately 600 carotenoids found in nature, only three are important precursors of vitamin A in humans: ß-carotene, α-carotene, and ß-cryptoxanthin. Of these, ß-carotene is the major provitamin A component of most carotenoid-containing foods.[4] Food composition tables are often used to estimate the amount of provitamin A carotenoids in foods. Only recently have accurate values for food carotenoids been determined.[5,6] Nonetheless, because cultivars and growing conditions differ in various localities, the actual content of carotenoids in a food may differ significantly from that reported in such tables.[6]

Dietary preformed vitamin A is absorbed efficiently by the intestinal tract in the presence of fat and transported in the blood as vitamin A esters.[1-3] Much of the absorbed vitamin is stored in the liver. When required by tissues, the vitamin A in this liver reserve is released and transported to the tissues by a highly regulated process. The absorption of preformed vitamin A is not significantly affected by its food source or by the amount ingested. Substantial amounts are absorbed even during gastrointestinal infections.[7]

> The carotenoid content of any fruit or vegetable can vary markedly because of the cultivars used, growing conditions, and its state of maturity

The absorption of dietary carotenoids, in contrast, is affected by a large number of factors, including their chemical nature; their physical binding within the food; the presence of dietary fat, conjugated bile salts, and pancreatic enzymes in the intestinal lumen; the presence of other food components that inhibit their absorption; the amount ingested; the relative size of the food particles ingested; and food preparation practices that disrupt the food to different degrees.[8, 9] Systemic and parasitic infections reduce carotenoid absorption. Vitamin A deficiency enhances, whereas protein deficiency reduces, the conversion of ß-carotene to vitamin A. Genetics plays an important but not yet well-defined role.[9]

Thus, whereas the nutritional value of a food containing preformed vitamin A can be fairly well predicted, that of a food containing carotenoids cannot. For example, if red palm oil is ingested in small amounts, the relative bioavailability of ß-carotene is approximately 10-fold greater than that in whole uncooked carrots. Despite these uncertainties, the ingestion of carotenoid-containing foods, in the apparent absence of preformed vitamin A, can meet the vitamin A needs of both children and adults.[10,11]

Carotenoid bioavailability

Carotenoids can show physiologic actions unrelated to their conversion into vitamin A. In a nutritional context, however, the desired products of carotenoid metabolism are vitamin A–active compounds, of which the major ones are retinyl esters, retinol, and retinoic acid. Bioavailability can be categorized as absolute or as relative.[12] Absolute bioavailability is defined as the mass of vitamin A–active compounds formed in the body following the ingestion of a given amount of a provitamin A carotenoid. Relative bioavailability is the response of a suitable indicator to a given form of a provitamin A carotenoid relative to a reference form. This could be, for example, the same amount of ß-carotene in oil or a known mass of preformed vitamin A in a highly utilizable form.

> The nutritional value of carotenoids ingested in foods can vary 10-fold or more as a result of food preparation practices

When the amount of provitamin A ingested is small (<1 mg), most of it is converted to vitamin A in the intestine. With larger amounts, an increasing proportion of the absorbed carotenoid is found in the plasma and in tissues. Adjustment must consequently be made for this absorbed-but-not-immediately-converted carotenoid in determining a bioavailability value.

The absolute bioavailability of provitamin A carotenoids from food sources is essentially unknown for any commodity. Thus, published values of bioavailability are all relative to either ß-carotene in oil or to vitamin A in a bioavailable form.

Estimated vitamin A equivalence of carotenoids

In 1967, an expert committee of the Food and Agriculture Organization (FAO) and the World Health Organization (WHO) suggested that a ratio of 6 μg all-*trans* ß-carotene in food is equivalent to 1 μg all-*trans* retinol in food.[13] Thus, the retinol equivalent (RE) was established, which could be expressed in any mass units, e.g., ng, μg, or mg. Generally, μg RE is employed. The FAO/WHO committee based its equivalency ratio on two assumptions: (1) that the mass ratio of the maximum conversion of ß-carotene in oil, its most bioavailable form, to vitamin A in vivo was 2:1, and (2) that the bioavailability of ß-carotene from foods *on average* was one-third that of ß-carotene in oil. Thus, $2 \times 3 = 6$ μg ß-carotene per μg retinol.

Other common carotenoids, like ß-cryptoxanthin and α-carotene, were considered to be half as active as ß-carotene. Later, *cis*-isomers were considered to be half as active as their all-*trans* counterparts. Thus, conversion ratios of 5.8:1 and 6.4:1 for ß-carotene in papaya and in amaranth, respectively, were calculated from a well-designed study with preschool children in India.[10]

New methods of determining carotenoid bioavailability should allow better estimates of the vitamin A content of diets

Many balance studies (see below) in humans have indicated that the absorption of provitamin A carotenoids from the diet is 50–80%.[13,14] India consequently defined a ratio of 4:1 for the food-based ß-carotene/vitamin A conversion.[14] The approach was similar to that used by the FAO/WHO committee, but the average bioavailability of ß-carotene in ingested vegetables and fruits relative to ß-carotene in oil was considered to be 50%, not 33.3%.

More recently, higher ratios (poorer bioavailability) of carotene to vitamin A have been suggested from feeding studies in Indonesia, namely, 26:1 for carrots and green leafy vegetables and 12:1 for fruits.[15] These studies have stimulated a reevaluation of the methods used to assess the bioavailability of carotenoids as sources of vitamin A in the diet.

Indicators used to measure carotenoid bioavailability, vitamin A deficiency, and serum retinol levels

Balance techniques

The amount of carotenoids absorbed is assumed to be the difference between the amount ingested and the amount found in the feces. This procedure overestimates absorption inasmuch as the extraction efficiency of carotenoids from undigested foods and the extent of carotenoid destruction in the gastrointestinal tract are not assessed.

Improvement in dark adaptation and/or electroretinogram responses

Responses to various indicators of vitamin A deficiency occur quickly at relatively low doses of vitamin A or ß-carotene. These methods have been most effective in controlled clinical studies of vitamin A deficiency.[16] The methods, however, are difficult to use with young children.

Increase in serum retinol

The increase in serum retinol relative to a reference compound, e.g., retinyl ester in a bioavailable form, produced by feeding a carotenoid-containing food for a given period can be determined. An unsupplemented control group must also be included. Subjects must be vitamin A-depleted; otherwise, no response will be noted. Because the relation between plasma retinol concentrations and vitamin A status is not linear, groups must be carefully matched. The rate of response as well as the ultimate increment in serum retinol should be measured. This technique has been most commonly used to evaluate the relative bioavailability of carotenoids.[10,15]

New approaches for determining carotenoid bioavailability

The absorption of carotenoids and their conversion into vitamin A in humans have recently been approached in several new ways:

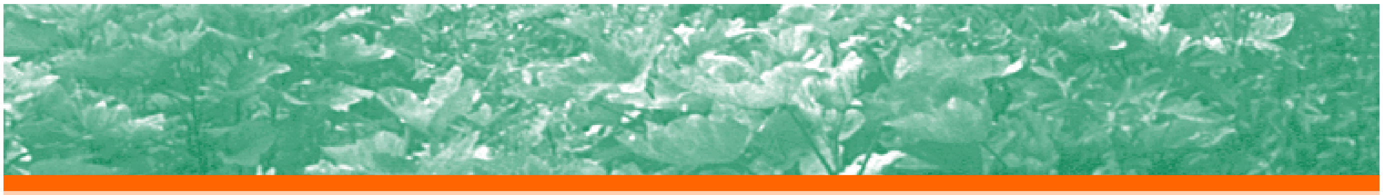
- the quantitation of absorbed carotenoids and newly formed vitamin A in the triglyceride-rich lipoprotein fraction of plasma by an area-under-the-curve (AUC) procedure,[17]
- in vivo kinetics of a single dose of deuterated ß-carotene by use of a sophisticated modeling technique,[18]
- comparison of the appearance of deuterated vitamin A in the plasma by the AUC method after the administration either of deuterated ß-carotene in oil or in food or of deuterated vitamin A,[19]
- comparison of the total body reserves, determined by an isotope-dilution technique, before and after feeding carotenoid-rich foods for several weeks,[20] and
- measurement of the steady-state labeling of ß-carotene or vitamin A after administering small doses of ß-carotene or vitamin A labeled with ^{13}C during an extended period.[21]

These methods in large part give relative bioavailability data. A general procedure for determining absolute bioavailability has not yet been formulated.

Educational measures should improve carotenoid utilization by improving food preparation practices

Summary

Our current knowledge about the bioavailability of provitamin A carotenoids is insufficient, fragmentary, and difficult to interpret. Nonetheless, provitamin A–containing foods, commonly available and eaten in almost all societies of the world, are generally able to meet the minimum vitamin A requirements of humans. Such foods must be prepared properly and eaten in sufficient quantities, however, to achieve this effect. Furthermore, any single average ratio for the conversion of carotenoids into vitamin A is at best a rough estimate that is not valid for all diets.



The Bioavailability of Dietary Carotenoids: Research Recommendations

- The bioavailability of carotenoids in foods ingested by humans should be determined by more quantitative procedures, including the use of carotenoids or foods labeled with heavy isotopes and appropriate pharmacokinetic and isotope-dilution methods.

- Ways of preparing and storing carotenoid-containing foods to enhance carotenoid bioavailability should be devised and disseminated by appropriate educational methods to populations at risk.

- Conversion ratios for categories of foods, e.g., dark green leafy vegetables and other carotenoid-containing vegetables and fruits, should be developed to enhance the accuracy of predicting vitamin A formation from ingested carotenoids. Modifiers of such ratios, e.g., mode of cooking, fat content of the diet, and particle size in the ingested food, might further improve these estimates.

- The extent to which the carotenoid content of ingested foods in a given culture accords with values found in food composition tables should be evaluated.

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Established in 1975, the International Vitamin A Consultative Group guides international activities for reducing vitamin A deficiency in the world. IVACG concentrates its efforts on stimulating and disseminating new knowledge, translating that new knowledge to assist others in its practical application, and providing authoritative policy statements and recommendations that others can use to develop appropriate prevention and control programs.

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