Telephone Counseling Intervention Increases Intakes of Micronutrient- and Phytochemical-Rich Vegetables, Fruit and Fiber in Breast Cancer Survivors


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ABSTRACT Although a large body of evidence suggests that diet may play an important role in cancer prevention, randomized controlled trials reported to date have not achieved sufficient increases in protective micronutrients and phytochemicals to adequately test the hypothesis that diet can reduce cancer risk. The Women’s Healthy Eating and Living (WHEL) Study, a randomized controlled trial of the role diet modification may play in future breast cancer events, introduced an innovative theory-based telephone counseling intervention to teach participants to consume a high fiber, low fat diet emphasizing vegetables and fruits rich in carotenoids and other potentially protective phytochemicals. This report examines the baseline to 12-mo changes in dietary intakes of 2970 participants, assessed through 24-h recalls and validated with plasma carotenoid concentrations. At 12 mo, the intervention group reported a significantly increased daily vegetable intake (+vegetable juice) of 7.1 servings (+82%) and fruit intake of 3.9 servings (+18%). Fiber intake increased from 3.04 to 4.16 g/(MJ d), whereas energy from fat decreased significantly from 28.6 to 23.7%. Plasma carotenoid concentrations increased significantly, i.e., α-carotene (+223%); β-carotene (+87%); lutein (+29%); and lycopene (+17%). In the comparison group, dietary intake and plasma carotenoid concentrations were essentially identical to those of the intervention group at baseline and were unchanged at 12 mo. The WHEL Study showed that a telephone counseling intervention can achieve major increases in micronutrient- and phytochemical-rich vegetables, fruit and fiber intakes, enabling an investigation of the potential cancer preventive effects of these food components.


KEY WORDS: • diet intervention • cancer prevention • breast cancer • telephone counseling

Current guidelines for the dietary pattern most likely to prevent cancer include a high consumption of vegetables and fruits and reduced intake of fat, especially animal fat (1–3). This dietary pattern emphasizes increased intakes of protective micronutrients and phytochemicals (such as carotenoids, flavonoids, terpenes, indoles and phenols) provided by dark green and orange vegetables, cruciferous and allium vegetables, tomatoes and citrus fruits (1,3–5). However, <5% of the adult female population in the United States reports consuming this recommended pattern (3). Thus, for most, adherence to the guidelines will require a large change in dietary pattern, and this change should lead to at least a 50% increase in circulating carotenoids, one recognized biomarker for nutrient-rich vegetable/fruit consumption (6–8).

Although considerable research supports the hypothesis that the recommended dietary pattern may help protect against cancer, crucial randomized trial evidence is missing. One problem is that interventions in trials have focused on increasing fruits and vegetables generally (9), and adherence to this general advice often does not lead to an increased consumption of protective micronutrients and phytochemicals (10). Such a result occurred in the Polyp Prevention Trial in which a 50% increase in self-reported vegetable and fruit consumption translated into only a 14% increase in serum total carotenoids at 12 mo and a much more modest 5% increase at 4 y (11,12).

To obtain an improved test of the role protective micronutrients and phytochemicals may play in cancer, the Women’s Healthy Eating and Living (WHEL) Study (9) introduced...
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an innovative intervention to motivate women to make major changes to their dietary pattern, i.e., frequent scheduled telephone counseling provided an individually tailored intervention based on social cognitive theory (13,14). This study is an ongoing multicenter, clinical trial designed to test whether diet change can reduce the risk of future breast cancer-related events (15). Broad, easily understandable behavioral goals were provided to help women achieve the target dietary pattern. Intervention participants were asked to consume a diet that included 5 vegetable servings/d, 16 oz (480 mL)/d of vegetable juice, 3 fruit servings/d, 30 g/d fiber and <20% of energy from fat. The vegetable juice goal was explained as a way of maximizing vegetable nutrients without excessive bulk. To minimize common increases in vegetable and fruit consumption that do not optimally meet cancer prevention goals (e.g., iceberg lettuce, French fried potatoes) (10), the study emphasized choosing colorful and flavorful vegetables and fruits with a higher content of potentially beneficial micronutrients and phytochemicals. A feasibility study showed that this intervention protocol could result in a major difference in plasma carotenoids between study groups at both 12 and 36 mo (16,17).

In this report, we describe the effectiveness of this intervention protocol in achieving major changes in the overall dietary pattern in the WHEL randomized trial. We provide evidence that this intensive intervention helped create differences between the study groups in the intake of vegetables and fruits reported to be rich in protective micronutrients and phytochemicals. Finally, we report plasma carotenoid concentrations for a random subsample as a validation of self-reported dietary intake.

SUBJECTS AND METHODS

Study population. This analysis includes all 2970 WHEL Study participants with complete dietary data at baseline who had not had a study end point (e.g., breast cancer event) by the 12 mo follow-up. The WHEL cohort includes 3088 women who were between the ages of 18 and 70 y when diagnosed with early stage breast cancer within the 4 y preceding study enrollment. Details of the study design and cohort characteristics, including evidence of the close comparability of study groups at baseline, have been published (15). The 2970 participants in the current analysis had an average age of 52 y and a mean BMI of 27.3 kg/m² at baseline. Over 50% had attended college, and 14% identified themselves as minorities. Approximately 40% had been diagnosed with a stage I (≥1 cm) breast cancer, 55% with Stage II and 5% with Stage IIIA.

Dietary assessment. Dietary intake was assessed through a set of four 24-h dietary recalls. Trained dietary assessors conducted these recalls over the telephone on randomly selected days that were stratified for weekend vs. weekdays over a 3-wk period. This paper reports on the baseline (before randomization) and 12-mo assessments. Quality assurance measures are reported elsewhere (15), and these include teaching participants to accurately estimate food intake (with food models, measuring cups, and spoons) and a multipass software-driven recall protocol. We used the Minnesota Nutritional Data System software to collect and estimate dietary and nutrient intakes (NDS version 4.01, 2001, University of Minnesota, Minneapolis, MN).

Participants were trained to estimate servings of vegetables, fruits, whole grains, and legumes using household measurements (volume rather than weight) as described in national dietary guidance documents (21). Printed documentation outlined a vegetable serving as ½ cup (120 mL) of cut-up vegetables, 1 cup (240 mL) of raw leafy green vegetables or 4 oz (120 mL) of 100% vegetable juice. A fruit serving was ½ cup (120 mL) of cut-up fruit, ¼ cup (60 mL) of dried fruit, 1 medium piece of fresh fruit (~100 g), or 4 oz (120 mL) of 100% fruit juice. A legume serving was defined as ½ cup (120 mL) cooked legumes (dried peas, beans, or lentils) or equivalent, and a whole grains serving was defined as 1 slice (309 g) of whole grain bread or ½ cup (120 mL) cooked whole grain product or equivalent.

Green vegetable servings included dark green leafy vegetables such as spinach, chard, greens, romaine and other dark green lettuce, bok choy, and leaf vegetables green throughout (not just the skin) such as broccoli. Orange vegetables included carrots, winter squash and sweet potatoes. Only cruciferous vegetables are reported as g/d, because cruciferous vegetables are included in other vegetable groups depending on their color (as an indicator of carotenoid content). For example, broccoli is included in the green vegetable group and cauliflower is included in the other vegetable group. Fatty acids included in (n-3) fatty acids are linolenic acid [18:3(n-3)], eicosapentaenoic acid [20:5(n-3)], and docosahexaenoic acid [22:6(n-3)].

At baseline, 90% of the participants had completed four dietary recalls, and 10% had completed three recalls. At 12 mo, 85% had completed four recalls, whereas 15% had completed three recalls. The comparability of the study groups on baseline dietary intake from these assessments as well as from FFQ was reported previously (15,18).

Validation of dietary intake. This study used plasma carotenoid concentrations as a biomarker of vegetable and fruit intake. Blood was collected, separated, and stored at −80°C during a scheduled study clinic visit at baseline and 12 mo. Height, weight, and waist and hip circumferences were also measured at the clinic visit and BMI was calculated. All participants completed the baseline visit and ~80% completed the 12 mo visit. Plasma carotenoids were measured for a random 27% sample of participants; a-carotene, b-carotene, lutein/zeaxanthin, lycopene and b-cryptoxanthin were separated and quantified using a HPLC method that was described previously (19). Zeaxanthin and lutein elute together with this method; thus, values presented as lutein are assumed to be lutein + zeaxanthin. The laboratory participates in the National Institute of Standards and Technology Standard round-robin quality assurance program, and a pooled plasma sample was analyzed with batches of study samples to monitor analytical precision, with day-to-day CV <10%.

Plasma total cholesterol concentrations were determined with the Kodak Ektachem Analyzer system (Johnson & Johnson Clinical Diagnostics, Rochester, NY) (20) and used in the interpretation of plasma carotenoid data (6). Standard reference materials from the manufacturer were used to validate the analytical precision of these procedures.

The intensive intervention and comparison group activities

Intervention group. The study used telephone counseling as the principal method to promote dietary change in the intervention group. Monthly cooking classes and monthly newsletters supported this individualized counseling. Each cooking class featured a nutrition theme to promote adherence and understanding of the intervention dietary pattern, and gave women an opportunity to taste new foods and learn to prepare recipes. The newsletters featured research updates, nutrition information and recipes to help motivate women to adopt and maintain the intervention dietary pattern.

The dietary counseling was provided by telephone from the WHEL Study coordinating center. Dietary counselors were trained in motivational interviewing techniques (13) and followed a three-phase protocol using strategies outlined by social cognitive theory (14). Phase 1 focused on education and the rapid development of self-efficacy to help participants realize that they could change their dietary intakes; phase 2 taught participants to self-monitor their dietary intake and overcome potential barriers to practical implementation of the dietary pattern; and phase 3 served as a motivational reminder of the study dietary pattern and a chance for counselors to help prevent relapse.

Comparison group. Women randomized to the comparison group received print materials that included dietary guidelines from the U.S. Department of Agriculture (21) and the National Cancer Institute (2), including the 5-a-Day program (22). They were also invited to four cooking classes based on food themes that focused on topics other than vegetables, fiber and fat (e.g., calcium). This group received a bimonthly cohort maintenance newsletter with updates.
about the study and general health and nutrition information unrelated to the intervention group’s dietary goals.

**Statistical methods.** Of the study sample, 304 women (10.2%) did not provide 24-h dietary recalls at 12 mo. This report uses a conservative intent-to-treat analysis that assumes these women had not changed their dietary pattern from baseline. We estimated distributions of average daily intakes of fruit servings, vegetable servings, fiber (g/MJ), and the percentage of energy from fat by study group at 12 mo. In addition, we computed intakes (means ± SEM) for categories of vegetables, fruit, legumes, whole grains, fiber, fat, and selected vitamins and minerals; we present 95% CI for change in these nutrients between baseline and 12 mo. Nonoverlapping CI indicate significant differences between the study groups. P-values for within-group differences over time were computed using paired t tests.

Mean plasma carotenoid concentrations at baseline and 12 mo were compared across time using paired t tests within each study group. Mixed-effects models (23) were used to assess the time profiles of plasma carotenoid concentrations by study group, while accounting for correlations in outcome due to repeated measures and to adjust for influencing factors, such as BMI and cholesterol concentrations. In these models, plasma concentrations were transformed via the natural logarithm (ln) to improve normality and to stabilize the variance. Separate models were developed for each response variable, namely, plasma concentrations (log-transformed) of α-carotene, β-carotene, lutein, lycopene and β-cryptoxanthin. The intercept term was included as a random effect, whereas group assignment, time, group by time interaction, BMI and cholesterol concentrations were modeled as fixed effects. Parameter (slope) estimates with standard errors are presented. Inference was based on standard asymptotic theory, and residual plots were used to investigate model fit (23). All analyses were performed using the Statistical Analysis System (version 8.01, SAS Institute, Cary, NC) and S-Plus (version 5, Insightful, Seattle, WA).

**RESULTS**

**Vegetable and fruit intake.** The distribution of vegetable and fruit intake did not differ between study groups at baseline (15). The comparison group distribution at 12 mo (Fig. 1A) was unchanged from that observed at baseline (3.9 ± 0.04 vegetable servings/d and 3.3 ± 0.04 fruit servings/d) (Table 1). Approximately 17% of the comparison group reported consuming an average of >10 servings/d and 27% reported consuming fewer than 5 servings/d.

The intervention group markedly increased their fruit and vegetable intake, i.e., at 12 mo, mean intakes were 7.1 servings/d of vegetables and 3.9 servings/d of fruit; 58% reported consuming 10 or more servings of fruits + vegetables/d, whereas only 9% reported consuming fewer than 5 servings/d.

The intervention group increased their consumption of green vegetables by ~60%, orange vegetables by 75%, tomatoes and tomato products by 30%, cruciferous vegetables by 50% and legumes by 25% (Table 1). Intakes of white potatoes and iceberg lettuce decreased by 30% (data not shown). The observed increase in vegetable consumption was facilitated in part by a marked increase in vegetable juice consumption (averaging 232 mL/d at 12 mo). Consumption of citrus fruit, berries and other fruit all increased by 50%. There was a significant 25% reduction in fruit juice consumption (P < 0.0001). In contrast, the comparison group made minimal changes to their vegetable and fruit intake.

**Dietary fiber.** Study groups had similar distributions of dietary fiber consumption at baseline, averaging 3.03 ± 0.02 g/(MJ · d) (15). At 12 mo, the intervention group reported an increase in fiber consumption: on average, this group consumed 4.16 g/(MJ · d) with only 20% consuming <2.87 g/(MJ · d) [12 g/(1000 kcal · d)] and 39% consuming >4.3 g/(MJ · d) [18 g/(1000 kcal · d)] (Fig. 1B). Consumption of soluble and insoluble fiber increased significantly by ~30% (P < 0.0001), and intakes of whole grains and whole grain products increased significantly by ~20%. In the comparison group, the pattern of fiber intake remained unchanged, with 46% of the group consuming <2.87 g/(MJ · d) and only 14% consuming >4.3 g/(MJ · d).

**Energy from fat.** At baseline, the percentage of energy from fat did not differ in the intervention and comparison groups (28.6 ± 0.13%) (Table 1). At 12 mo, the intervention group reported a mean intake of energy from fat of 23.7 ± 0.2%, with 36% consuming <20% energy from fat and 19% consuming >30% energy from fat (Fig. 1C). Intakes of saturated fat declined by 20%, polyunsaturated fat declined by 15%, monounsaturated fat declined by 20% and (n-3) fatty acids declined by 15%.

In the comparison group, the percentage of energy from fat did not change significantly from baseline. Only 12% of the comparison group reported consuming <20% energy from fat at 12 mo and 41% reported consuming >30% energy from fat. A small but significant decrease in intakes of saturated fat and (n-3) fatty acids was observed in the comparison group.

![Figure 1A](https://example.com/figure1a.png)

**Figure 1A** Mean daily fruit and vegetable servings (upper panel), fiber intake [g/(MJ · d)] (middle panel) and the percentage of energy from fat (lower panel) at the 12 mo follow-up for the 2970 breast cancer survivors in the Women’s Healthy Eating and Living (WHEL) Study who did (Intervention) and did not (Comparison) receive telephone counseling.

![Figure 1B](https://example.com/figure1b.png)

**Figure 1B** Daily fiber g/(MJ·d) for the 2970 breast cancer survivors in the Women’s Healthy Eating and Living (WHEL) Study who did (Intervention) and did not (Comparison) receive telephone counseling.

![Figure 1C](https://example.com/figure1c.png)

**Figure 1C** Percentage energy from fat for the 2970 breast cancer survivors in the Women’s Healthy Eating and Living (WHEL) Study who did (Intervention) and did not (Comparison) receive telephone counseling.
Other Nutrients. Other changes in nutrient intakes were also observed (data not shown). The intervention group increased their folate intake by 35% (P < 0.001) (compared with a 7% increase in the comparison group) and increased their vitamin C intake by 50% (P < 0.001) (no change in the comparison group). Magnesium intake increased by ~16% (P < 0.001) in the intervention group, whereas there was a slight 3% decrease in the comparison group (P < 0.05).

Change in plasma carotenoids. Plasma α-carotene concentrations were similar in the analyzed samples of both study groups at baseline (mean 0.230 μmol/L) (Table 2). At 12 mo, α-carotene concentration in the intervention group had increased twofold to 0.749 μmol/L, whereas mean α-carotene concentration remained unchanged in the comparison group. Plasma β-carotene concentrations were similar in both groups at baseline. At 12 mo, β-carotene concentration had increased significantly by 87% to 1.749 μmol/L in the intervention group (P < 0.05), with no significant change in the comparison group. Plasma lutein concentrations were also similar in both groups at baseline (0.407 μmol/L) but only the intervention group's lutein concentration had increased significantly at 12 mo (increasing by 29%). Plasma lycopene concentration similarly increased significantly in the intervention (17%) but not in the comparison group. β-Cryptoxanthin concentration did not differ either between or within groups at baseline and 12 mo. At 12 mo, the plasma total carotenoid concentrations were 66% higher in the intervention group than in the comparison group (P < 0.001).

The mixed models analysis was parameterized in such a way that the intercept corresponds to the comparison group mean plasma concentration and the “Group” term denoted the contrast between the intervention and comparison groups (Table 3). As expected, there were no group differences at baseline (lack of significance of the “Group” term) or differences across time for the comparison group (lack of significance of the “Time” term). The group-by-time interaction was significant for all plasma carotenoid concentrations, indicating that, after adjusting for BMI and plasma cholesterol concentration, the intervention group had significant increases in plasma concentrations of α-carotene, β-carotene, lutein and lycopene.

DISCUSSION

The results of this intent-to-treat analysis indicate that the WHEL Study intervention was successful in changing the dietary pattern of the intervention group, while minimizing a change in the dietary pattern of the comparison group, as evidenced by dietary assessment and differences between accepted plasma biomarkers of vegetable and fruit intake. To our knowledge, the degree of change in the dietary pattern observed in the intervention group participants in this study considerably exceeds that reported in earlier cancer prevention studies.

The change was achieved by altering the distribution of key dietary factors including vegetables, fruit, fiber and energy from fat. Given the importance of vegetables as a source of cancer-protective dietary constituents (4), including vegetable juice as a dietary target, helped to maximize the intake of micronutrients and phytochemicals, while minimizing potential side effects of very high fiber diets (24). It is important to note that although the dietary pattern led to substantial increases in participants’ β-carotene concentrations, the level
attained was lower than levels observed in previous \( \beta \)-carotene supplement studies \( [46\% \text{ lower than those attained in the Beta-Carotene and Retinol Efficacy Trial (25), and 31\% lower than those attained in the Alpha-Tocopherol, Beta Carotene Cancer Prevention study (26)] \}. The intervention appeared to be successful in modifying the overall dietary pattern to emphasize foods thought to be important in cancer prevention. If participants maintain these changes, this study is expected to have the power to address the question of whether such a dietary pattern can improve prognosis in women with early stage breast cancer.

This study differs from other cancer prevention trials through its use of an innovative health communication and behavior change approach. Although the intervention also included the more standard dietitian-led cooking classes and supplementary printed materials, the primary intervention strategy was telephone counseling provided from a centralized resource where a research dietitian (V.A.N.) supervised counselors. A standard counseling protocol delivered through scheduled telephone calls allowed the intervention to adhere closely to the principles of social cognitive theory (14) and be tailored to participants’ needs. Goal setting was an important component of the counseling program, and the counselor participated in performance review and judgment in a relapse-sensitive protocol (27,28). Motivational interviewing techniques optimized the counselors’ communication with participants (13).

Equally important to the primary WHEL Study design objectives is the evidence that the comparison group did not substantially change their dietary pattern. We cannot determine whether the absence of dietary change in this group is due to the absence of telephone counseling, the lower frequency of other intervention-oriented contacts or the difference in dietary recommendations; however, what we offered to the comparison group might be regarded as a minimal intervention, i.e., printed materials, quarterly cooking classes and bimonthly newsletters.

Women who have been diagnosed with breast cancer are one of the population groups most likely to change their dietary intake in response to intervention efforts (29). Indeed, after diagnosis and before enrollment, our study population reported considerable change toward the recommended cancer prevention dietary pattern (30). That the comparison group did not change their dietary intake between baseline and 12 mo suggests that women motivated by their cancer diagnosis to change their diets had already done so before study enrollment. The study allowed women to enroll up to 4 y after diagnosis, and the average time from diagnosis to randomization was almost 24 mo (15).

Although a large-scale dietary change that was specific to the intervention group is a major strength of this study, the overall baseline dietary pattern that was maintained in the comparison group is quite different from the dietary pattern of women in the general population. Dietary intake data show that in the mid-1990s, 26\% of U.S. women aged 40–59 consumed two or more fruit servings/d, which was half the level observed at baseline in our study; 49\% consumed three or more vegetables servings/d (compared with 69% in our study); 11\% chose colorful vegetables as at least one third of their vegetable servings (compared with 35% in our study). For fat and fiber intake, only 33\% of U.S. women consumed <30\% percent of energy from fat (compared with 58% in our study), and 42\% consumed <10\% of energy from saturated fat (compared with 55\% in our study) (3). Thus, breast cancer survivors appear to be far more motivated to introduce dietary changes than the general population, and application of the study intervention to the general population might not achieve as large a change.

### TABLE 2

**Plasma carotenoid concentrations at baseline and 12 mo in breast cancer survivors in the Women’s Healthy Eating and Living (WHEL) Study who did (Intervention) and did not (Comparison) receive telephone counseling**

<table>
<thead>
<tr>
<th>Carotenoid/Term</th>
<th>Coefficient ± se</th>
<th>Repeated measures P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \alpha )-Carotene</td>
<td>-0.046 ± 0.036</td>
<td>0.21 *</td>
</tr>
<tr>
<td>( \beta )-Carotene</td>
<td>0.026 ± 0.051</td>
<td>0.66</td>
</tr>
<tr>
<td>Lutein</td>
<td>0.012 ± 0.019</td>
<td>0.25</td>
</tr>
<tr>
<td>Lycopene</td>
<td>-0.024 ± 0.034</td>
<td>0.66</td>
</tr>
</tbody>
</table>

**Mixed models of log-transformed plasma carotenoid concentrations subsample (n = 791) of breast cancer survivors in the Women’s Healthy Eating and Living (WHEL) Study who did (Intervention) or did not (Comparison) receive telephone counseling**

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1 Models were adjusted for BMI and plasma cholesterol concentration.
The group targeted for behavior change in the present study, i.e., women who have been diagnosed with primary breast cancer and who have completed initial treatments, comprises an expanding population of individuals in whom diet may have an important effect on prognosis or risk of future breast cancer events (31). Numerous ecological and analytical epidemiologic investigations and laboratory studies have suggested that dietary factors may influence the risk of breast cancer. It is biologically feasible, and even likely, that factors influencing the risk for the primary breast cancer could continue to exert an influence on the progression of cancer, including risk for recurrence and new primary breast cancer. Results from several epidemiologic studies suggest that a pre-diagnosis diet that is high in micronutrients provided by vegetables and fruits and low in fat may be associated with improved prognosis (32–43). Diet intervention studies targeting this population have shown reductions in dietary fat intake (44–46), but substantially smaller increases in intakes of fiber and vegetables compared with the WHEL Study.

This trial is an efficacy study on the effect of a major change in dietary pattern on prognosis after breast cancer, and we did not consider preenrollment dietary pattern among the criteria for enrollment. However, women self-selected into this clinical trial, and more educated women appeared to be much more likely to volunteer than the general population of women who had been diagnosed with early stage breast cancer, thus limiting our ability to generalize the results to the entire population of breast cancer survivors.

There is considerable concern about the validity of self-reported measures of dietary pattern (18,47–49) and we documented the probability that ~25% of our population may be low energy reporters (50). A strength of our study is that we can use plasma carotenoid concentrations to validate self-reported intake of colorful vegetables and fruits. A limitation of all studies of dietary pattern is that valid biomarkers for other dietary components, including overall energy intake, fat and fiber, are not feasible for large trials.

In summary, results from this study demonstrate that an intensive intervention based primarily on telephone counseling, supplemented by cooking classes and monthly newsletters, can produce a substantial change in overall dietary pattern, with significant increases in micronutrient- and phytochemical-rich vegetables, fruit and fiber. The magnitude of the change in intakes of vegetables, fruit, fiber and fat will permit testing the effect of the scale of differences in dietary intake observed in cross-cultural comparisons. Although women diagnosed with breast cancer may be highly motivated to change their behavior to reduce their cancer risk, the dietary intervention methodology is likely to be applicable in other areas in which diet modification may be efficacious for disease prevention.

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LITERATURE CITED


