The challenge to reach nutritional adequacy for vitamin A: β-carotene bioavailability and conversion—evidence in humans

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ABSTRACT

β-Carotene is an important dietary source of vitamin A for humans. However, the bioavailability and vitamin A equivalency of β-carotene are highly variable and can be affected by food- and diet-related factors, including the food matrix, food-processing techniques, size of the dose of β-carotene, and the amounts of dietary fat, fiber, vitamin A, and other carotenoids in the diet as well as by characteristics of the target population, such as vitamin A status, nutrient deficiencies, gut integrity, and genetic polymorphisms associated with β-carotene metabolism. The absorption of β-carotene from plant sources ranges from 5% to 65% in humans. Vitamin A equivalency ratios for β-carotene to vitamin A from plant sources range from 3.8:1 to 28:1, by weight. Vitamin A equivalency ratios for β-carotene from biofortified Golden Rice or biofortified maize are 3.8:1 and 6.5:1, respectively, and are lower than ratios for vegetables that have more complex food matrices (10:1 to 28:1). The vitamin A equivalency of β-carotene is likely to be context-specific and dependent on specific food- and diet-related factors and the health, nutritional, and genetic characteristics of human populations. Although the vitamin A equivalency of β-carotene is highly variable, the provision of vegetable and fruit sources of β-carotene has significantly increased vitamin A status in women and children in community settings in developing countries; these results support the inclusion of dietary interventions with plant sources of β-carotene as a strategy for increasing vitamin A status in populations at risk of deficiency. Am J Clin Nutr doi: 10.3945/ajcn.112.034850.

INTRODUCTION

Provitamin A carotenoids are an important source of dietary vitamin A that are found primarily in dark-green leafy vegetables (DGLVs), such as spinach, and in orange and yellow vegetables and fruit, such as carrot, mango, and papaya. Provitamin A carotenoids provide ≤30% of daily vitamin A intake in the United States, whereas animal products that contain preformed vitamin A, such as dairy products, egg yolk, and liver, provide ≥70% of daily vitamin A intake (1). In contrast, in low-income populations in developing countries, dietary carotenoids provide ~80% of daily vitamin A intake (2). This is an important difference because preformed dietary vitamin A is well absorbed by humans, whereas provitamin A carotenoids from plant sources are less well absorbed and need to be converted to vitamin A in human intestinal cells (3). Of the provitamin A carotenoids commonly found in foods, β-carotene has the greatest vitamin A activity (3). The other provitamin A carotenoids are assumed to have approximately half the vitamin A activity of β-carotene, although recent data suggest that the bioavailability of β-cryptoxanthin and α-carotene is greater than previously assumed (4). The vitamin A equivalency ratio for β-carotene to vitamin A is currently estimated as 12:1, by weight (12 μg β-carotene is equal to 1 μg retinol), for plant sources of β-carotene in a mixed diet. The ratio is based on ~17% absorption of β-carotene from a mixed diet (6 μg plant β-carotene = 1 μg pure β-carotene) and a conversion ratio to vitamin A of 2:1 (2 μg β-carotene = 1 μg retinol) (5). However, vitamin A equivalency ratios are highly variable for both pure β-carotene in oil and β-carotene from plant sources and can be affected by food- and diet-related factors and health, nutritional, and genetic characteristics of human populations.

β-Carotene, as a dietary source of vitamin A, is important to human health. Vitamin A deficiency is a public health problem in preschool-age children and in pregnant and lactating women in developing countries and is most prevalent in parts of Africa and South and Southeast Asia (6). Globally, ~190 million preschool-age children and 19.1 million pregnant women have low serum retinol concentrations, and ~5.2 million preschool-age children and 9.8 million pregnant women are night blind (6). Vitamin A deficiency is still a leading cause of preventable childhood blindness and is associated with reduced immune function and increased risk of mortality from gastrointestinal disease and measles (7, 8).

Dietary β-carotene is a safe source of vitamin A because intestinal conversion of β-carotene to vitamin A decreases as an oral dose of β-carotene increases (9). In contrast, preformed dietary vitamin A is well absorbed in humans and has been associated with adverse effects on health, if consumed in high amounts. Diets high in preformed vitamin A were associated with an increased risk of hip fracture in postmenopausal women, whereas dietary β-carotene intake was not (10). Moreover, be

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cause preformed vitamin A is potentially teratogenic, pregnant women are advised to avoid consuming large amounts of preformed vitamin A (11) and may rely more on plant sources of β-carotene to meet their vitamin A needs (12). However, there has been concern that large doses of supplemental β-carotene may have adverse effects on human health. Supplementation trials to assess the effect of β-carotene on the incidence of lung cancer and cardiovascular disease indicated that large doses of β-carotene (20–30 mg/d) were not associated with a reduced risk of cancer or cardiovascular disease and may be harmful to smokers or to workers exposed to asbestos (13–15). The amounts of β-carotene that were given to participants in the trials are much higher than the amounts that are commonly consumed in the diet. The majority of people in the United States and United Kingdom consume 1–2 mg dietary β-carotene/d, and vegans and vegetarians consume ~4–9 mg/d (16). There are no known adverse health effects associated with the consumption of physiologic doses of β-carotene from foods.

Because β-carotene is an important dietary source of vitamin A, it is important to understand factors that affect the vitamin A equivalency of β-carotene to provide appropriate dietary recommendations for maintaining adequate vitamin A status in human populations. This review summarizes evidence on the bioavailability and intestinal conversion of β-carotene to vitamin A in humans. Although postabsorptive conversion of β-carotene does occur, and has been reported to account for ~30% of the total conversion of an oral dose of β-carotene to vitamin A (17, 18), the information presented here will focus only on intestinal absorption and conversion of β-carotene to vitamin A.

**FACTORS THAT AFFECT THE BIOAVAILABILITY OF β-CAROTENE**

Food- and diet-related factors that affect the bioavailability of β-carotene include the food matrix, food-preparation techniques, size of the dose of β-carotene, and the amounts of fat, fiber, preformed vitamin A, or other carotenoids in the diet (3, 16, 19, 20). The bioavailability of β-carotene tends to be lower in foods with complex food matrices, such as DGLVs, and higher in foods with simpler food matrices, such as fruit and red palm oil (19). β-Carotene must be released from the food matrix to be absorbed, and food-processing techniques that disrupt the food matrix such as mild cooking and homogenization increase the bioavailability of β-carotene (21–23). The vitamin A equivalency of β-carotene is lower when large doses are administered. In US adults, the plasma β-carotene response (AUC) increased 2-fold when an oral dose of β-carotene was doubled from 20 to 40 mg, whereas the plasma vitamin A response (AUC) increased by only 36%, indicating that conversion to vitamin A decreases as the dose of β-carotene increases, but that absorption does not appear to be affected (9). Similarly, a very high vitamin A equivalency ratio of 55:1 was reported for a US woman in response to an oral dose of 126 mg β-carotene in oil, whereas the ratio was reported as 3.8:1 in the same woman in response to a smaller oral dose of 6 mg β-carotene in oil (24). The effect of the size of the β-carotene dose on absorption is less clear; in an earlier study, absorption efficiency decreased slightly when the oral dose of β-carotene was increased from 12 to 30 mg (25). Dietary fat is required for intestinal absorption of β-carotene and facilitates incorporation of β-carotene into mixed micelles (3). The amount of fat that is required for optimal absorption of β-carotene has been reported to range from 2.4 to 5 g/meal for cooked vegetables. In Filipino children who consumed β-carotene from cooked vegetables containing either 2, 4, 5, or 10 g fat/meal, the observed increases in total body vitamin A pool size did not differ by amount of fat in the diet (26). Similarly, no differences in improvement in vitamin A status were observed in Indian children who consumed spinach with either 5 or 10 g of added fat (27). However, the apparent uptake of β-carotene from raw vegetables in salads was significantly greater when salads were consumed with dressings containing 28 g fat compared with dressings with 6 g fat in US adults (28). Larger amounts of dietary fat may be required for optimal absorption of β-carotene from raw vegetables than from cooked vegetables because the food matrix of uncooked vegetables may reduce bioavailability to a greater extent. In contrast, sucrose polyester, a nonabsorbable fat found in some processed foods, has been shown to reduce the plasma β-carotene response by 21% (29). Water-soluble dietary fibers can also affect β-carotene bioavailability; pectin, guar, and alginates reduced absorption of carotenoids by ~33–43% in German women, whereas wheat bran and cellulose had no effect (30). Dietary intakes of preformed vitamin A and other carotenoids may also affect intestinal absorption and/or conversion of β-carotene to vitamin A. Supplemental preformed vitamin A (3 mg/d) reduced intestinal conversion of β-carotene to vitamin A in 2 US women (31). Combined administration of lutein (15 mg) and β-carotene (15 mg) reduced the appearance of β-carotene in triglyceride-rich lipoproteins (TRLs) by ~34%, compared with administration of β-carotene alone, but did not affect the conversion of β-carotene to vitamin A (32).

The nutritional status, health, and genetic characteristics of human populations can also affect the vitamin A equivalency of β-carotene. Intestinal conversion of β-carotene to vitamin A is affected by vitamin A status. Recently, vitamin A deficiency has been shown to induce BCMO1 (β,β-carotene 15,15'-monooxygenase 1) expression, which is the key enzyme that converts β-carotene to vitamin A in intestinal cells (33). Moreover, in Filipino children, conversion of plant β-carotene to vitamin A varied inversely with vitamin A status (34). Animal studies suggest that nutritional deficiencies of iron, zinc, and protein may also affect estimates of the vitamin A equivalency of β-carotene. This has implications for populations in developing countries because deficiencies of these nutrients tend to coexist (35). Iron deficiency disrupts retinol homeostasis and results in decreased mobilization of vitamin A from the liver and low serum retinol concentrations in rats (36). Marginal zinc deficiency results in a significant reduction in β-carotene absorption in rats (37) and may also limit production of retinol-binding protein and interfere with retinol homeostasis. Protein deficiency is associated with reduced intestinal conversion of β-carotene to vitamin A in rats (33) and may interfere with production of chylomicrons, lipoproteins, and retinol binding, which may affect β-carotene and/or vitamin A metabolism (19). Intestinal parasites and bacterial overgrowth can damage intestinal mucosal cells and result in increased permeability and decreased absorption of nutrients (38). In Indonesian children who were...
supplemented with red sweet potato, serum retinol concentrations increased to a greater extent when children who were infected with intestinal helminthes were dewormed, when the intensity of infection was high (39). Other gastrointestinal infections that interfere with fat digestion and absorption may also affect the absorption of β-carotene (19). Serum retinol concentrations decrease transiently in response to systemic inflammation or infection (40) and may affect estimates of the vitamin A equivalency of β-carotene when the response in serum retinol concentration is used to estimate vitamin A equivalency ratios for β-carotene. Fever has been shown to reduce absorption of vitamin A in children (41, 42) and may also affect absorption of β-carotene.

Genetic polymorphisms also affect the vitamin A equivalency of β-carotene. Recently, 2 common genetic polymorphisms of the BCMO1 gene were identified and were associated with a reduction in intestinal conversion of β-carotene to vitamin A of ~32–69% in UK women (43). This recent finding may account for much of the observed interindividual variability in estimates of the vitamin A equivalency of β-carotene in human populations.

### ABSORPTION OF PURE β-CAROTENE

The absorption of pure β-carotene has been reported to range from 8.7% to 65% in humans (Table 1). β-Carotene absorption was first assessed by administering radiolabeled β-carotene to 2 hospitalized patients and by measuring the radioactivity recovered in thoracic lymph (44). Because administration of large doses of radioactivity was no longer considered ethical shortly thereafter, estimates of β-carotene absorption were not reported again until the mid-1990s when a nonisotopic method was introduced in which an oral dose of β-carotene is administered and responses curves (AUC) for newly absorbed β-carotene and retinyl esters are measured in the TRL fraction of plasma (45). At approximately the same time, stable isotopes of β-carotene became available and were used to study β-carotene metabolism safely in humans (46). Shortly thereafter, accelerator mass spectrometry, which requires administration of very small doses of [14C]-labeled substrates that are considered safe for humans, was first used to study β-carotene metabolism (47–50). More recently, β-carotene absorption has been estimated by measuring β-carotene recovered in feces after administration of an unlabeled oral dose in adults with ileostomies and in healthy volunteers (absorbed β-carotene = the oral dose of β-carotene minus β-carotene recovered in feces) (51, 52). A limitation of this method is that β-carotene absorption may be overestimated in healthy volunteers because of incomplete collection of feces or degradation of β-carotene by microflora in the large intestine or underestimated because of secretion of endogenous β-carotene into the large intestine. However, degradation of β-carotene by microflora is less likely in adults with ileostomies.

On the basis of isotopic methods, absorption of pure β-carotene ranged from 8.7% to 65%. Estimates of absorption were higher (~43–65%) when absorption was estimated by administering very small oral doses of [14C]-β-carotene (0.270–306 μg) and measuring recovery of radioactivity in feces by using accelerator mass spectrometry, which is an extremely sensitive and precise analytic method (47–50). In a small group of US

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**TABLE 1**

<table>
<thead>
<tr>
<th>Study population (reference)</th>
<th>Vitamin A status</th>
<th>Method of estimating apparent absorption</th>
<th>14C-β-carotene in oil, single dose</th>
<th>14C-β-carotene in oil, single dose</th>
<th>14C-β-carotene in oil, single dose</th>
<th>Method of estimating apparent absorption</th>
<th>14C-β-carotene in oil, single dose</th>
<th>14C-β-carotene in oil, single dose</th>
<th>14C-β-carotene in oil, single dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>US man, aged 35 y (47)</td>
<td>Adequate</td>
<td>Measurement of radioactivity recovered in thoracic lymph duct</td>
<td>100 mg [14C]-β-carotene in oil, single dose</td>
<td>100 mg [14C]-β-carotene in oil, single dose</td>
<td>100 mg [14C]-β-carotene in oil, single dose</td>
<td>Measurement of radioactivity recovered in thoracic lymph duct</td>
<td>100 mg [14C]-β-carotene in oil, single dose</td>
<td>100 mg [14C]-β-carotene in oil, single dose</td>
<td>100 mg [14C]-β-carotene in oil, single dose</td>
</tr>
</tbody>
</table>
adults, mean (±SD) absorption was reported as 47 ± 13% in response to an oral dose of 0.541 μg β-carotene, and the interindividual variability was reported as a CV of 28% (49). On the basis of nonisotopic methods, the absorption of pure β-carotene was reported to range from 11% to ~30–35% when the oral doses of β-carotene were much larger (15 and ~3 mg/d, respectively) (45, 51, 52).

The absorption of pure β-carotene is highly variable across studies. Most studies were carried out in healthy adults from developed countries, and although vitamin A status was not reported in all studies, it is likely that vitamin A status was adequate, with the possible exception of the 2 hospitalized patients in the early study (44). The variability in absorption is likely to be related to differences in the size of the oral doses of β-carotene and differences in measurement error associated with the methods used to assess absorption.

**ABSORPTION OF β-CAROTENE FROM PLANT SOURCES**

The absorption of β-carotene from plant sources has been reported to range from ~7% to 65% in humans (Table 2). It is more challenging to quantify β-carotene absorption from foods. As mentioned above, isotopic methods exist for quantifying β-carotene absorption from single doses of isotopically labeled pure β-carotene (47–50), but this is much more difficult to accomplish with foods because of the complexities of labeling β-carotene in plants and measuring labeled β-carotene recovered in feces. As shown in Table 2, β-carotene absorption from plant sources has been estimated mostly by using nonisotopic methods, with the exception of the study by Edwards et al (53) in which an extrinsic isotopic reference method was used.

β-Carotene absorption from mixed diets in adults was reported to range from 11.9% to 16% (51, 52, 54). The absorption of β-carotene from specific foods was reported to range from ~5% to 26% for spinach (55, 56) and from ~7% to 65% for carrots (53, 57) and was 12% for broccoli (58). In all studies, adequate amounts of dietary fat (~10–40 g) were administered with the test meals to facilitate absorption of β-carotene. The high variability in β-carotene absorption may be related to differences in food matrices of the test foods, differences in composition of meals administered with the test foods, and/or differences in food preparation techniques. Within studies, β-carotene tended to be better absorbed from foods that were more highly processed. Absorption was significantly greater from liquefied spinach than from whole leaf spinach (55), and significantly greater from cooked carrots than from raw carrots (57). However, absorption of β-carotene from cooked chopped leaf spinach did not differ from that from cooked whole leaf spinach (56). It is also possible that the amounts and types of dietary fiber in the diets that were administered with the test foods differed and may have affected β-carotene absorption. The vitamin A status of the study participants was reported as adequate for most studies, however, serum retinol concentrations were reported as >0.1 μmol/L for adults with ileostomies in the UK studies (56, 57), suggesting that some participants may have had marginal vitamin A status.

**VITAMIN A EQUIVALENCY OF PURE β-CAROTENE IN OIL**

The vitamin A equivalency of pure β-carotene in oil has been reported to range from 2.1 to 55:1, by weight, in humans (Table 3). The vitamin A equivalency of pure β-carotene was first estimated by comparing the amount of β-carotene intake or preformed vitamin A intake that was required to correct abnormal dark adaptation in vitamin A–depleted adults (59, 60). More recently, various isotopic methods have been used to estimate the vitamin A equivalency of pure β-carotene in oil (17, 18, 24, 47, 51, 52, 61, 62). The vitamin A equivalency of β-carotene has also been estimated by administering an oral dose of unlabeled β-carotene and comparing response curves (AUC) for newly absorbed β-carotene and retinyl esters in the TRL fraction of plasma with a reference dose of vitamin A (62).

The high variability in vitamin A equivalency ratios across studies (2.1–55:1) appears to be related to the size of the oral dose of pure β-carotene administered, as would be expected given that intestinal conversion of β-carotene to vitamin A decreases as an oral dose of β-carotene increases (9). Estimates of vitamin A equivalency ratios ranged from 2:1 to 9:1 when doses of β-carotene were ≤6 mg, whereas the ratios were ≥16:1 when oral doses of ≥16:1 mg were administered (Table 3). Nevertheless, the reported vitamin A equivalency ratios are still highly variable (2:1–9:1) for doses of pure β-carotene ≤6 mg. The interindividual variability in vitamin A equivalency ratios within studies was also high (CVs of 60–69%) (17, 18, 51, 52, 61, 62). Genetic polymorphisms related to β-carotene metabolism probably account for some of the observed variability in vitamin A equivalency ratios. Wang et al (18) reported that 4 of 15 study participants showed very little response to oral doses of β-carotene and were “poor converters,” suggesting that there are genetic differences in β-carotene metabolism among study participants. Differences in vitamin A status may have also contributed to the observed variability. Vitamin A equivalency ratios tended to be lower (2.1–2.4:1) in vitamin A–depleted US men (60) and in Indonesian children with marginal to adequate vitamin A status (61) when small doses of β-carotene (≤2 mg/d) were administered. However, the vitamin A equivalency ratio was also low (2.3:1) in US women, with presumably adequate vitamin A status, when the dose of β-carotene was very small (595 μg) (62).

**VITAMIN A EQUIVALENCY OF β-CAROTENE FROM PLANT SOURCES**

Vitamin A equivalency ratios for plant β-carotene range from 3.8:1 to 28.1 in humans (Table 4). Vitamin A equivalency ratios have been estimated in populations in developed and developing countries by assessing various response indicators for β-carotene and vitamin A to either single meals (62–66) or to longer-term provision (~50–60 d) of β-carotene–containing foods (67–70). Vitamin A equivalency ratios are highly variable across and within studies; the reported CVs for ratios within studies ranged from 36% to 54% (Table 4) (62–65).

The vitamin A equivalency of β-carotene appears to be greater from foods with simpler food matrices. Vitamin A equivalency ratios for Golden Rice, spirulina, red palm oil, and biofortified maize range from 3.8:1 to 6.5:1 and are lower than those for vegetable or fruit sources of β-carotene, which range from 10:1 to 28:1 (Table 4). It is encouraging that the vitamin A equivalency ratios are lower for the biofortified staple foods that are meant to be targeted to populations at risk of vitamin A deficiency in developing countries; however, the ratios were estimated in healthy, well-nourished US adults and may not be as
<table>
<thead>
<tr>
<th>Study population (reference)</th>
<th>n</th>
<th>Vitamin A status¹</th>
<th>β-Carotene supplement, duration of supplementation</th>
<th>Method of estimating apparent absorption</th>
<th>Estimated apparent absorption %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dutch men, aged 18–50 y (52)</td>
<td>24</td>
<td>Adequate</td>
<td>~ 6.9 mg/d β-carotene as mixed fruit and vegetables for 3 wk</td>
<td>Measurement of β-carotene recovered in feces</td>
<td>11.9 (95% CI: 0.6, 23.2)</td>
</tr>
<tr>
<td>Dutch adults, aged 18–35 y (54)</td>
<td>22</td>
<td>Adequate</td>
<td>5.1 mg/d β-carotene as a mixed-vegetable diet for 4 wk</td>
<td>Comparison of plasma β-carotene response to mixed-vegetable diet vs reference dose of pure β-carotene</td>
<td>14.0 ± 1.1²</td>
</tr>
<tr>
<td>Dutch adults with ileostomies, aged 23–75 y (51)</td>
<td>17</td>
<td>Adequate</td>
<td>~ 7.6 mg/d β-carotene as mixed fruit and vegetables for 2 wk</td>
<td>Measurement of β-carotene recovered in feces</td>
<td>16 (95% CI: 6, 24)</td>
</tr>
<tr>
<td>Dutch adults, aged 18–58 y (55)</td>
<td>12/food group</td>
<td>Not reported</td>
<td>10.4 mg/d β-carotene as whole-leaf spinach, 8.8 mg/d as minced spinach, or 9.0 mg/d as liquefied spinach for 3 wk</td>
<td>Comparison of plasma β-carotene response for spinach vs reference dose of pure β-carotene</td>
<td>5.1 (whole)</td>
</tr>
<tr>
<td>UK adults with ileostomies, aged 51 ± 7.6 y (56)</td>
<td>7/food group</td>
<td>Uncertain (serum retinol reported as &gt;0.1 μmol/L)</td>
<td>10 mg β-carotene as cooked whole spinach or cooked finely chopped spinach</td>
<td>Measurement of β-carotene recovered in feces</td>
<td>26 ± 14.5 (whole)</td>
</tr>
<tr>
<td>US adults, aged 25–35 y (53)</td>
<td>3/food group</td>
<td>Adequate</td>
<td>~ 5.6 mg β-carotene as raw carrots or ~6.2 mg β-carotene as raw spinach</td>
<td>β-carotene and retinyl ester response curves in TRLs³ in relation to a reference dose of [²H₄]vitamin A</td>
<td>7 (vegetables combined; range: 3–16)</td>
</tr>
<tr>
<td>UK adults with ileostomies, aged 38–75 y (57)</td>
<td>8</td>
<td>Uncertain (serum retinol reported as &gt;0.1 μmol/L)</td>
<td>15 mg β-carotene as cooked carrots or as raw carrots</td>
<td>Measurement of β-carotene recovered in feces</td>
<td>65 ± 7 (cooked)</td>
</tr>
<tr>
<td>US men, aged 20–45 y (58)</td>
<td>5/food group</td>
<td>Adequate</td>
<td>29 mg/d β-carotene as carrots or 6 mg/d β-carotene as broccoli</td>
<td>Comparison of plasma β-carotene response to vegetables vs reference dose of pure β-carotene</td>
<td>18 (carrots)</td>
</tr>
</tbody>
</table>

¹ "Adequate" status was determined on the basis of serum retinol concentrations.

² Mean ± SD (all such values).

³ TRLs, triglyceride-rich lipoproteins.
<table>
<thead>
<tr>
<th>Study population (reference)</th>
<th>n</th>
<th>Vitamin A status</th>
<th>β-Carotene supplement, duration of supplementation</th>
<th>Method of estimating vitamin A equivalency</th>
<th>Vitamin A equivalency (ratio, by weight)</th>
</tr>
</thead>
<tbody>
<tr>
<td>US women, aged 18–30 y (62)</td>
<td>6</td>
<td>Not reported, assumed adequate</td>
<td>595 μg β-carotene, single dose added to white maize porridge</td>
<td>Measurement of plasma ratio of retinol formed from [13C10]β-carotene vs reference dose of [13C10]vitamin A</td>
<td>2.3:1 (range: 0.8:1–5:1; CV: 69%)</td>
</tr>
<tr>
<td>UK man (59)</td>
<td>1</td>
<td>Deficient⁵</td>
<td>&lt;2 mg β-carotene/d</td>
<td>Comparison of plasma responses (AUC) for retinol formed from [13C10]β-carotene vs reference dose of [13C10]vitamin A</td>
<td>3.8:1</td>
</tr>
</tbody>
</table>

1 Amount of β-carotene that has the same vitamin A activity as 1 μg retinol.
2 Determined on the basis of serum retinol concentrations.
3 Determined on the basis of reported vitamin A intake.
4 TRLs, triglyceride-rich lipoproteins.
5 Determined on the basis of impaired dark adaptation.
<table>
<thead>
<tr>
<th>Study population (reference)</th>
<th>n</th>
<th>Vitamin A status</th>
<th>Plant source of β-carotene, amount, duration of supplementation</th>
<th>Method of estimating vitamin A equivalency ratio</th>
<th>Vitamin A equivalency ratio, by weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemic Indonesian children, aged 7–11 y (67)</td>
<td>45–49/group</td>
<td>Marginal&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Orange fruit, ~3 mg/d, DGLVs/carrots, ~4.1 mg/d, or DGLVs, 5.6 mg/d, 6 d/wk for 9 wk</td>
<td>Comparison of change in serum retinol concentration in β-carotene food groups vs preformed vitamin A food group</td>
<td>12:1 for fruit (95% CI: 6:1, 29:1) 26:1 for vegetables (95% CI: 3:1, 76:1)</td>
</tr>
<tr>
<td>Anemic lactating Vietnamese women, aged ~26 y (68)</td>
<td>68–73/group</td>
<td>Low to adequate&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Orange/yellow fruit, 4.8 mg/d, or DGLVs, 5.6 mg/d, 6 d/wk for 10 wk</td>
<td>Comparison of change in serum retinol concentration in β-carotene food groups vs preformed vitamin A food group</td>
<td>12:1 for fruit (95% CI: 8:1, 22:1) 28:1 for vegetables (95% CI: 17:1, 84:1)</td>
</tr>
<tr>
<td>Bangladeshi men, aged ~22 y (69)</td>
<td>14/group</td>
<td>Marginal&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Indian spinach, ~4.5 mg/d, or sweet potato, ~4.5 mg/d, 60 d</td>
<td>Comparison of change in total-body vitamin A pool in β-carotene food groups vs vitamin A supplemented group</td>
<td>10:1 for spinach 13:1 for sweet potato</td>
</tr>
<tr>
<td>Chinese children, aged 5–6 y (70)</td>
<td>19–22/group</td>
<td>Adequate&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Green/yellow vegetables, ~4.6 mg/d, 5 d/wk for 10 wk</td>
<td>Comparison of change in total-body vitamin A pool in response to β-carotene foods vs light-colored vegetable group</td>
<td>27:1 (range: 19:1–48:1)</td>
</tr>
<tr>
<td>US adults, aged ~57 y (63)</td>
<td>14 Adequate&lt;sup&gt;2&lt;/sup&gt;</td>
<td>[&lt;sup&gt;3&lt;/sup&gt;H]-labeled spinach, ~11 mg, single dose</td>
<td>Comparison of plasma responses (AUC) for retinol formed from [&lt;sup&gt;3&lt;/sup&gt;H]-spinach vs reference dose of [&lt;sup&gt;13&lt;/sup&gt;C&lt;sub&gt;37&lt;/sub&gt;]vitamin A</td>
<td>21:1 (range: 10:1–47:1; CV: 43%)</td>
<td></td>
</tr>
<tr>
<td>US men, aged ~59 y (63)</td>
<td>7 Adequate&lt;sup&gt;2&lt;/sup&gt;</td>
<td>[&lt;sup&gt;3&lt;/sup&gt;H]-labeled carrots, ~11 mg, single dose</td>
<td>Comparison of plasma responses (AUC) for retinol formed from [&lt;sup&gt;3&lt;/sup&gt;H]-carrots vs reference dose of [&lt;sup&gt;13&lt;/sup&gt;C&lt;sub&gt;37&lt;/sub&gt;]vitamin A</td>
<td>15:1 (range: 8:1–25:1; CV: 44%)</td>
<td></td>
</tr>
<tr>
<td>US women, aged 18–30 y (62)</td>
<td>6 Not reported, assumed adequate</td>
<td>β-carotene biofortified maize, 527 μg β-carotene, single dose as maize porridge</td>
<td>Comparison of responses (AUC) of retinyl esters formed from β-carotene maize vs reference dose of vitamin A in TRLs</td>
<td>6.5:1 (range: 3.9–13.3; CV:54%)</td>
<td></td>
</tr>
<tr>
<td>US adults, aged ~41–70 y (65)</td>
<td>5 Adequate</td>
<td>[&lt;sup&gt;3&lt;/sup&gt;H]-labeled β-carotene biofortified Golden Rice, 0.99–1.53 mg β-carotene single dose as cooked rice</td>
<td>Comparison of plasma responses (AUC) for retinol formed from [&lt;sup&gt;3&lt;/sup&gt;H]-Golden Rice vs reference dose of [&lt;sup&gt;13&lt;/sup&gt;C&lt;sub&gt;37&lt;/sub&gt;]vitamin A</td>
<td>3.8:1 (range: 1.9:1–6.4:1; CV: 45%)</td>
<td></td>
</tr>
<tr>
<td>US adults (66)</td>
<td>12 Not reported, Assumed adequate</td>
<td>Red palm oil, 2.37 mg β-carotene, added to juice-based drink, single dose as beverage</td>
<td>Comparison of responses (AUC) of retinyl esters formed from palm oil vs reference dose of [H&lt;sub&gt;4&lt;/sub&gt;]vitamin A in TRLs</td>
<td>5:7:1</td>
<td></td>
</tr>
<tr>
<td>Chinese men, aged 41–57 y (64)</td>
<td>10 Adequate&lt;sup&gt;2&lt;/sup&gt;</td>
<td>[&lt;sup&gt;3&lt;/sup&gt;H]-labeled spirulina, ~4.2 mg, single dose</td>
<td>Comparison of plasma responses (AUC) for retinol formed from [&lt;sup&gt;3&lt;/sup&gt;H]-spirulina vs reference dose of [&lt;sup&gt;13&lt;/sup&gt;C&lt;sub&gt;37&lt;/sub&gt;]vitamin A</td>
<td>4.5:1 (range: 2.3:1–7:1; CV: 36%)</td>
<td></td>
</tr>
</tbody>
</table>

<sup>1</sup> DGLVs, dark-green leafy vegetables; TRLs, triglyceride-rich lipoproteins.
<sup>2</sup> Determined on the basis of reported serum retinol concentrations.
### TABLE 5
Effect of fruit and vegetable sources of β-carotene on vitamin A status in humans

<table>
<thead>
<tr>
<th>Study population (reference)</th>
<th>n/group</th>
<th>Vitamin A status</th>
<th>Amount, plant source of β-carotene, duration of supplementation</th>
<th>Method of estimating efficacy of food supplement</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemic, iron-deficient, lactating Indonesian women (71)</td>
<td>53–62</td>
<td>Marginal&lt;sup&gt;2&lt;/sup&gt;</td>
<td>3.5 mg/d as stir-fried DGLVs (containing 4.4 g fat) for 7 d/wk for 12 wk</td>
<td>Comparison of change in serum and milk retinol concentrations in food group vs control group (CRP/AGP not measured)</td>
<td>No effect of food supplement on serum or milk retinol</td>
</tr>
<tr>
<td>Lactating Zimbabwean women (72)</td>
<td>48–50</td>
<td>Marginal to adequate&lt;sup&gt;2&lt;/sup&gt;</td>
<td>~1.1 mg/d as puréed papaya or grated carrots, with meal containing 10 g fat, for 60 d</td>
<td>Comparison of change in serum retinol concentrations or change in RDR in food group vs control group (CRP measured)</td>
<td>Significant increase in serum retinol concentrations in both food groups compared with placebo group; reduction in percentage of women with low liver vitamin A stores in papaya group compared with placebo group</td>
</tr>
<tr>
<td>Anemic lactating Vietnamese women, aged ~26 y (68)</td>
<td>68–73</td>
<td>Low to adequate&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Orange/yellow fruit, 4.8 mg/d, or DGLVs, 5.6 mg/d, 6 d/wk for 10 wk</td>
<td>Change in serum and milk retinol concentrations in food group vs control group (CRP/AGP not measured)</td>
<td>Significant increase in serum and milk retinol concentrations for both food groups compared with the control group</td>
</tr>
<tr>
<td>Mozambiquean children, aged 4–38 mo (73)</td>
<td>Intervention area: 498 Control area: 243</td>
<td>Marginal&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Promotion of production and consumption of OFSP for 2 y</td>
<td>Change in serum retinol concentrations in children in OFSP study area vs control area (CRP measured)</td>
<td>Significant increase in serum retinol concentrations in children in intervention area vs control area</td>
</tr>
<tr>
<td>Gambian children, aged 2–7 y (74)</td>
<td>43–45</td>
<td>Marginal&lt;sup&gt;2&lt;/sup&gt;</td>
<td>~1.8 mg/d as dried mango with 5 g fat, 5 d/wk for 4 mo</td>
<td>Comparison of change in serum retinol concentrations in food group vs control group (CRP measured)</td>
<td>Significant increase in serum retinol concentrations in the food group compared with control group</td>
</tr>
<tr>
<td>Chinese children, aged 5–6 y (70)</td>
<td>19–22</td>
<td>Adequate&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Green/yellow vegetables, ~4.6 mg/d, 5 d/wk for 10 wk</td>
<td>Comparison of change in total-body vitamin A pool size in food group vs control group (CRP/AGP not measured)</td>
<td>Total-body vitamin A pool size was maintained in the vegetable group but declined significantly in the control group (by 7.7 mg on average)</td>
</tr>
<tr>
<td>Anemic Indonesian children, aged 7–11 y (67)</td>
<td>45–49</td>
<td>Marginal&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Orange fruit, ~3 mg/d DGLVs/carrots, ~4.1 mg/d 6 d/wk for 9 wk</td>
<td>Change in serum retinol concentrations in food groups vs control group (CRP/AGP not measured)</td>
<td>Significant increase in serum retinol concentrations in both food groups compared with the control group</td>
</tr>
<tr>
<td>Filipino schoolchildren, aged 9–12 y (26)</td>
<td>38–39</td>
<td>Marginal to adequate&lt;sup&gt;2&lt;/sup&gt;</td>
<td>4.2 mg as cooked, mixed vegetables in meals containing 2.4 g fat, 5 d/wk for 9 wk</td>
<td>Comparison of change in serum retinol concentrations and change in total-body vitamin A pool size in food group vs control group (CRP measured)</td>
<td>No effect of food supplement on serum retinol; 2-fold increase in vitamin A pool size; percentage of children with estimated low liver vitamin A (&lt;0.07 μmol/g) declined from 35% to 7%</td>
</tr>
</tbody>
</table>

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<sup>1</sup> AGP, α<sub>1</sub> acid glycoprotein; CRP, C-reactive protein; DGLVs, dark-green leafy vegetables; OFSP, orange-fleshed sweet potato; RDR, relative dose-response test.

<sup>2</sup> Determined on the basis of serum retinol concentrations.

<sup>3</sup> Determined on the basis of milk retinol concentrations.
favorable when the biofortified foods are consumed by populations in developing countries who may have multiple nutritional deficiencies and a high prevalence of intestinal parasites, diarrhea, and other infections.

The high variability in vitamin A equivalency ratios across studies may also be related to differences in vitamin A status, nutritional deficiencies, gut integrity, and genetic variation among study participants. Vitamin A equivalency ratios for DGLVs range from 10:1 to 28:1 (63, 67–69). The vitamin A equivalency ratio was lowest (10:1) when spinach was cooked, puréed, and consumed by Bangladeshi men with marginal vitamin A status who were treated for intestinal helminthes (69). These factors would tend to increase bioavailability and favor a lower vitamin A equivalency ratio. The ratio was higher (21:1) when a larger dose of β-carotene (~11 mg) was consumed as cooked, puréed spinach by healthy, vitamin A–replete US adults (63). The larger dose and replete vitamin A status of the study participants may have reduced intestinal conversion of β-carotene to vitamin A. The ratio was highest (26:1 or 28:1) when cooked vegetables were consumed by anemic Indonesian schoolchildren or by anemic lactating Vietnamese women with marginal vitamin A status and a high prevalence of intestinal helminthes (≥48% and ≥62%, respectively) (67, 68). The iron status of the schoolchildren was inadequate; the iron status of the women was not reported. The vitamin A equivalency ratios were estimated by comparing changes in serum retinol concentration in response to consumption of plant sources of β-carotene or food sources of preformed vitamin A. Retinol homeostasis can be disrupted in iron deficiency, resulting in low serum retinol concentrations (36), and by systemic inflammation or infection, which was not assessed in these studies; thus, the serum retinol response may have been affected by these conditions. These factors combined would tend to reduce bioavailability and favor a higher vitamin A equivalency ratio. Collectively, the results of these studies show that the vitamin A equivalence of β-carotene is likely to be context-specific and dependent on food- and diet-related factors and the nutritional, health, and genetic characteristics of human populations.

EFFECT OF SUPPLEMENTATION WITH PLANT SOURCES OF β-CAROTENE ON VITAMIN A STATUS IN COMMUNITY SETTINGS

Supplementation with plant sources of β-carotene in community settings has had mixed effects on the vitamin A status of lactating women and children (Table 5). In lactating Indonesian women, daily consumption of stir-fried DGLVs for 12 wk had no effect on serum or milk retinol concentrations compared with a control group who received a nonfortified wafer (71). In contrast, the provision of puréed papaya or grated carrots for 60 d increased serum retinol concentrations in lactating Zimbabwean women compared with a control group who received pink-colored water, and the percentage of women with low liver vitamin A stores, on the basis of the relative dose-response test, declined in women who received puréed papaya compared with the control group (72). Similarly, serum and milk retinol concentrations increased in lactating Vietnamese women who received either DGLVs or orange/yellow fruit for 10 wk compared with a control group who received a diet low in both provitamin A and preformed vitamin A (68). The promotion of production and consumption of orange-fleshed sweet potatoes in Mozambique resulted in increased serum retinol concentrations in preschool children in the intervention area compared with children in the control area after a 2-y period (73). The consumption of dried mango for 4 mo increased serum retinol concentrations in Gambian children compared with a control group who received a single placebo capsule (40 mg α-tocopherol) followed by no treatment for 4 mo (74). In young Chinese children, daily consumption of meals containing β-carotene–rich vegetables for 10 wk prevented a decline in total body vitamin A pool size compared with a control group who received light-colored vegetables (70). Similarly, serum retinol concentrations increased in Indonesian schoolchildren who received either DGLVs or orange-colored fruit for 9 wk in comparison with a control group who received a diet low in both provitamin A and preformed vitamin A (67). Finally, total body vitamin A pool size increased 2-fold above baseline values in Filipino schoolchildren in response to meals containing β-carotene–rich vegetables for 9 wk (26). Overall, these studies showed that consumption of fruit and vegetable sources of β-carotene can increase the vitamin A status of lactating women and children at risk of deficiency in community settings. However, the extent of improvement in vitamin A status is difficult to quantify in studies in which serum retinol was used to assess status because serum retinol is homeostatically controlled and does not provide information on the magnitude of change in vitamin A status in response to an intervention. Moreover, infection status and other nutritional deficiencies were not assessed in all of the studies and may have affected serum retinol concentrations.

CONCLUSIONS

In summary, plant β-carotene is an important dietary source of vitamin A for human populations. The bioavailability and vitamin A equivalency of β-carotene are highly variable and can be affected by food- and diet-related factors and nutritional, health, and genetic characteristics of human populations. Nevertheless, daily consumption of usual portion sizes of fruit and vegetable sources of β-carotene can increase vitamin A status in populations at risk of vitamin A deficiency. However, the effectiveness of plant sources of β-carotene for increasing vitamin A status is likely to be context-specific and dependent on the factors mentioned above. Dietary interventions with plant sources of β-carotene should be considered as a concurrent strategy to existing programs for increasing vitamin A status in populations at risk of deficiency. More information is needed on genetic variations that may affect β-carotene and vitamin A metabolism and on other diet- and population-related factors that can affect the bioavailability of β-carotene, so that appropriate dietary recommendations can be made for maintaining adequate vitamin A status in human populations.

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