Plasma Carotenoids as Biomarkers of Vegetable Intake: The University of Minnesota Cancer Prevention Research Unit Feeding Studies

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Abstract

High vegetable intake has been associated with a decreased risk for various human cancers in epidemiological studies. Carotenoids are plant compounds that may both possess chemopreventive activity and be useful biomarkers of vegetable and fruit intake. Nineteen men and women were randomized into a controlled cross-over feeding study to measure the effect of vegetable intake on plasma carotenoid concentrations. Participants consumed each of 4 experimental diets for 9 days. The control diet consisted of commonly consumed foods and was essentially carotenoid free. High vegetable diets (carotenoid, cruciferous, and soy) consisted of the control diet plus carrots and spinach (carotenoid), broccoli and cauliflower (cruciferous), and tofu and FriChik (soy). Plasma carotenoid concentrations were highest on the carotenoid and cruciferous diets. When compared to the control, mean plasma α-carotene, β-carotene, and lutein concentrations were 5.2, 3.3, and 2.2 times higher on the carotenoid diet, respectively (P < 0.001). Mean plasma lutein concentrations were 2.1 times higher on the cruciferous versus the control diet (P < 0.001). There were no differences between diets in plasma β-cryptoxanthin and lycopene concentrations. These data indicate that plasma α-carotene, β-carotene, and lutein may be useful biomarkers of carotenoid-rich food intake and that lutein may act as an intake biomarker of commonly consumed vegetables in the Cruciferae family. These findings should prove useful in undertaking dietary intervention trials because they suggest the feasibility of monitoring intake of some plant foods and of distinguishing among plant food groups.

Introduction

High intakes of plant foods, including carotenoid-rich, cruciferous, and soy vegetables, have been associated with decreased risks for certain human cancers in epidemiological studies (1, 2). Certain phytochemicals present in these plant foods have shown antineoplastic activity in animal and cell models, thereby supporting their potential role in cancer risk reduction (3, 4). Irrespective of their physiological role, phytochemicals may act as biomarkers of intake of a broad array of vegetables and fruits and, thus, be of value in studies of disease risk and in dietary intervention studies. The identification of such biomarkers is important in epidemiological studies measuring dietary intake because traditional data collection methods are prone to misclassification and other types of bias and are especially problematic in dietary intervention studies where neither the researcher nor the participant is blind to the intervention.

Carotenoids are widely distributed phytochemicals in plant foods, and we have shown that plasma concentrations of these compounds distinguish individuals with high and low intakes of vegetables and fruits (5). Thus, plasma carotenoids may be useful biomarkers of total vegetable and fruit intake. Over 40 carotenoids are present in the human diet (6), but little is known about the absorption, metabolism, and potential interactions among them in response to intake of specific plant foods. Plasma carotenoid concentrations have been measured after intake of carotenoid supplements (β-carotene and canthaxanthin) in clinical trials (7–10) and following intake of single vegetables or vegetable products (broccoli, carrots, and carrot and tomato juices) in controlled feeding studies (11–13). Additional identification and evaluation of plasma carotenoid concentrations in humans in response to feeding specific vegetables and combinations of vegetables may aid in understanding human carotenoid absorption and metabolism and facilitate the development of objective exposure markers for chemoprevention studies.

The purpose of this study was to measure plasma α-carotene, β-carotene, lutein/zeaxanthin, lycopene, and β-cryptoxanthin concentrations after consistent daily intakes of various vegetable combinations against the background of a controlled diet consisting of typical American food items.

Materials and Methods

Experimental Design. Participants were randomized into a controlled cross-over feeding study and consumed 4 experimental diets for 9 days, with at least a 10-day washout between diet periods. Body weights were measured on the first and last days of each diet period, and blood was drawn on day 10 after a 12-h fast. Preceding the experimental diets, a 5-day self-select period allowed evaluation of the typical dietary intakes and plasma carotenoid concentrations of study participants. Typical dietary intakes were measured with the use of 4-day diet records. Blood was drawn on day 5, and heights and fasting weights were measured. The design of the study was approved by the Institutional Review Board: Human Subjects Committee at the University of Minnesota (Minneapolis, MN), and in-
formed written consent was obtained from all participants before the start of the study.

**Participants.** Twenty-three male and female nonsmokers, ages 20–34 years, were recruited from the University of Minnesota community to participate in a vegetable feeding study conducted October 1992–February 1993. Potential participants were screened in a telephone interview for the following exclusion criteria: (a) medical history of gastrointestinal disorders; (b) body allergies; (c) weight loss or gain greater than 4.5 kg within the past year; (d) major changes in eating habits within the past year (e.g., adoption of a faddish diet); (e) exercise regimens requiring significant short-term dietary changes; (f) antibiotic use within the past 3 months; (g) body weight >130% of ideal; (h) current treatment for a diagnosed disease; (i) alcohol intake >2 drinks/day (2 drinks were defined as 720 ml of beer, 240 ml of wine, or 90 ml of liquor); (j) oral contraceptive use; and (k) unwillingness to consume all foods provided in the study. In addition, participants were instructed to maintain their usual exercise levels, to take no medications (except for infrequent over-the-counter pain relievers), and to take no nutritional supplements during the experimental feeding periods. Nutritional supplements (including a multivitamin and vitamins B, C, and E) were taken less than by 3 participants during the washout periods. Because β-carotene was not a component of these supplements, their use was not prohibited when participants were off the experimental diets.

**Experimental Diets.** The four experimental diets were: control, carotenoid, cruciferous, and soy. The four experimental diets provided 8.3–9.0 MJ (1980–2150 kcal) total energy and 17–19%, 50–56%, and 27–31% energy as protein, carbohydrate, and fat, respectively; the diets supplied at least two-thirds of the RDA for most micronutrients. Daily nutrient intakes on each experimental diet are shown in Table 1. Foods consumed on the control diet included: crisp rice and corn flake cereals, bagel, white bread, instant chicken noodle soup, rice, canned chicken, saltine and club crackers, 1% milk, margarine, processed American cheese, shortbread and chocolate sandwich cookies, and vanilla pudding. The remaining experimental diets consisted of the control diet plus specific plant foods. Thus, the carotenoid diet consisted of the control diet plus daily servings of 165 g (1 cup) frozen carrot coins (J. R. Simplot Co., Caldwell, ID), 125 g (0.5 cup) frozen carrot puree (Stahlbush Island Farms, Inc., Corvallis, OR), and 250 g (0.9 cups) frozen chopped spinach (J. R. Simplot Co., Caldwell, ID). The cruciferous diet consisted of the control diet plus daily servings of 390 g (2 cups) frozen broccoli (J. R. Simplot Co., Boise, ID) and 300 g (1.55 cups) frozen cauliflower (J. R. Simplot Co., Boise, ID). The soy diet consisted of the control diet plus daily servings of 86 g (3 ounces) firm tofu (Morinaga Nutritional Foods, Inc., Los Angeles, CA) and 45 g Frinchik, a textured vegetable protein product (Worthington Foods, Inc., Worthington, OH). Bulk foods, including plant foods, were purchased in advance from the same case lot and supplier to meet the differing caloric requirements of participants because pudding macronutrient proportions and carotenoid content resembled the control diet. Despite this flexibility in pudding intake, participants lost weight when consuming the experimental diets, with the average loss ranging from 0.41 to 0.73 kg (0.9–1.6 pounds). Participants successfully consumed each experimental diet and did not appear to change their activity levels. In general, besides occasional days of illness, all study food and only small amounts of additional foods were consumed.

**Study Protocol.** Participants were required to check in during the feeding periods at least every other day, when they would eat breakfast and pick up food for the remainder of that day and the next, if appropriate. Food was picked up on Friday for the weekend. Participants were instructed to consume all food given to them each day and to consume no additional foods (such as candy, gum, breath mints, alcohol, coffee, tea, or soda). Participants were allowed to consume the study foods at any time during a 24-h period and in any combination. Coolers with ice packs were available for the participants to store their food if they did not have access to refrigerators during the day. Although most of the food was prepackaged, other foods (e.g., raw rice) required preparation by the participants. Compliance with the feeding regimen was assessed by a daily checklist, which required participants to check off the experimental foods when eaten and list any additional (nonstudy) foods consumed.

**Diet Assessment.** Macro- and micronutrient intakes, except for individual carotenoids, were assessed with the use of the Minnesota Nutrition Data System software, developed by the Nutrition Coordinating Center (Food Database Ver. 5A; Nutrient Database Ver. 20; University of Minnesota, Minneapolis, MN). Updated carotenoid food composition data, specifically median values for vegetables and fruits, were used to calculate individual carotenoid intakes during the self-select and experimental diet periods (14). These updated carotenoid food composition data, available as part of the Nutrition Data System, were used because they provide the most precise estimate of the

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**Table 1** Daily dietary intake on the experimental diets: the University of Minnesota CPRU Feeding Studies

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Control</th>
<th>Carotenoid</th>
<th>Cruciferous</th>
<th>Soy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Megajoules (MJ)</td>
<td>8.3</td>
<td>9.0</td>
<td>8.9</td>
<td>9.0</td>
</tr>
<tr>
<td>Calories (kcal)</td>
<td>1980.0</td>
<td>2150.0</td>
<td>2130.0</td>
<td>2140.0</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>85.6</td>
<td>93.9</td>
<td>101.5</td>
<td>100.6</td>
</tr>
<tr>
<td>Carbohydrate (g)</td>
<td>263.4</td>
<td>301.3</td>
<td>293.5</td>
<td>286.7</td>
</tr>
<tr>
<td>Fat (g)</td>
<td>70.0</td>
<td>63.3</td>
<td>63.6</td>
<td>73.1</td>
</tr>
<tr>
<td>Dietary fiber (g)</td>
<td>7.4</td>
<td>17.5</td>
<td>23.2</td>
<td>8.7</td>
</tr>
</tbody>
</table>

* Nutrient values do not include vanilla pudding, which was consumed in variable amounts by participants.

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4 The abbreviations used are: MJ, megajoule; kcal, kilocalorie; CPRU, Cancer Prevention Research Unit.
five primary carotenoids present in vegetables and fruits based on a compilation of food analyses. Although updated carotenoid data are unavailable for foods other than vegetables and fruits, an accurate estimate of carotenoid intake is obtained since the primary sources of carotenoids in the American diet are vegetables and fruits (15), and the only potential sources of carotenoids on the experimental diets were the vegetables. The control diet was, by design, essentially carotenoid free. The carotenoid contents of the experimental diets are shown in Table 2.

### Plasma Analyses
After an overnight fast, on the morning of day 5 of the self-select period and day 10 of each experimental diet period, 30 ml of blood were collected in red dye-coated EDTA tubes (Becton Dickinson Vacutainer Systems, Rutherford, NJ). Red dye-coated tubes were used to minimize carotenoid exposure to light. Samples were immediately placed on ice and spun (1500 x g; 20 min; 4°C). Plasma was transferred under subdued light into red dye-coated polystyrene centrifuge tubes and placed on ice. Aliquots of plasma were flushed with nitrogen and stored in amber Wheaton vials at -70°C until later analysis. The plasma carotenoids, α-carotene, β-carotene, lutetin/zeaxanthin (hereafter referred to as lutein), lycopene, and β-cryptoxanthin, were determined by the method of Bieri et al. (16) with the use of HPLC. Quality control procedures included calibration with the use of crystalline standards (Hoffman-LaRoche, Basel, Switzerland; Sigma Chemical Co., St. Louis, MO) and the routine analysis of plasma control pools containing high and low concentrations of each analyte. In addition, our laboratory routinely analyzes National Institutes of Standards and Technology reference sera and is a participant in the National Institutes of Standards and Technology Fat-Soluble Vitamin Quality Assurance group.

Plasma cholesterol was measured with the use of an enzymatic, timed end point method on a SYNCHRON CX5 system (Beckman Instruments, Inc., Brea, CA; Refs. 17-19). This total cholesterol test on SYNCHRON CX5 systems has been certified by the National Cholesterol Education program.

### Randomization
A random permutation of the 24 possible diet sequences was generated with participants assigned in order to the permuted sequence. Sealed envelopes containing the diet sequences were used so that neither participant nor feeding study staff had knowledge of the next randomization sequence. Because not all 24 sequences were used, and because some of the participants did not complete the study, the design was only approximately balanced on period and sequence orders.

### Statistical Analyses
Plasma carotenoid concentrations between diets were compared with the use of repeated measures ANOVA. Factors in the model included period and diet. Pairwise comparisons were made among the diets at the 0.01 level of significance. One-period carryover effects were estimated by adding a factor to the model for the previous diet completed by the participant. Adjustment of plasma carotenoid concentrations for plasma cholesterol did not alter the significance of the differences between treatment means; therefore, unadjusted values and analyses are reported here. Lycopene was the only plasma carotenoid correlated with plasma cholesterol, and this was observed only following the self-select diet. Log transformation of the data did not significantly alter the results obtained with the use of the untransformed data.

### Results
Nineteen participants, 11 men and 8 women, completed the self-select period and 4 experimental diet treatments. Four of the initial 23 recruits did not complete adequate data collection for all experimental diets. The baseline characteristics of the participants are presented in Table 3. The mean age, height, weight, and body mass index of the participants were 25.7 years, 171.5 cm, 66.4 kg, and 22.4 kg/m², respectively. Plasma carotenoid concentrations measured at the end of the self-select diet period representing free-living carotenoid concentrations were 0.10, 0.34, 0.35, 0.15, and 0.55 μmol/liter for α-carotene, β-carotene, lutein, β-cryptoxanthin, and lycopene, respectively. The self-select diets of the study population were similar to typical American diets. Over the 4-day period, mean energy intake was 9.5 MJ/day (2267 kcal); the percentage of energy from protein, carbohydrate, and fat was 15, 57, and 30, respectively. Mean daily intakes of α-carotene, β-carotene, lutein, β-cryptoxanthin, and lycopene were 0.45, 1.96, 1.95, 0.04, and 1.93 mg, respectively.

Mean plasma carotenoid concentrations on each experimental diet are presented in Table 4. α-Carotene, β-carotene,
Plasma Carotenoids as Biomarkers of Vegetable Intake

Table 3  Participant characteristics measured during the self-select period: the University of Minnesota CPRU Feeding Studies

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Men Mean (SD)</th>
<th>Women Mean (SD)</th>
<th>Total Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>25.60 (3.5)</td>
<td>25.80 (3.7)</td>
<td>25.70 (3.5)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>176.30 (6.6)</td>
<td>164.90 (10.7)</td>
<td>171.50 (9.9)</td>
</tr>
<tr>
<td>Wt (kg)</td>
<td>73.30 (8.5)</td>
<td>57.00 (9.1)</td>
<td>66.40 (11.9)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.60 (2.6)</td>
<td>20.80 (1.8)</td>
<td>22.40 (2.6)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Plasma carotenoids</th>
<th>Mean (SD)</th>
<th>Mean (SD)</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>a-Carotene</td>
<td>0.28 (0.18)</td>
<td>0.84 (0.38)</td>
<td>0.42 (0.44)</td>
</tr>
<tr>
<td>b-Carotene</td>
<td>0.34 (0.20)</td>
<td>0.56 (0.14)</td>
<td>0.45 (0.18)</td>
</tr>
<tr>
<td>lutein</td>
<td>0.12 (0.06)</td>
<td>0.14 (0.05)</td>
<td>0.13 (0.07)</td>
</tr>
<tr>
<td>lycopene</td>
<td>0.32 (0.12)</td>
<td>0.30 (0.08)</td>
<td>0.29 (0.13)</td>
</tr>
<tr>
<td>b-Cryptoxanthin</td>
<td>0.15 (0.12)</td>
<td>0.13 (0.06)</td>
<td>0.14 (0.09)</td>
</tr>
</tbody>
</table>

* Mean (SD).

Table 4  Mean plasma carotenoid concentrations after each experimental diet: the University of Minnesota CPRU Feeding Studies

<table>
<thead>
<tr>
<th>Plasma carotenoid</th>
<th>Control Mean (SD)</th>
<th>Carotenoid Mean (SD)</th>
<th>Cruciferous Mean (SD)</th>
<th>Soy Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>a-Carotene</td>
<td>0.09 (0.05)</td>
<td>0.48 (0.21)b</td>
<td>0.09 (0.07)</td>
<td>0.13 (0.10)</td>
</tr>
<tr>
<td>b-Carotene</td>
<td>0.26 (0.13)</td>
<td>0.84 (0.38)b</td>
<td>0.37 (0.19)</td>
<td>0.29 (0.15)</td>
</tr>
<tr>
<td>Lutein</td>
<td>0.26 (0.09)</td>
<td>0.58 (0.16)b</td>
<td>0.53 (0.16)b</td>
<td>0.25 (0.06)</td>
</tr>
<tr>
<td>Lycopene</td>
<td>0.32 (0.12)</td>
<td>0.30 (0.08)</td>
<td>0.29 (0.13)</td>
<td>0.34 (0.15)</td>
</tr>
<tr>
<td>b-Cryptoxanthin</td>
<td>0.15 (0.12)</td>
<td>0.13 (0.06)</td>
<td>0.15 (0.13)</td>
<td>0.13 (0.09)</td>
</tr>
</tbody>
</table>

* Mean (± SD).

Discussion

Results from this vegetable feeding study illustrate that plasma a-carotene, b-carotene, and lutein concentrations increase differentially after intake of carotenoid-containing vegetable combinations. Thus, individual plasma carotenoids, or combinations thereof, may be useful exposure markers of high intakes of vegetables and may allow some specific association of vitamins thereof. The representativeness of these study participants for investigating plasma carotenoids is confirmed by their initial plasma carotenoid concentrations. Self-select blood concentrations showed that lycopene, lutein, b-carotene, b-cryptoxanthin, and a-carotene were present in the following proportions: 37:23:23:10:7, respectively. Micozzi et al. (12) found plasma concentrations of a- and b-carotene to constitute 43, 19, and 14% of total carotenoids, respectively, when they measured individual plasma carotenoids as part of a total plasma carotenoid determination. These data illustrate, as others have, that in the United States, similar proportions and absolute concentrations of the five aforementioned carotenoids are found in human plasma, and that lycopene, lutein, and b-carotene are predominant (20, 21).

Feeding high doses of carotenoid-containing vegetables changed both the absolute and relative amounts of specific carotenoids in plasma. Because so little is understood about human absorption and metabolism of dietary carotenoids other than b-carotene, studying the relationships among dietary carotenoids in plasma may help explain these processes. For example, the dietary b-carotene:lutein ratio was 1.0, 1.3, 0.7, and 1.0, in the control, carotenoid, cruciferous, and soy diets, respectively; plasma ratios observed on these diets were 1.0, 1.5, 0.7, and 1.2. These ratios suggest a direct relationship between intakes of these carotenoids and plasma concentrations at these high dietary levels. In contrast, the relationship between dietary intake and plasma concentrations of a- and b-carotene is difficult to assess in this study. On the carotenoid diet, the mean plasma b-carotene:a-carotene ratio was 1.8, whereas the ratio of these carotenoids in the diet was 3.9. This may be due to an interaction between dietary a- and b-carotene or inadequate a-carotene composition data for cooked spinach and broccoli (14). Historically, analytic techniques have not been sensitive enough to quantify a-carotene in foods (22). Therefore, the relationship between a-carotene intake and plasma concentrations cannot be assessed with certainty until better food composition data become available.

Despite similar b-carotene:lutein ratios in the experimental diets and in plasma, a potential interaction between dietary b-carotene and lutein was suggested based on the relationship between absolute intake and plasma concentrations after the carotenoid and cruciferous diets. Although lutein intake was lower on the cruciferous diet (approximately 75% lower than the carotenoid diet), mean plasma lutein concentrations were similar, whereas plasma b-carotene concentrations corresponded more closely to b-carotene intake. This may indicate competition for absorption, which has been suggested in other studies (12, 23). With low b-carotene intake, dietary lutein may be absorbed preferentially in the small intestine. This was suggested in a feeding study by Micozzi et al. (12) where plasma lutein concentrations were observed to increase after 6-week administration of a placebo and decrease with 6-week b-carotene supplementation (12 and 30 mg) when compared to baseline carotenoid concentrations. The control diet used in the Micozzi study may have included a single daily serving of lutein-rich vegetables, which would help explain why plasma lutein concentrations increased steadily with placebo administration and decreased with supplemental b-carotene if there is indeed an interaction between lutein and b-carotene (11).

To our knowledge, six controlled feeding studies have measured changes in plasma carotenoid concentrations after intake of single vegetables in healthy human adults (11–13, 24–26). These studies provide some kinetic data on the
time it takes certain carotenoids to appear in the blood, to peak after a specified dose, and their persistence within a tissue. However, only two of these studies have measured more than two plasma carotenoids after vegetable intake. One of the strengths of this study is that five plasma carotenoids were measured after intake of vegetable combinations, not of just a single vegetable, thus, more closely mimicking real life dietary patterns. Nonetheless, comparisons between these data and that of other studies furthers our understanding of carotenoid metabolism. For example, in the study reported here, it is not known whether plasma carotenoid concentrations plateaued by day 10 (indicating tissue saturation). Micozzi et al. (12) showed that mean plasma β-carotene concentrations stabilized and α-carotene continued to increase with daily intake of 272 g carrots over a 6-week period; mean plasma lutein concentrations continued to increase at 6 weeks with daily intake of 300 g broccoli. Likewise, Kim et al. (25) observed similar results for serum α- and β-carotene concentrations with daily intake of 452.6 g of carrot juice throughout the duration of their 2-week study; Jensen et al. (26) observed similar results for serum α- and β-carotene when participants were fed 207.3 g carrots/day for 1 week. These data suggest that plasma carotenoid concentrations measured on day 10 of our feeding study may not be indicative of maximum plasma carotenoid concentrations. However, this study provides excellent data on our question of primary interest: are changes in vegetable intake able to be monitored with the use of plasma carotenoids?

Some of the feeding studies mentioned above have measured plasma carotenoid clearance and have shown that the 10-day washout used in this study may not be long enough to attenuate elevated plasma carotenoid concentrations achieved after a high carotenoid feeding. However, this study showed no significant carryover effects. Brown et al. (11) noted that plasma β-carotene concentrations continued to decline 9–10 days following the peak concentration achieved after a single dose of 272 g carrots. Micozzi et al. (12) observed that plasma α-carotene, β-carotene, and lutein concentrations continued to fall 28 days after cessation of their 6-week feeding regimen. Jensen et al. (26) observed a half-life of approximately 7 days for serum α- and β-carotene concentrations with consumption of a carotenoid depletion diet after daily carrot intake; the week after 7 days of carrot juice consumption showed no change in serum α- and β-carotene concentrations in the study of Kim and Simpson (25). Therefore, there appears to be a residual effect of carotenoid-rich food intake on plasma carotenoid concentrations. Although this residual effect may be problematic for biomarker development (it did not appear to be so here), it is advantageous from a chemopreventive standpoint. If blood concentrations provide a measure of the dose reaching target tissues, then a more persistent agent may confer protection over a longer period of time.

The bioavailability of plant food carotenoids in humans has been the subject of much debate and data are lacking for the wide variety of carotenoids present in the human diet. Bioavailability may be affected by food processing and preparation, the presence of other foods in the diet, and innate physiological differences among individuals (6, 10, 13, 27–29). In this study the effects of these variables were minimized as much as possible in the following manner: (a) participants consumed a controlled diet; (b) vegetables were prepared from frozen; (c) participants followed study guidelines for vegetable preparation; and (d) macronutrient compositions of the diets were similar. Dietary fiber intake did differ among the diets in this study, which was inevitable due to the variety of vegetable feedings. However, the effects of fiber on carotenoid absorption cannot be assessed at these high levels of intake because the highest plasma carotenoid concentrations were observed with the carotenoid and cruciferous diets, the two diets highest in fiber and carotenoid content.

**Implications.** In this study, plasma α-carotene, β-carotene, and lutein concentrations were shown to reflect ingestion of specific carotenoid-containing vegetables. Therefore, if intake of carotenoid-rich vegetables and fruits decreases cancer risk, then plasma carotenoids appear to be adequate markers of a modifiable chemopreventive exposure. If total vegetable and fruit intake is protective because of other unidentified chemopreventive phytochemicals, plasma carotenoids may still be useful biomarkers of intake due to the fact that carotenoids are widespread in vegetables and fruits and many people typically consume some carotenoid-rich vegetables and fruits as part of their daily intakes (15). Our work and that of others have shown that plasma carotenoids are strong predictors of self-reported total vegetable and fruit intake in a free-living population (5) and are potential markers of compliance in dietary vegetable and fruit interventions (30).
Acknowledgments

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