A combination of prebiotic short- and long-chain inulin-type fructans enhances calcium absorption and bone mineralization in young adolescents[1-4]

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ABSTRACT

Background: Short-term studies in adolescents have generally shown an enhancement of calcium absorption by inulin-type fructans (prebiotics). Results have been inconsistent; however, and no studies have been conducted to determine whether this effect persists with long-term use.

Objective: The objective was to assess the effects on calcium absorption and bone mineral accretion after 8 wk and 1 y of supplementation with an inulin-type fructan.

Design: Pubertal adolescents were randomly assigned to receive 8 g/d of a mixed short and long degree of polymerization inulin-type fructan product (fructan group) or maltodextrin placebo (control group). Bone mineral content and bone mineral density were measured before randomization and after 1 y. Calcium absorption was measured with the use of stable isotopes at baseline and 8 wk and 1 y after supplementation. Polymorphisms of the *Fok1* vitamin D receptor gene were determined.

Results: Calcium absorption was significantly greater in the fructan group than in the control group at 8 wk (difference: $8.5 \pm 1.6\%$; $P < 0.001$) and at 1 y (difference: $5.9 \pm 2.8\%$; $P = 0.04$). An interaction with *Fok1* genotype was present such that subjects with an *ff* genotype had the least initial response to fructan. After 1 y, the fructan group had a greater increment in both whole-body bone mineral content (difference: 35 ± 16 g; $P = 0.03$) and whole-body bone mineral density (difference: 0.015 ± 0.004 g/cm^2; $P = 0.01$) than did the control group.

Conclusion: Daily consumption of a combination of prebiotic short- and long-chain inulin-type fructans significantly increases calcium absorption and enhances bone mineralization during pubertal growth. Effects of dietary factors on calcium absorption may be modulated by genetic factors, including specific vitamin D receptor gene polymorphisms. *Am J Clin Nutr* 2005;82:471–6.

KEY WORDS Calcium absorption, vitamin D receptor, stable isotopes, inulin, prebiotics, pubertal growth, bioavailability

INTRODUCTION

Absorption of an adequate amount of calcium is particularly important during early adolescence to help achieve peak bone mass. The current recommended daily intakes of calcium are largely based on dose-effect relations to maximize net calcium retention, which in adolescents is primarily determined by calcium absorption (1). In addition to dietary intake, intestinal absorption is a key factor that controls the retention of calcium. This is especially important, given the large disparity between recommended and typical intakes of calcium in adolescents.

Recent data have shown that prebiotic inulin-type fructans (ITFs) added to the daily diet significantly increase the absorption of both calcium and magnesium in growing animals and in adolescents. Numerous animal studies have shown that ITFs significantly increase calcium absorption (2) and bone mineralization (3). In humans, the most convincing data, up until now, have been obtained in adolescents (4–6) and in postmenopausal women (7, 8). These data suggest that a mixed short and long degree of polymerization (DP) fructan product is most effective for enhancing mineral absorption (2, 5, 6).

However, all of the reported studies in humans have been relatively short term and none have directly assessed the potential benefits of supplementation with ITFs on bone mineralization. It is important that such data be available in considering the inclusion of ITFs in the diet on a daily basis, as would occur with more widespread food fortification with ITF. We therefore evaluated the effects of a mixed short- and long-DP fructan on calcium absorption and bone mineralization in young adolescents. We further sought to evaluate the interactions of genetic factors in the response of calcium and bone mineral metabolism to ITFs.

SUBJECTS AND METHODS

Subjects

Through public advertising, we identified 50 girls and 50 boys for this study. All subjects were between 9.0 and 13.0 y of age and had a body mass index between the 5th and 95th percentiles for age and sex. The subjects were selected to approximately match the ethnic distribution of the greater Houston area. All subjects received a screening physical examination, which included Tanner staging. To be enrolled in the study, the subjects had to be healthy and have a Tanner stage of 2 or 3 (breast stage for girls and pubic hair stage for boys). Girls had to be premenarcheal. Subjects with any chronic illnesses requiring them to take medications regularly were ineligible for the study.

Written informed consent was obtained from a parent or legal guardian for each subject; written assent was obtained from all of the study subjects. The Institutional Review Board of Baylor College of Medicine and Affiliated Hospitals approved this protocol.

Initial study visit

Within 8 wk of the screening visit described above, the subjects were admitted for 24 h to the General Clinical Research Center of Texas Children's Hospital in Houston, TX. During this stay, calcium absorption and bone mineralization were measured as described below. Blood was collected for DNA analysis of vitamin D receptor polymorphisms.

At the end of the baseline study, the subjects were randomly assigned in a double-blinded fashion and stratified by sex to 1 of 2 carbohydrate supplement groups: fructan group (8 g/d oligosaccharides of an inulin-type fructan, Raftilose Synergy1; Orafti NV, Tienen, Belgium) or control group (maltodextrin placebo). The ITF was a cospray dried 1:1 mixture of oligofructose (average DP:DP_{av} = 4) and long-chain inulin (DP_{av} = 25). Subjects were instructed to mix the carbohydrate supplement with 180–240 mL of calcium-fortified orange juice and to drink it with breakfast daily for 12 mo. Maltodextrin (Glucidex IT38; Roquette Freres, Lestrem, France) was chosen as the placebo control because, contrary to the ITF, it is completely digested in the upper intestinal tract and does not interfere with the metabolic activity of the colonic flora. Its sensory and other characteristics were virtually indistinguishable from those of the ITF; therefore, it served as a better control than did sucrose. To provide some dietary variation, the subjects were also allowed to use milk to mix the carbohydrate supplement. However, they were provided the orange juice free of charge. Dietary recalls and discussions with families showed that all subjects primarily used orange juice on >95% of the study days.

After 8 wk of receiving the carbohydrate supplement to which they had been randomly assigned, the subjects returned for a repeat calcium absorption study. Twelve months after the initial baseline study, the subjects returned for a follow-up visit during which time calcium absorption and bone mineralization were measured.

Calcium absorption measurements

Stable-isotope studies were performed as previously described (9, 10). Most of the subjects received a breakfast that contained approximately one-third of their daily intake of calcium (including the tracer-containing juice). For subjects with low calcium intakes (<800 mg/d), the total breakfast represented a higher proportion of their total daily calcium intake (≤50%), consistent with their usual dietary practices. Subjects with higher usual intakes had other meal components (primarily dairy products) provide up to an additional 350 mg with their meal, depending on their usual intake. Toward the end of breakfast, the subjects were given 20 μg ^{46}Ca, which had been mixed with 240 mL calcium-fortified orange juice. Different breakfast items were used to reflect the usual pattern of calcium intake of the subjects, but the calcium content of the isotope-containing meals was the same in each subject in all 3 studies.

After breakfast, ^{42}Ca (1.2 mg) was infused over 2 min via a heparin-lock catheter. Beginning with breakfast, a complete 24-h urine collection was obtained. Subsequently, subjects collected a second 24-h urine collection at home after discharge from the General Clinical Research Center (6). Calcium absorption was calculated from the relative recovery of the oral and the intravenous tracers during the entire 48-h study period. A 48-h time period was chosen because of evidence that ITFs may increase the absorption of calcium in the large intestine. This would necessitate a longer collection period than the 24-h time period usually used in such studies to fully identify an effect (5, 11, 12). The subjects were required to note any lost urine or failure to collect a urine sample at home.

Dietary methods

At the screening visit, the study dietitian asked the subjects what foods they usually ate on a normal day to determine food preferences. Inpatient menus for the overnight study visit were based on normal calcium intake (13). All foods and beverages used during the inpatient and outpatient visits were weighed before and after intake to accurately determine intake. The subjects were instructed to keep weighed food records for 6 d during the study: a 2-d period after the first overnight visit, a 2-d period 2 mo later, and a 2-d period after the 1-y visit. The subjects were called at home during the 1-y period to obtain a 24-h dietary recall of the previous day's intake and to ensure that the subject maintained a relatively consistent calcium intake. To reflect the marketplace changes in dietary food contents during the study, dietary intake data were collected with the use of the NUTRITION DATA SYSTEM FOR RESEARCH software (versions 4.03 and 4.05; Nutrition Coordinating Center, University of Minnesota, Minneapolis, MN).

To monitor compliance, subjects were provided with a calendar and instructed to put a sticker on the calendar for every day that they remembered to drink the juice with the supplement. They were instructed to keep all supplement packets after they had mixed them into the orange juice and return them to the research center every 3 mo along with their calendars and any unused supplement packets. The study staff counted compliant days and the number of supplement packets consumed. Subjects were mailed a small gift if they returned their calendars and packets in a timely fashion. If subjects chose to consume the supplement with milk, they were required to indicate this in writing on the calendar.

Analytic methods

Urine samples were prepared for thermal ionization mass spectrometric analysis as previously described by using an oxalate precipitation technique (9, 10). Samples were analyzed for

isotopic enrichment with a magnetic sector thermal ionization mass spectrometer (model MAT 261; Finnigan Bremen, Germany). The accuracy and precision of this technique for natural-abundance samples compared with standard data are 0.15%.

Dual-energy X-ray absorptiometry

Bone mineralization measurements were performed by using a Hologic QDR-4500A dual-energy X-ray (DXA) absorptiometer (Hologic, Inc, Waltham, MA). The whole body was scanned in the fan-beam mode. Whole-body bone mineral content (BMC) and whole-body areal bone mineral density (BMD) were measured. Whole-body BMD precision was <1%, whereas whole-body BMC precision was <1.5% (14, 15).

Genetic methods

Genomic DNA was isolated from 3 mL whole blood collected in EDTA-coated tubes with the use of the Wizard TM Genomic DNA Purification Kit (Promega, Madison, WI). The DNA was analyzed for *Fok1* genetic polymorphisms by the Gene Expression Core of the Texas Coast Digestive Disease Center. The VDR receptor phenotypes (*Fok1*) were analyzed as previously described (16). Primer sequences for *Fok1* were obtained from Mark Johnson, Creighton University School of Medicine, Omaha, NE.

Statistical methods

Comparisons of carbohydrate supplement and genotype groups for fractional absorption of calcium were made by using analysis of variance and analysis of covariance (ANCOVA) techniques, in which changes over the time course of the study were determined by repeated-measures ANCOVA with subsequent determination of differences at specific measurement time points by ordinary ANCOVA. Covariate adjustments were based on the specific analysis conducted. Sex, ethnicity, and Tanner stage at enrollment were included as covariates in models of calcium absorption. These analyses were implemented by using the general linear models (univariate and repeated-measures options) provided in SPSS 13.0 for WINDOWS (SPSS Inc, Chicago, IL). In addition, the proportion of responders with an increase in calcium absorption of ≥3% after 8 wk of the ITF treatment was determined by using the multiple logistic regression option of this program. All data are presented as means ± SEMs.

Sample size was determined on the basis of our earlier study, in which we found a 6% change (SD: 9%) in fractional calcium absorption in girls after adding an ITF to their diet for 3 wk. Therefore, enrollment of 80 subjects had a power >0.9 (P < 0.05) to identify this difference. We enrolled 100 subjects (50 of each sex) based on a 20% dropout rate by 1 y, whereas ultimately only 8% of the subjects failed to complete all aspects of the study.

We have separately reported the relation between vitamin D receptor polymorphisms, including the *Fok1* gene, and calcium absorption and bone mineralization (17). Because we found a significant *Fok1* genotype–related effect on calcium absorption and bone mineralization, *Fok1* genotype was used as a covariate in evaluating the effects of the carbohydrate supplement on calcium absorption and bone mineralization.

TABLE 1
Anthropometric characteristics of the children at baseline[1]

	Fructan group (n = 48)	Control group (n = 50)	P[2]
Age (y)	11.8 ± 0.2[3]	11.4 ± 0.2	0.10
Height (cm)	148.9 ± 1.3	148.3 ± 1.2	0.74
Weight (kg)	42.7 ± 1.3	41.4 ± 1.4	0.48
Tanner stage 2 (%)[4]	73	76	0.73

[1] Children were randomly assigned to receive 8 g/d of either inulin-type fructan or maltodextrin placebo (control).

[2] ANOVA.

[3] $\bar{x} \pm$ SEM (all such values).

[4] All subjects were either Tanner stage 2 or Tanner stage 3.

RESULTS

Subject and dietary description

A total of 100 subjects met the study criteria and were randomly assigned to the fructan or the control group; 98 subjects completed the baseline and 8-wk absorption studies. Both dropouts were from the fructan group, which left 48 subjects in the fructan group and 50 in the control group. One subject dropped out because of a failure to tolerate the ITF (increased stool frequency and diarrhea), and the other subject dropped out because of noncompliance with the study procedures, which was unrelated to the carbohydrate assignment. All other subjects tolerated the study protocol well. Three additional subjects (all in the control group) dropped out between 8 wk and 1 y for personal reasons that were unrelated to the group assignment. At 1 y, 3 additional subjects were unable to complete the absorption studies, but did complete the bone mineral measurements. Thus, the total sample number at 1 y was 95 for the bone mineral measurements and 92 for the calcium absorption measurements.

Anthropometric characteristics of the study subjects are shown in **Table 1**. The mean (±SEM) age of the subjects at the start of the study was 11.6 ± 0.1 y. The fructan group consisted of 24 whites, 5 African Americans, 11 Hispanics, and 8 Asians; the control group consisted of the 28 whites, 9 African Americans, 11 Hispanics, and 2 Asians. Compliance with daily carbohydrate supplementation was not significantly different between groups (84% in the fructan group and 81% in the control group). There was no significant relation between fractional absorption and compliance at any time period.

Total urinary calcium at the 3 time points was compared. Mean (±SEM) urinary calcium was 81 ± 7 mg/d at baseline, 78 ± 5 mg/d at 8 wk, and 87 ± 6 mg/d at 1 y (P = 0.10, repeated-measures analysis of variance). These results suggest no differences in the completeness of the urine samples collected at home and those collected while the subjects were inpatients. There were no differences in urinary calcium between the fructan and control groups at baseline or any time point (P > 0.2 at each time point after correction for ethnicity, sex, and Tanner stage).

Calcium intake was maintained throughout the study at the subject's usual intake, and there were no significant differences in calcium intake between the carbohydrate supplement groups. The mean (±SEM) calcium intake at baseline was 907 ± 33 mg/d, at 8 wk was 959 ± 33 mg/d, and at 1 y was 906 ± 29 mg/d.

TABLE 2
Calcium absorption in the children at baseline, 8 wk, and 1 y[1]

Time of study	Fructan group	Control group	P
	%	%	
Baseline	29.9 ± 1.4 [48][2]	29.4 ± 1.5 [50]	0.76
8 wk[3]	38.5 ± 1.2 [48]	30.0 ± 1.3 [50]	<0.001
1 y[3]	37.7 ± 2.1 [47]	31.7 ± 2.3 [45]	0.04

[1] Children were randomly assigned to receive 8 g/d of either insulin-type fructan or maltodextrin placebo (control). All values were adjusted for genotype, ethnicity, Tanner stage at enrollment, sex, and calcium intake. Repeated-measures analysis of covariance showed a significant interaction of time of measurement and use of fructan ($P = 0.04$). Subsequent comparisons were made by using ordinary analysis of covariance.

[2] $\bar{x} \pm$ SEM; n in brackets (all such values).

[3] Adjusted for calcium absorption at baseline.

Calcium absorption at 8 wk and 1 y

The effects of the fructan and control groups on the fractional absorption of calcium during the study year were compared by repeated-measures ANCOVA at the baseline, 8- wk, and 1-y time points ($n = 92$). After adjustment for ethnicity ($P = 0.04$), sex ($P = 0.54$), *Fok1* genotype ($P = 0.007$), calcium intake at each visit ($P = 0.03$ at baseline; $P > 0.1$ at 8 w and 1 y), and Tanner stage at enrollment ($P = 0.15$), the effect of fructan on the fractional absorption of calcium was significant ($P = 0.02$). The interaction of time point of measurement and carbohydrate group was significant ($P < 0.01$).

We further evaluated the results for calcium absorption at 8 wk and 1 y relative to the baseline absorption values by ordinary ANCOVA (**Table 2**). After adjustment for baseline values and other covariates, calcium absorption was significantly greater at 8 wk (difference 8.5 ± 1.6%, $P < 0.001$) and 1 y (difference 5.9 ± 2.8%, $P = 0.04$) in the fructan group than in the control group.

Inclusion of the 25-hydroxyvitamin D concentration in the model had no effect on the relation between carbohydrate groups and calcium absorption. The 25-hydroxyvitamin D concentration was not significantly related to calcium absorption at 8 wk ($P = 0.83$) or at 1 y ($P = 0.51$).

Effects of genotype on results at 8 wk and 1 y

We previously showed a significant effect of *Fok1* genotype on calcium absorption (16, 17). Therefore, we sought to identify whether there was a nutrient-gene interaction by evaluating whether fractional calcium absorption at 8 wk and 1 y was related to an interaction of genotype with carbohydrate supplementation. The three-factor interaction of genotype with carbohydrate supplementation and time point of measurement was significant ($P = 0.04$). Additionally, the interaction of genotype with carbohydrate supplementation was significant at 8 wk ($P = 0.03$) but not at 1 y ($P = 0.43$). We analyzed each genotype group at 8 wk and 1 y for the effects of the carbohydrate supplement, and the results indicate a preferential effect of fructan in the subjects with genotypes associated with higher calcium absorption (*FF* and *Ff*) at 8 wk (**Table 3**).

Additionally, we determined the proportion of individuals who were "responders" to the carbohydrate supplement. In this analysis, we chose an increase of 3% to represent a responder a priori. This evaluation was only done at the 8-wk time period because there was a mean 2.3% increase in calcium absorption in

TABLE 3
Effect of genotype on calcium absorption in children at 8 wk and 1 y[1]

Fok1 genotype	Fructan group	Control group	P
8 wk			
FF	45.6 ± 1.7 [12][2]	33.2 ± 1.3 [22]	<0.001
Ff	37.3 ± 1.7 [26]	30.2 ± 2.0 [20]	0.02
ff	31.9 ± 1.6 [10]	28.5 ± 1.8 [8]	0.22
1 y			
FF	44.9 ± 4.5 [11]	35.8 ± 3.3 [20]	—
Ff	38.9 ± 2.5 [26]	30.6 ± 3.1 [18]	—
ff	31.0 ± 3.5 [10]	32.1 ± 4.2 [7]	—

[1] Children were randomly assigned to receive 8 g/d of either inulin-type fructan or maltodextrin placebo (control). All values were adjusted for baseline absorption, calcium intake at baseline and 8 wk or 1 y, Tanner stage, sex, and ethnicity. Repeated-measures analysis of covariance showed a significant genotype by carbohydrate treatment by time of measurement interaction ($P = 0.04$). Subsequent pairwise comparisons of genotypes were made by using ordinary analysis of covariance. The interaction of genotype with carbohydrate supplementation was significant at 8 wk ($P = 0.03$) but not at 1 y ($P = 0.43$).

[2] $\bar{x} \pm$ SEM; n in brackets (all such values).

the control group compared with baseline at 1 y, which would have made the 3% definition of a responder difficult to interpret. The interaction of carbohydrate supplement group with *Fok1* genotype was significant in determining responders at 8 wk ($P = 0.01$) with sex, Tanner stage, and ethnicity as covariates. The percentage of responders by genotype is shown in **Table 4**. Overall, 67% (32/48) of the fructan group and 34% (17/50) of the control group were responders ($P = 0.004$).

Bone mineralization results

Comparisons of groups for changes during the study year in whole-body BMC and BMD are shown in **Table 5**. After 1 y, fructan resulted in a greater increase in whole-body BMC (35 ± 16 g; $P = 0.03$) and BMD (0.015 ± 0.004 g/cm^2; $P = 0.01$) than did the control treatment. To calculate the approximate effect of this difference in whole body BMC on daily calcium accretion, we used a factor of 0.322 for the fraction of calcium per mg of BMC (14). This leads to a calculation of an average net difference of 30 mg/d in calcium accretion between groups.

TABLE 4
Percentage of children with an increase in calcium absorption of ≥3% after 8 wk of treatment[1]

Fok1 genotype	Fructan group	Control group	P
	%	%	
FF	92 [12]	18 [22]	0.002
Ff	62 [26]	40 [20]	0.07
ff	50 [10]	63 [8]	0.53

[1] n in brackets. Children were randomly assigned to receive 8 g/d of either inulin-type fructan or maltodextrin placebo (control). All values were adjusted for sex, Tanner stage, and ethnicity. In the initial 2-factor multiple logistic regression, the interaction of genotype by carbohydrate treatment was significant ($P = 0.01$). Subsequent pairwise comparisons of genotypes were made by using a single-factor logistic regression.

TABLE 5
Calcium accretion and bone mineral density (BMD) in the children after 1 y of treatment[1]

	Fructan group (n = 47)		Control group (n = 48)	
	Baseline	Change after 1 y	Baseline	Change after 1 y
Whole-body BMC (g)	1338 ± 35	245 ± 11	1256 ± 35	210 ± 10[2]
Whole-body BMD (g/cm^2)	0.888 ± 0.009	0.047 ± 0.004	0.872 ± 0.009	0.032 ± 0.004[3]

[1] All values are $\bar{x}$ ± SEM and were adjusted for ethnicity, sex, Tanner stage at enrollment, and *Fok1* genotype. Children were randomly assigned to receive 8 g/d of either inulin-type fructan or maltodextrin placebo (control). BMC, bone mineral content.

[2,3] Significantly different from change after 1 y in the fructan group (analysis of covariance): [2] $P = 0.03$, [3] $P = 0.01$.

DISCUSSION

We showed a greater enhancement in calcium absorption and in bone mineralization in young adolescents provided 8 g ITF/d than in those given the same amount of maltodextrin, a placebo control that itself appeared to have had a small effect on calcium absorption in some subjects. Our data further suggest that, at least initially, the magnitude of the benefit was affected by genetic modifiers of calcium absorption, including polymorphisms of the *Fok1* gene.

Although animal studies have uniformly shown enhancement of calcium (and magnesium) absorption by ITF (2, 3), results of investigations in humans have been mixed (12). Recent studies have tended to confirm such an effect in both adolescents (4–6) and in adults (7, 8, 18), but available data are limited by their short-term nature. Our finding of a benefit of ITF after 1 y of use is relevant because a failure to show a persistent change would suggest no clinical benefit of ITF. Indeed, the types of food in which ITF products are likely to be supplemented are products such as yogurts and juices, which are consumed over a long period of time.

We did not evaluate the relation between calcium intake and the magnitude of the effect of the ITF. We chose to give the ITF with a substantial calcium load at breakfast to reflect the equivalent calcium intake of a whole glass of milk or juice given with a typical breakfast for that subject. Future investigations, therefore, need to evaluate the specific effects of ITF on calcium absorption at very low intakes of calcium (eg, <450 mg/d) because such low intakes were not evaluated in the present study.

The mechanism of action of ITF responsible for the enhancement of calcium absorption remains unclear. It may be related to an increased absorption of calcium in the colon by scavenging unabsorbed calcium (11). ITFs typically are fermented in the proximal and distal colon. This fermentation results in the production of short-chain fatty acids (acetate, propionate, and butyrate) and lactate. These may increase the solubility of minerals, enhancing their absorption. Alternatively, it is possible that a trophic effect occurs throughout the intestines that enhances passive calcium absorption (2, 3, 11). In this regard, our finding of an interaction of ITF and *Fok1* genotype suggests that a vitamin D–mediated enhancement of absorption may also be involved. However, this hypothesis is not supported by our failure to find any significant relation between vitamin D status at the start of the study and calcium absorption at 8 wk or vitamin D status at 1 y and calcium absorption at 1 y.

These genetic interactions indicate how difficult it is to determine the effects of a dietary intervention when it is short term or when the sample size is small, especially a dietary intervention that affects trophic gut function. Our study was larger than previous physiologic studies of ITFs. Although even larger population-based studies would be ideal, they are impractical because of the costs associated with the assessment of endpoints such as calcium absorption and bone mineralization in large populations.

The net benefit associated with ITF supplementation in the present study was the average increase in calcium accretion ($\approx$30 mg Ca/d) to the skeleton, an increase equivalent to $\approx$11 g each year during pubertal growth. Although this increase is considerable, it is much less than the deficit of up to 80 g/y that we recently reported to be associated with extremely low-calcium diets providing an average of 450 mg Ca/d (13). Therefore, the addition of an ITF to the diet, although beneficial for net calcium balance, does not have the same magnitude of effect during puberty as do large changes in dietary calcium intake.

Nevertheless, an increase in calcium absorption and bone calcium deposition of 15–20% of the nonsupplemented amount may represent a substantial additional health benefit with negligible risks. Additionally, numerous other potential health benefits are associated with an increased intake of ITF (19). Supplementation with 8 g inulin/d appeared safe for virtually all of the study subjects; gastrointestinal symptoms were reported by only one subjects ($\approx$2%), and these symptoms rapidly resolved after the ITF was discontinued.

It is important to consider the potential public health benefits of advocating enhanced calcium absorption from the diet through the use of more bioavailable calcium sources or, as in the present study, through the use of a nonabsorbable carbohydrate. This issue has been discussed extensively with regard to the relative merits of different sources of calcium in supplements and whether a potential small absorptive benefit of calcium citrate or calcium citrate malate over calcium carbonate is of enough clinical importance to affect the consumers choice of supplement (20, 21). In these cases, a cost-benefit analysis may be useful; however, consumers may choose what they consider to be the optimal supplement on the basis of scientific data, even if that supplement has a higher relative cost per absorbed milligram of calcium.

It is likely that ITFs are, and will likely remain, a premium food and beverage supplement. It is probable that calcium absorption can be increased with a calcium supplement (or increased food and beverage calcium intake) as readily as with an ITF-fortified product. However, these 2 decisions have different benefit and safety profiles. The mineral-absorptive benefit of ITF products is an important component of overall gastrointestinal health, even though this benefit is generally not the primary or sole reason for

their being chosen by consumers. Furthermore, we have shown that a benefit of ITF on calcium absorption exists across a range of calcium intakes (5), which indicates that consumers have several strategies to choose from to enhance their calcium status.

We conclude that the daily inclusion of a modest amount of a commercially available nonabsorbable ITF with a mixture of short and long DP enhances calcium absorption and bone mineralization in pubertal adolescents. Genetic interactions, however, may modulate this affect.

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