ABSTRACT Watermelon is a rich natural source of lycopene, a carotenoid of great interest because of its antioxidant capacity and potential health benefits. Assessment of bioavailability of lycopene from foods has been limited to tomato products, in which heat processing promotes lycopene bioavailability. We examined the bioavailability of lycopene from fresh-frozen watermelon juice in a 19-wk crossover study. Healthy, nonsmoking adults (36–69 y) completed three 3-wk treatment periods, each with a controlled, weight-maintenance diet. Treatment periods were preceded by “washout” periods of 2–4 wk during which lycopene-rich foods were restricted. All 23 subjects consumed the W-20 (20.1 mg/d lycopene, 2.5 mg/d β-carotene from watermelon juice) and C-0 treatments (controlled diet, no juice). As a third treatment, subjects consumed either the W-40 (40.2 mg/d lycopene, 5.0 mg/d β-carotene from watermelon juice, n = 12) or T-20 treatment (18.4 mg/d lycopene, 0.6 mg/d β-carotene from tomato juice, n = 10). After 3 wk of treatment, plasma lycopene concentrations for the W-20, W-40, T-20 and C-0 treatments were (least squares means ± SEM) 1078 ± 106, 1183 ± 139, 960 ± 117 and 272 ± 27 nmol/L, respectively. Plasma concentrations of β-carotene were significantly greater after W-20 (574 ± 49 nmol/L) and W-40 (694 ± 73 nmol/L) treatments than after the C-0 treatment (313 ± 27 nmol/L). Plasma lycopene concentrations did not differ at wk 3 after W-20, W-40 and T-20 treatments, indicating that lycopene was bioavailable from both fresh-frozen watermelon juice and canned tomato juice, and that a dose–response effect was not apparent in plasma when the watermelon dose was doubled. J. Nutr. 133: 1043–1050, 2003.

KEY WORDS: • lycopene • β-carotene • bioavailability • watermelon • tomato

Watermelon is one of few foods rich in lycopene, a non-provitamin A carotenoid that has up to twice the antioxidant capacity of β-carotene in vitro (1–3). Data from epidemiological studies suggest lycopene may have protective effects against certain types of cancers (4–7) and cardiovascular disease (8,9).

Previous investigations of lycopene bioavailability have focused on tomato products (10–18), which represent 80% of lycopene intake in the U.S. diet (19). Other natural food sources of lycopene include guava, pink grapefruit, apricots, persimmons and red-fleshed papaya, although the contribution of these foods to dietary lycopene is limited (19–21). The mean lycopene concentration of watermelon (4868 μg/100 g) is about 40% higher than the year-round mean for raw tomato (3025 μg/100 g) (21), and watermelon ranks 5th among the major contributors of lycopene in the U.S. diet (19). However, the bioavailability of lycopene from watermelon has not been evaluated.

Carotenoid absorption from plants is generally poor relative to carotenoid supplements (12) and varies with several factors, including accessibility from the plant matrix (22). The crystalline nature of lycopene in tomato may account in part for its apparently low absorption efficiency from the tomato plant matrix (16,23). The bioavailability of both lycopene and β-carotene from tomato products has been shown to increase with heat and/or homogenization, processes that break down plant cell walls, allowing release of carotenoids (16). Although trans isomers of lycopene are generally stable in the plant matrix, once liberated they are susceptible to heat-induced isomerization to cis isomers (24), which may be more readily absorbed (10,25). Watermelon has a carotenoid profile similar to that of tomato (26), but it is not typically heat treated, a factor that might be expected to limit lycopene bioavailability.

The primary objective of this study was to assess the bioavailability of lycopene from watermelon juice using tomato juice as a comparative lycopene-rich food. As secondary objectives, we sought to determine whether a measurable dose-
response in plasma lycopene occurs when the amount of watermelon juice consumed is doubled and to compare the plasma lycopene response to tomato and watermelon juices providing a similar amount of lycopene. Plasma responses from other carotenoids present in watermelon and tomato, including β-carotene, phytoene and phytofluene, were also examined.

SUBJECTS AND METHODS

Study design. Over 19 wk, subjects consumed three of four possible treatments according to a repeated measures crossover design. Treatments were as follows: 1) C-0, control or base diet only; 2) W-20, base diet plus 20.1 mg/d lycopene and 2.5 mg/d β-carotene from watermelon; 3) W-40, base diet plus 40.2 mg/d lycopene and 5.0 mg/d β-carotene from watermelon; and 4) T-20, base diet plus 18.4 mg/d lycopene and 0.6 mg/d β-carotene from tomato juice. Subjects consumed W-20 and C-0 in separate treatment periods, plus either T-20 or W-40 in a third treatment period. Twelve distinct treatment sequences (i.e., triplets) were assigned to 24 subjects, with each sequence order assigned to two subjects. Subjects were matched by gender, age and body mass index (BMI) to have a nonbiased profile of subjects represented in the split treatments (W-40 and T-20).

Four-week washout periods, during which subjects limited consumption of lycopene-containing foods, were completed between treatment periods 1 and 2, and 2 and 3 to minimize carryover effects on plasma lycopene. A 2-wk washout period was completed before treatment period 1 to allow plasma lycopene to reach stable baseline levels before treatment. Subjects consumed their own foods, but kept written records of fruit, vegetable and beverage intake during the washout periods.

Subjects. The Committee on Human Research of the Johns Hopkins School of Public Health and Hygiene approved the study procedures. Before enrollment in the study, subjects signed consent forms. Twelve men and 12 women, all healthy, nonsmoking and between the ages of 36–69 y from the Beltsville, MD area were recruited. Subjects’ mean BMI was 27 ± 4 kg/m² (range: 20–35 kg/m²) and mean age was 51 ± 10 y. Subjects were determined to be healthy by a physician and by routine blood and urine indicators, height, weight and blood pressure. Subjects had no hyperlipidemias, current pregnancy, diabetes, liver disease or kidney disease. Subjects did not take lipid-lowering drugs or supplements high in carotenoids. Eleven men and 11 women completed all three treatments; one subject dropped out of the study before the first treatment and another completed only the C-0 and W-20 treatments.

Watermelon juice. Watermelon juice was prepared at the USDA Citrus and Subtropical Products Lab (Winter Haven, FL) from Millionaire variety seedless Sunripe™ watermelons (Falls Church, VA). Melon flesh was fed into a screw finisher and the pulp was forced through a stainless steel screen tube with perforations of 0.1 mm diameter. The juice was bottled in 0.25 L-capacity high density polyethylene containers (each 260 g or ˜1 cup) and frozen immediately without pasteurization. Bottling, freezing and microbial analysis of the juice was done by The Fresh Juice Company/Saratoga Bottling Co. (Winter Haven, FL). The juice was maintained for 1–6 mo at −20°C before consumption or food analysis.

Watermelon juice was thawed in the refrigerator 1–2 d before serving to subjects. Three containers, one at each meal, were provided daily for the W-20 treatment, whereas two containers were provided at each meal for the W-40 treatment. Mean doses of individual carotenoids for each treatment are shown in Table 1. Watermelon juice provided 150 kJ energy per 100 g (Covance Laboratories, Madison, WI), and contained <0.1 g/100 g total dietary fiber by AOAC Method 991.43 (Medallion Labs, Minneapolis, MN).

Tomato juice. A single lot of commercially available canned tomato juice was purchased locally (Greenbelt, MD), and was not given further heat treatment. For the T-20 treatment, two servings (122 g each, ˜0.5 cup) of tomato juice were given daily at breakfast and at dinner. Tomato juice provided 84 kJ energy per 100 g (Covance Laboratories) and 0.6 ± 0.05 g total dietary fiber per 100 g (Medallion Labs). The actual amount of lycopene provided with the tomato juice treatment (18.4 mg) was slightly less than the desired dose of 20 mg lycopene because of natural product variability.

Controlled diet. Subjects were fed controlled, weight-mainte- nance diets at the Beltsville Human Nutrition Research Center (BHNRC) Human Study Facility. Menus, ranging from 6700 to 15,000 kJ, were prepared in 840-kJ increments by proportionately scaling each food item. Subjects were weighed daily and the diet was adjusted if necessary to maintain starting body weights. Breakfast and dinner were consumed in the dining facility Monday through Friday under the supervision of a registered dietitian. Lunches and weekend meals, including treatments, were packed for take-out. Proportions of macronutrients in the base diet were controlled within narrow ranges and provided a mean of 34% energy from fat, 15% from protein and 51% from carbohydrate. Macronutrient contents of the base diets were calculated using Nutritionist Five™ (First DataBank; San Bruno, CA), with nutrient values from the USDA Nutrient Database for Standard Reference, Release 14 (28). Diets were designed to meet the recommended dietary allowances of known required nutrients. Diets provided a stable, daily intake of nonlycopene carotenoids, which were held constant as a function of energy required to maintain body weight. The carotenoid content of the base diet was calculated using the 1998 USDA-NCC Carotenoid Database for U.S. Foods (21). For example, the 10,040 kJ (2400 kcal) diet contained a mean of 2.2 mg carotenoids, including α-carotene (0.03 mg), β-carotene (0.84 mg) and lutein/zeaxanthin (1.3 mg). Once per wk, subjects consumed a salad dressing containing 0.9–2.0 mg lycopene, depending on the energy level of the base diet. This was the only source of lycopene on the C-0 (base) diet.

TABLE 1
Carotenoids, energy and fiber content of juice treatments and typical base diet

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Amount (mg/d)</th>
<th>cis LYC1</th>
<th>trans LYC1</th>
<th>β-Carotene</th>
<th>Phytoene</th>
<th>Phytofluene</th>
<th>Energy (kJ/d)</th>
<th>Fiber (g/d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>W-202</td>
<td>780</td>
<td>1.2</td>
<td>18.9</td>
<td>2.5</td>
<td>0.90</td>
<td>0.45</td>
<td>1160</td>
<td>&lt; 13</td>
</tr>
<tr>
<td>W-402</td>
<td>1560</td>
<td>2.4</td>
<td>37.8</td>
<td>5.0</td>
<td>1.80</td>
<td>0.89</td>
<td>2320</td>
<td>&lt; 13</td>
</tr>
<tr>
<td>T-202</td>
<td>244</td>
<td>2.0</td>
<td>16.4</td>
<td>0.6</td>
<td>2.10</td>
<td>1.10</td>
<td>204</td>
<td>1.6</td>
</tr>
<tr>
<td>C-04</td>
<td>0</td>
<td>&lt; 0.2</td>
<td>&lt; 0.2</td>
<td>0.84</td>
<td>n/a6</td>
<td>n/a9</td>
<td>10040</td>
<td>25.2</td>
</tr>
</tbody>
</table>

1 LYC, lycopene.
2 Watermelon (W-20, W-40) and tomato (T-20) juice treatments were consumed in addition to base diet (C-0).
3 Fiber content of watermelon juice was below detection limit (0.1 g/100 g total dietary fiber) of AOAC Method 991.43 (27).
4 Carotenoid and fiber content of 10,040 kJ base diet (C-0), which provided 1.3 mg LYC/wk or < 0.2 mg LYC/d.
5 Values for phytoene and phytofluene in base diet are not available (n/a).

4 Abbreviations used: BMI, body mass index; C-0, control or base diet; LSM, least squares mean(s); LYC, lycopene; T-20, 18.4 mg/d lycopene from tomato juice; W-20, 20.1 mg/d lycopene from watermelon juice; W-40, 40.2 mg/d lycopene from watermelon juice.
**Results**

Treatment main effects were significant for total lycopene, \( \beta \)-carotene, cis lycopene, trans lycopene, phytoene and phytofluene, but not significant for lutein and retinol. Treatment \( \times \) wk interaction effects for plasma \( \beta \)-carotene, total lycopene, cis lycopene, trans lycopene, phytoene and phytofluene indicate that significant differences between treatments occurred as the time subjects consumed a diet increased from 0 to 3 wk.

For plasma total lycopene, effects of gender, gender \( \times \) wk, treatment, treatment \( \times \) wk and treatment \( \times \) wk \( \times \) wk effects were significant. The wk and preintervention baseline covariance were significant, with \( \log_{10} \) lycopene changing both as a linear and quadratic function of wk and as a linear function of preintervention baseline plasma lycopene. Linear models of plasma lycopene fit each treatment as a function of wk, including both genders and setting the covariate for preintervention baseline lycopene at the mean, are shown in Figure 1A. The LSM for plasma lycopene for W-20, W-40 and T-20 treatments were significantly greater than control at wk 1, 2 and 3 (Table 2). There were no significant differences in plasma lycopene LSM for the W-20, W-40 and T-20 treatments at any time. The W-40 treatment produced a twofold increase in plasma lycopene at wk 3, reaching a mean of 1183 nmol/L. This value was not significantly different from the LSM for W-20 (1078 nmol/L) or T-20 (960 nmol/L) treatments at wk 3.

For \( \beta \)-carotene, treatment, gender, and treatment \( \times \) wk effects were significant. Log \( \beta \)-carotene values increased linearly with age, preintervention baseline plasma \( \beta \)-carotene and wk within treatment. Linear models of plasma \( \beta \)-carotene fit to each treatment as a function of wk, including both genders and setting covariates of age and preintervention baseline at their means, are shown in Figure 1B. The W-20 and W-40 treatments resulted in significantly greater plasma \( \beta \)-carotene LSM (Table 2) than either C-0 (wk 1, 2, 3) or T-20 (wk 2, 3). Plasma \( \beta \)-carotene increased 100% from wk 0 (348 nmol/L) to wk 3 (694 nmol/L) for the W-40 treatment, but this value did not differ from the W-20 (574 nmol/L) treatment at wk 3. The T-20 treatment did not differ from the C-0 treatment at any time for \( \beta \)-carotene.

The increase in plasma total lycopene with watermelon or tomato treatments was attributed to increases in both cis and trans isomers of lycopene (Fig. 2). Baseline-adjusted values were obtained by subtracting wk 0 values for cis and trans lycopene from the corresponding wk 3 values for each individual subject. LSM of baseline-adjusted values were then
generated for each treatment. There were significant increases from wk 0 to wk 3 in both cis and trans lycopene for W-20, W-40 and T-20 treatments that did not occur for C-0. The increase in cis lycopene was significantly greater for the W-20 and W-40 treatments than for C-0, whereas the increase in trans lycopene did not differ among W-20, W-40 and T-20 treatments. The cis and trans lycopene concentrations decreased similarly after the C-0 treatment.

The LSM were generated for percentages of individual lycopene isomers at wk 0 and wk 3. At wk 0, plasma lycopene was 30–32% trans and did not differ among treatments. At wk 3, there were differences in percentages of individual lycopene isomers among treatments (Fig. 3). Isomer percentages did not differ between the W-20 and W-40 treatments; thus, only the W-20 treatment is shown in Figure 3. At wk 3 of treatments, the percentage of total lycopene in the trans form was significantly greater for W-20 (44%), W-40 (46%) and T-20 (38%) “treatments” than for control (27%). At wk 3, the percentage of “other”-cis isomers was significantly greater for control (12%) and T-20 (10%) treatments than for either the W-20 (7%) or the W-40 (7%) treatment. The percentage of 13-cis lycopene was greater for T-20 (22%) than for control (20%) at wk 3. The 9-cis and 15-cis lycopene percentages did not differ for any treatment–time combinations.

Women had significantly higher plasma concentrations of total lycopene, total cis lycopene, trans lycopene and β-carotene at the onset of each treatment (wk 0); however, the gender × wk interaction was significant for both total and trans lycopene, so that gender differences for these variables diminished by wk 3 for all lycopene-containing treatments. Regardless of preintervention baseline covariate lycopene level or treatment, women had significantly greater mean cis lycopene concentrations at wk 0 and 3, as shown for the T-20 treatment (Fig. 4A). β-Carotene levels were significantly and consistently higher for women at wk 0 and at wk 3, regardless of treatment, as shown for the W-20 treatment (Fig. 4B).

For plasma phytoene and phytol, effects of treatment and treatment × wk were significant. Log_{10} phytoene and phytol values linearly increased with wk in a treatment-dependent manner. Log_{10} phytoene increased linearly with respect to the preintervention baseline concentration. Plasma phytoene and phytol responses were determined by fitting a linear model to each treatment as a function of wk, including both genders, and setting covariates at their means. The LSM for phytoene were significantly greater after the W-40 and T-20 treatments than after the C-0 treatment at wk 2 and 3 (Table 2). Phytoene and phytol concentrations after the W-20 treatment did not differ from those after the W-40 or C-0 treatments at any time. The LSM for phytoene were significantly greater after the T-20 treatment than for the C-0, W-20 or W-40 treatments at wk 1–3 (Table 2). Effects of treatment × age interaction were significant for phytoene, and when the age covariate was varied, the LSM for T-20 and W-40 were not consistently different from C-0 at wk 2 and 3. The treatment × preintervention baseline interaction was significant for phytol. Although the LSM after the T-20 treatment were consistently greater than those of the C-0 treatment at wk 3, regardless of preintervention baseline phytol, the LSM after the W-40 treatment was greater than that of C-0 only when the preintervention baseline was high (230 nmol/L).

**DISCUSSION**

Fresh-frozen watermelon juice produced a significant increase in plasma lycopene, comparable to the increase observed with a similar amount of lycopene from canned tomato juice. Within 1–2 wk, consumption of ~20 mg/d lycopene from either watermelon or tomato juice resulted in a 100 to 200% increase in plasma lycopene in human subjects. Heat treatment was thus not required for lycopene absorption from fresh-frozen watermelon juice.

Although there has been some doubt about the bioavailability of lycopene from tomato juice (4,12), we demonstrated an increase in plasma lycopene from 428 to 960 nmol/L over 3 wk using 18.4 mg/d lycopene from 240 g (~1 cup/d) of tomato juice. This finding is in agreement with that of Sakamoto et al. (13), who reported an increase in plasma lycopene from 425 to 807 nmol/L over 4 wk using 18 mg/d lycopene from tomato juice. Similarly, Paetau et al. (18) reported an increase in plasma lycopene from 580 to 820 nmol/L over 4 wk using 75 mg/d lycopene from tomato juice. Single-dose studies have not consistently shown changes in plasma lycopene with commercially processed tomato juice unless it is given additional heat treatment (10,11). However, the tricyglycerol-rich lipoprotein fraction of plasma has been shown to respond to raw (15) and canned tomatoes (16), suggesting whole
plasma may not reveal small lycopene responses to single meals.

After W-20, W-40 and T-20 treatments, plasma lycopene concentrations were significantly elevated above control by wk 1, reaching a maximum at wk 2 and a plateau between wk 2 and wk 3. This plateau effect was reported previously (18) in response to continued doses of lycopene supplements or tomato juice. In the W-40 treatment, the watermelon dose was doubled, although the plasma lycopene response was similar to that for W-20. Similarly, Sakamoto et al. (13) reported no difference in plasma lycopene concentrations in treatment groups fed 18 and 36 mg lycopene/d from tomato juice for 4 wk. These chronic study data support findings from acute studies that suggest absorption of lycopene is more efficient at lower doses (10,34). It is not clear whether this apparent reduction in absorption efficiency is attributable to a greater proportion of the lycopene dose being excreted or metabolized or to an accumulation of lycopene in nonplasma tissues. Lycopene has been shown to accumulate in prostate tissue of men consuming tomato products (35), and it is possible that lycopene accumulates in tissues other than plasma in a dose-responsive manner.

Gender effects were significant for both β-carotene and lycopene, whereas BMI was not a significant covariate for

**TABLE 2**

Plasma carotenoids in humans that consumed watermelon, tomato or control diets for 3 wk

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Wk 0</th>
<th>Wk 1</th>
<th>Wk 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Wk 0</td>
<td>Wk 1</td>
</tr>
<tr>
<td></td>
<td>n</td>
<td>nmol/L</td>
<td>nmol/L (%)</td>
</tr>
<tr>
<td>Lycopene</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>23</td>
<td>377 ± 31</td>
<td>373 ± 33a (-1)</td>
</tr>
<tr>
<td>W-20</td>
<td>23</td>
<td>452 ± 37</td>
<td>845 ± 75b (87)</td>
</tr>
<tr>
<td>W-40</td>
<td>12</td>
<td>402 ± 41</td>
<td>929 ± 97b (131)</td>
</tr>
<tr>
<td>T-20</td>
<td>10</td>
<td>428 ± 45</td>
<td>797 ± 86b (86)</td>
</tr>
<tr>
<td>β-Carotene</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>23</td>
<td>354 ± 26</td>
<td>363 ± 25a (2.5)</td>
</tr>
<tr>
<td>W-20</td>
<td>23</td>
<td>338 ± 24</td>
<td>431 ± 29b (27)</td>
</tr>
<tr>
<td>W-40</td>
<td>12</td>
<td>348 ± 31</td>
<td>468 ± 37b (34)</td>
</tr>
<tr>
<td>T-20</td>
<td>10</td>
<td>352 ± 34</td>
<td>368 ± 31ab (4)</td>
</tr>
<tr>
<td>Phytoene</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>23</td>
<td>69 ± 4</td>
<td>66 ± 4a (-4)</td>
</tr>
<tr>
<td>W-20</td>
<td>23</td>
<td>73 ± 4</td>
<td>76 ± 4ab (4)</td>
</tr>
<tr>
<td>W-40</td>
<td>12</td>
<td>80 ± 7</td>
<td>87 ± 7b (8)</td>
</tr>
<tr>
<td>T-20</td>
<td>10</td>
<td>67 ± 6</td>
<td>86 ± 7ab (28)</td>
</tr>
<tr>
<td>Phytofluene</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>23</td>
<td>44 ± 4</td>
<td>36 ± 3a (-19)</td>
</tr>
<tr>
<td>W-20</td>
<td>23</td>
<td>47 ± 5</td>
<td>39 ± 4a (-15)</td>
</tr>
<tr>
<td>W-40</td>
<td>12</td>
<td>44 ± 6</td>
<td>38 ± 4a (-16)</td>
</tr>
<tr>
<td>T-20</td>
<td>10</td>
<td>52 ± 9</td>
<td>70 ± 11b (34)</td>
</tr>
</tbody>
</table>

1 Values are least square means ± SEM. Means for a variable at a time with superscripts without a common letter differ, P < 0.05.
2 Treatments: control (base diet only), W-20 (base diet plus 780 g watermelon juice/d), W-40 (base diet plus 1560 g watermelon juice/d), T-20 (base diet plus 244 g tomato juice/d).
3 Percentage change from wk 0.

**FIGURE 2** Baseline-adjusted plasma concentrations for all trans and cis lycopene (LYC) at wk 3 of treatment for watermelon (W-20, W-40), tomato juice (T-20) and base (control) diet (C-0). Cis isomers include the 5-, 9-, 13-, 15- and “other” isomers. Values are least squares means ± SEM, and are wk 0 baseline-adjusted” within each subject to represent the change in plasma lycopene between wk 0 and wk 3 of each treatment: control (C-0, n = 23); 20.1 mg lycopene (18.9 mg trans, 1.2 mg cis) from watermelon (W-20, n = 23); 40.2 mg lycopene (37.8 mg trans, 2.4 mg cis) from watermelon (W-40, n = 23); and 18.4 mg lycopene (16.4 mg trans, 2.0 mg cis) from tomato juice (T-20, n = 10). Means without a common letter differ, P < 0.05.

**FIGURE 3** Percentages of individual lycopene isomers at wk 3 for control (C-0, n = 23), watermelon juice (W-20, n = 23) and tomato juice (T-20, n = 10) treatments. Values are least squares means ± SEM. Major isomers of lycopene, including trans, 5-cis, 13-cis, and “other” isomers are shown as individual percentages. Percentages of minor isomers 9-cis and 15-cis did not differ after treatment; hence, these values were combined into a single percentage. Means for an isomer without a common letter differ, P < 0.05.
either β-carotene or lycopene, and age was a significant covariate for β-carotene only. Serum concentrations of β-carotene were previously found to be lower in men than in women (36,37), as found in the present study. Serum concentrations of lycopene (total, cis and trans) were greater in women than in men at baseline, whereas this difference remained only for cis lycopene after treatment. Previous studies have not shown a consistent relationship between gender and plasma lycopene (20). BMI did not remain a significant covariate for β-carotene or lycopene once factors such as age, preintervention baseline carotenoids and gender were included in the models. We did not, however, assess the effect of body weight alone on carotenoid response. Previous studies found that β-carotene, but not lycopene, was inversely associated with BMI (36–38). \( \text{Log}_{10} \) β-carotene increased linearly with age in the present study, a finding that agrees with some studies (36,37) but not others (38–41).

Tomato products are typically 90% or greater trans lycopene (24). In contrast, plasma carotenoids are generally >50% cis lycopene (42,43). The relative percentages of cis and trans isomers in plasma have been suggested to represent an equilibrium state in plasma (25,30). In the present study, trans (30–32%) and 5-cis (29–31%) lycopene isomers predominated at baseline, a finding consistent with other reports (29,43,44). The percentage trans remained similar at wk 3 of C-0 (27%) treatment, but increased significantly from wk 0 to wk 3 for W-20 (44%), W-40 (46%) and T-20 (38%) treatments. Similarly, Holloway et al. (29) reported that 40–45% of plasma lycopene in human subjects was in the trans form after 2 wk supplementation with 21 mg/d tomato paste (84% trans). They also reported a greater (nonsignificant) percentage of cis isomers in HDL than in either LDL or VLDL, and suggested cis-lycopene may be taken up from tissues by HDL in a manner analogous to reverse cholesterol transport. These data (29) and those from the present study suggest that, in addition to equilibrium forces that may influence isomer distribution in plasma, the relative proportions of cis and trans isomers are influenced by the balance between uptake and clearance of plasma lycopene by lipoproteins.

Plasma cis and trans isomers of lycopene in plasma were significantly greater than those for C-0 after W-20, W-40 and T-20 treatments, despite the fairly low concentration of cis lycopene isomers in the lycopene-containing treatments (<11%). This is in agreement with earlier human studies, in which an increase in both trans and cis isomers of plasma lycopene occurred after a single dose of heated tomato juice (15) and a 15-d dietary intervention with vegetable juice and tomato sauce (14). Accumulating evidence in humans (10,15) and in animal models (25) supports the hypothesis that cis lycopene is preferentially absorbed. Isomerization of trans to cis lycopene is likely to occur during digestion (30), but only after trans lycopene is released from the food matrix, in which it is fairly stable (24). The increase in trans lycopene was greater for W-20 (and W-40) than for T-20, a finding that may be explained by the difference in trans lycopene consumed per day for the W-20 (18.9 mg trans) and T-20 (16.4 mg trans) doses. Another possibility is that trans lycopene was more readily released from the watermelon matrix than from tomato, although this latter explanation is speculative.

Absorption of carotenoids from plants is influenced by matrix features including the type of chromoplast(s) present and the association of protein with carotenoids (45). In the red tomato, lycopene accumulates in long crystalloids, whereas β-carotene is dissolved in lipid droplets or globules (46). This difference in chromoplast types may explain the preferential absorption of β-carotene from tomato products (16). Red watermelon and red tomato have similar carotenoid patterns (26), and both have crystalline chromoplasts containing lycopene (46–48), but other similarities or differences in ultrastructure and release of carotenoids during digestive processes remain to be elucidated.

Plasma β-carotene increased fairly linearly and significantly after W-20 and W-40 treatments, although the plasma response did not differ between these treatments. This may be explained by the large interindividual variation in responses and the reduction in statistical power that occurred because only half of subjects consumed the W-40 treatment. A β-carotene response was not seen for the T-20 treatment, which contained less β-carotene than did the W-20 or W-40 treatments. Previous studies showed significant increases in plasma β-carotene after consumption of 1 mg β-carotene for 4 d from heated-homogenized tomatoes (16) and after consumption of 0.6 mg (13) and 2.1 mg (18) β-carotene from tomato juice over 4 wk. Although the dose of β-carotene provided in the T-20 treatment was small (0.6 mg), the low-carotenoid background diet of the present study produced a general downward trend in plasma carotenoids, which may have masked subtle

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**FIGURE 4** Gender differences are illustrated by models for plasma concentrations of (A) lycopene (cis, trans) and (B) β-carotene for selected 3-wk treatments. For T-20, baseline plasma trans and cis lycopene were set to means of 159 and 308 nmol/L, respectively, for generating model equations separated by gender. For women, Log10 \( (\text{trans}_{T-20} + 1) \) = 2.1791 + 0.3585 \( \times \) wk - 0.0820 \( \times \) wk²; Log10 (cis_T-20 + 1) = 2.5440 + 0.2117 \( \times \) wk - 0.0397 \( \times \) wk². For men, Log10 (trans_T-20 + 1) = 2.0251 + 0.4032 \( \times \) wk - 0.0820 \( \times \) wk²; Log10 (cis_T-20 + 1) = 2.3881 + 0.2416 \( \times \) wk - 0.0397 \( \times \) wk². For W-20 and C-0 treatments, baseline plasma β-carotene (B) was set to a mean of 395 nmol/L for generating model equations by gender. For women, Log10 (β-caroteneW-20 + 1) = 2.5737 + 0.1481 \( \times \) wk - 0.0188 \( \times \) wk²; Log10 (β-caroteneC-0 + 1) = 2.5981 - 0.0207 \( \times \) wk + 0.0188 \( \times \) wk². For men, Log10 (β-caroteneW-40 + 1) = 2.4536 + 0.1481 \( \times \) wk - 0.0188 \( \times \) wk²; Log10 (β-caroteneC-0 + 1) = 2.4780 - 0.0207 \( \times \) wk + 0.0188 \( \times \) wk². Differences between genders are indicated by different letters, \( P < 0.05 \).
changes in plasma \( \beta \)-carotene that might have occurred with the T-20 treatment. \( \beta \)-Carotene absorption from watermelon appeared to be more responsive to dose than was lycopene, a finding in agreement with animal studies that showed the absorption efficiency of lycopene to be poorer than that of other carotenoids (49,50).

Phytoene and phytofluene are of interest because they may have protective effects against chronic disease (51–53). Both phytofluene and phytoene concentrations doubled after 3 wk of T-20 treatment, which is consistent with a previous study (18). Phytoene was bioavailable from both tomato and watermelon juices, but particularly from tomato juice. Plasma phytofluene increased for T-20 only, although this increase was dramatic despite the fairly small amount (1.1 mg) present in the tomato juice. The significant interactions observed for phytoene (treatment \( \times \) age) and phytofluene (treatment \( \times \) preintervention baseline) may not be biologically relevant, given that they were not consistent for the two watermelon treatments.

The means for plasma lycopene at wk 0 (374–452 nmol/L) are similar to the 50th percentile value of 410 nmol/L for adults over age 20 \( \gamma \) based on data from NHANES III (54) and baseline values from previous studies (55,56). The population marginal means (LSM) at wk 0 baseline in the present study, although lower than those in some studies (12,44), were not atypical. The LSM for plasma lycopene after 3 wk of consumption of dietary treatments including watermelon or tomato juice ranged from 960 to 1183 nmol/L, values that are consistent with lycopene supplementation studies (13,18) and also within ranges reported for free living adults (44,54). NHANES III data show that the 50th, 90th and 99th percentiles for mean, 1-d intake of lycopene from food are 2.1, 22.3 and 65.5 mg/d, respectively (57). The dietary intervention with T-20 and W-20 treatments was within the 90th percentile for usual intake for the U.S. diet, whereas that for W-40 was close to the upper end of the typical U.S. intake. If the mean lycopene concentration of watermelon is 4.800 \( \mu \)g/100 g (21) and 1 wedge (1/6th) of a medium-sized watermelon weighs \( \sim \)286 g, and \( \sim \)48% or 137 g of this is the edible portion (27), then 20 mg of lycopene could be obtained from three wedges of watermelon. Similarly, if 1 cup diced watermelon (152 g edible portion) provides a mean of 7.3 mg lycopene, then 2 \( \frac{1}{2} \) cups of watermelon would provide 20 mg of lycopene. The dose of lycopene provided and resulting plasma levels in this study are physiologically relevant based on these comparisons.

In healthy human subjects, in the presence of ample fat, lycopene was bioavailable from watermelon juice and produced an increase in plasma lycopene similar to that of tomato juice. This is the first report to demonstrate that lycopene is bioavailable from a watermelon product. We used watermelon in juice form to provide a consistent product across the months of controlled feeding. This would not have been possible with the whole fruit because of the large interindividual variability in lycopene content of watermelons (58). Although use of the juice limits the extrapolation of our data to whole watermelon, the juice contained pulp from fresh watermelon and was not heat processed, factors supporting the concept that lycopene is bioavailable from whole watermelon.

In conclusion, we evaluated lycopene bioavailability from two food sources, with no additional heat treatment, and found that lycopene was bioavailable from both fresh-frozen watermelon and canned tomato juices. Plasma concentrations of lycopene were significantly and similarly elevated from 18 to 20 mg lycopene per day from fresh-frozen watermelon juice or canned tomato juice. Heat treatment was not necessary for lycopene absorption from watermelon juice. There was no apparent dose–response effect for plasma lycopene when the amount of watermelon juice consumed was doubled. Watermelon may serve as a bioavailable source of lycopene in the diet.

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LITERATURE CITED


