

## Effects of oligofructose-enriched inulin on intestinal absorption of calcium and magnesium and bone turnover markers in postmenopausal women

Leah Holloway<sup>1</sup>, Sharon Moynihan<sup>1</sup>, Steven A. Abrams<sup>2</sup>, Kyla Kent<sup>1</sup>, Andrew R. Hsu<sup>1</sup>  
and Anne L. Friedlander<sup>1\*</sup>

<sup>1</sup>Clinical Studies Unit and Geriatric Research Education and Clinical Center, VA Palo Alto Health Care System, Palo Alto, California, USA

<sup>2</sup>USDA/ARS Children's Nutrition Research Center, Baylor College of Medicine, Houston, Texas, USA

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Deficiency of oestrogen at menopause decreases intestinal Ca absorption, contributing to a negative Ca balance and bone loss. Mg deficiency has also been associated with bone loss. The purpose of the present investigation was to test the hypothesis that treatment with a spray-dried mixture of chicory oligofructose and long-chain inulin (Synergy1; SYN1) would increase the absorption of both Ca and Mg and alter markers of bone turnover. Fifteen postmenopausal women (72.2 (SD 6.4) years) were treated with SYN1 or placebo for 6 weeks using a double-blind, placebo-controlled, cross-over design. Fractional Ca and Mg absorption were measured using dual-tracer stable isotopes before and after treatment. Bone turnover markers were measured at baseline, 3 and 6 weeks. Fractional absorption of Ca and Mg increased following SYN1 compared with placebo ( $P < 0.05$ ). Bone resorption (by urinary deoxypyridinoline cross-links) was greater than baseline at 6 weeks of active treatment ( $P < 0.05$ ). Bone formation (by serum osteocalcin) showed an upward trend at 3 weeks and an increase following 6 weeks of SYN1 ( $P < 0.05$ ). Closer examination revealed a variation in response, with two-thirds of the subjects showing increased absorption with SYN1. *Post hoc* analyses demonstrated that positive responders had significantly lower lumbar spine bone mineral density than non-responders (dual X-ray absorptiometry  $0.887 \pm 0.102$  v.  $1.104 \pm 0.121$  g/cm<sup>2</sup>;  $P < 0.01$ ), and changes in bone turnover markers occurred only in responders. These results suggest that 6 weeks of SYN1 can improve mineral absorption and impact markers of bone turnover in postmenopausal women. Further research is needed to determine why a greater response was found in women with lower initial spine bone mineral density.

**Synergy1: Mineral absorption: Bone turnover: Bone density: Oligofructose: Inulin**

Despite recent advances in the pharmacological prevention and treatment of osteoporosis, women who elect not to take hormone or drug therapy are at particular risk of developing osteoporosis. Thus, there remains a substantial need for additional strategies for maintenance of skeletal health after menopause. Oestrogen deficiency at menopause leads to a decrease in intestinal Ca absorption and a corresponding increase in renal Ca excretion, leading to a negative Ca balance that contributes to bone mineral loss (Prince, 1994). Evidence from clinical trials suggests that an increase in Ca balance will positively affect bone mass and bone mineral density (BMD; Prince *et al.* 1995). Although Ca supplementation is not as effective as anti-resorptive agents in maintaining BMD, it has been shown to alter the balance of bone turnover markers (Riggs *et al.* 1998) and to decrease fracture risk in both peri- and postmenopausal women (Report of the North American Menopause Society, 2001). Unfortunately, the solution is not as straightforward as simply consuming more Ca because the percentage absorption is inversely related to intake (Heaney *et al.* 1990) so that increasing Ca intake may be partially negated by a corresponding decrease in the efficiency of Ca absorption.

The primary method of increasing Ca absorption is by increasing circulating levels of 25 hydroxyvitamin D (25(OH) vitamin D) from 'low normal' to 'high normal' (Heaney *et al.* 2003). Another possible way to increase fractional Ca absorption may be through the consumption of non-digestible oligosaccharides such as oligofructose-enriched inulin, a prebiotic carbohydrate (Abrams *et al.* 2005). Non-digestible oligosaccharides may influence Ca absorption indirectly by stimulating hypertrophy of the intestinal mucosa, thereby increasing the surface area for diffusion, or directly by increasing transcellular transport through the production of SCFA (Greger, 1999). These fatty acids may decrease pH, thus allowing an additional exchange of H ions for Ca ions (van den Heuvel *et al.* 2000; Raschka & Daniel, 2005). Oligosaccharides have also been shown to increase the absorption of Mg ions in postmenopausal women (Tahiri *et al.* 2001). Although the role of Mg in bone health is less clear, serum and bone Mg are reduced in postmenopausal women (Yano *et al.* 1985; Cohen, 1988), and supplementation with Mg has been shown to increase bone mass in osteoporotic women (Stendig-Lindberg *et al.* 1993). Therefore, the purpose

**Abbreviations:** 25(OH) vitamin D, 25 hydroxyvitamin D; BMD, bone mineral density; DP, degree of polymerisation; PTH, parathyroid hormone.

\* **Corresponding author:** Dr Anne L. Friedlander, fax +1 650 849 0535, email friedlan@stanford.edu

of the current investigation was to determine whether a product containing oligofructose from chicory plus long-chain inulin enriched with oligofructose (Synergy1; SYN1) could alter Ca and Mg absorption in healthy postmenopausal women. We hypothesised that 6 weeks of treatment with SYN1 would increase the efficiency of intestinal mineral absorption, resulting in a reduction in bone resorption.

## Subjects and methods

### Subjects

Fifteen healthy, free-living postmenopausal women were recruited by letter and flyer from the surrounding community. All participants were a minimum of 10 years past the onset of menopause. Exclusion criteria included use of hormone replacement therapy either currently or within the previous year, use of any pharmacological osteoporosis treatment, use of thiazide diuretics or glucocorticoids, diabetes or any illness known to affect either intestinal absorption or bone metabolism. The protocol was approved by the Stanford University Administrative Panel on Human Subjects in Medical Research and the Institutional Review Board for Human Subject Research of Baylor College of Medicine, and each subject gave written informed consent.

Volunteers underwent a screening visit that included a health history questionnaire, electrocardiogram and routine blood and urine chemistry. At this visit, they were given 3 d food record forms to complete at home. The records were subsequently analysed using a commercially available software program, Nutritionist V (First DataBank, Inc., San Bruno, CA, USA). Participants with intakes of less than 800 mg/d Ca were given a CaCO<sub>3</sub> supplement (500 mg) to take for 3 weeks prior to their first study evaluation (equilibrium phase) and for the remainder of the study. No participant had a Ca intake greater than 1300 mg/d. The data from one subject were deleted from the analysis of mineral absorption due to non-compliance with the urine collection protocol during the 6-week active phase measurement period.

### General study design

Participants were randomised to receive either SYN1 or placebo (completely digestible maltodextrin) in a cross-over fashion for 6 weeks followed by a 6-week washout period. After the washout period, each subject received the other treatment for an additional 6 weeks. Fasting blood and urine samples were collected at baseline, 3 weeks and 6 weeks of each treatment period for measurement of bone turnover markers parathyroid hormone (PTH) and 25(OH) Vitamin D. Measurements were made in the Clinical Studies Unit, VA Palo Alto Health Care System on subjects who had been fasting for 8 or more hours and were well hydrated. Samples were collected between 08.00 and 10.00 hours. Mineral absorption studies were performed at baseline and 6 weeks of each treatment period. Absorption was measured by dual stable isotope on 72 h urine collections. Bone density of the hip and spine was also measured on each subject by dual X-ray absorptiometry at the Musculo-Skeletal Research Laboratory at the Menlo Park Division of the VA Palo Alto Health Care System.

### Intervention treatment

At the start of each intervention period, subjects received packets of either SYN1 or placebo in a randomised, double-blind manner. Participants were instructed to consume one packet with breakfast and one packet with dinner for 6 weeks and to record the time of consumption. They were advised that the packet contents would more easily dissolve in a heated liquid, and it was recommended that the packet be taken with coffee or hot tea.

Each active packet contained 5 g Raftilose Synergy1 (Orafti, Tienen, Belgium), which is a co-spray dried 1:1 mixture of chicory oligofructose (a  $\beta(2-1)$  chicory fructan with a degree of polymerisation (DP) of 3–8, average DP 4) and long-chain inulin (a  $\beta(2-1)$  chicory fructan with DP 10–65, average DP 25). The commercial SYN1 product contains 92% fructans and 8% sugars (glucose, fructose, sucrose; Van Loo, 2004). Inulin (DP 3–65, average DP 10) is extracted from chicory roots with hot water. Inulin is present as a storage carbohydrate in such foods as leeks, onions, bananas, garlic and wheat (Van Loo *et al.* 1995). It is resistant to absorption in the small intestine and arrives in the colon where it is selectively fermented. Oligofructose (DP 3–8, average DP 4) is produced by means of a partial enzymatic hydrolysis of inulin. A long-chain inulin fraction (DP 12–65, average DP 25) is extracted from inulin by means of a physicochemical separation technique. SYN1 is a 1:1 combination of oligofructose and the long-chain inulin fraction (Coudray *et al.* 2003). The placebo packets contained a digestible matodextrin.

### Calcium and magnesium absorption testing

Ca and Mg absorption were measured at baseline and at 6 weeks of each treatment period. To measure absorption, each subject was given 22  $\mu$ g stable isotope <sup>46</sup>Ca and 23 mg <sup>26</sup>Mg in 118 ml Ca-fortified orange juice as part of a test meal. The remainder of the standardised test meal consisted of an English muffin with one pat of margarine and one pat of jelly, 118 additional ml Ca-fortified orange juice and 237 ml decaffeinated coffee or tea, providing a total intake of 396 mg Ca and 58 mg Mg. The time of completion of the test meal was recorded. Subjects were then given 1.2 mg <sup>42</sup>Ca and 11.5 mg <sup>25</sup>Mg intravenously over a 30 min period. The intravenous line was flushed with saline after the stable isotopes had been given. Subjects were discharged with collection supplies and an additional 118 ml Ca-fortified orange juice to be consumed with dinner. All voided urine was collected for the next 72 h in two 36 h collection periods. During the 72 h collection period, food intake was recorded using the 3 d food records. These were analysed for Ca and Mg intake using Nutritionist V.

### Calcium and magnesium absorption analyses

Ca and Mg absorption analyses were performed at Baylor College of Medicine Houston, Texas, USA. Ca samples were prepared for mass spectrometric analysis using an oxalate precipitation technique (Yergey *et al.* 1980). Mg samples were prepared using cation exchange chromatography (Vieira *et al.* 1994). Ca isotopic ratios were measured using magnetic

sector thermal ionisation mass spectrometry (MAT 261; Finnigan, Bremen, Germany). Mg samples were analysed by inductively coupled plasma mass spectrometry (ICP-MS) (Vieira *et al.* 1994). A ratio was calculated between each Ca isotope and  $^{43}\text{Ca}$ , and each Mg isotope and  $^{24}\text{Mg}$ .

#### Bone mineral density measurements

BMD in the lumbar spine (L2–L4) and hip was measured using dual X-ray absorptiometry (QDR 4000; Hologic, Waltham, MA, USA). The long-term precision of these measurements in our laboratory is 1.5% at each site for this age group. To reduce the precision error, duplicate measurements were obtained and mean values analysed. Dual X-ray absorptiometry measurements were made in the Musculoskeletal Research Center at the Menlo Park Division of the VA Palo Alto Health Care System.

#### Biochemical analyses

Fasting serum and urine samples were stored at  $-70^{\circ}\text{C}$  until analysed. All biochemical analyses were run on batched specimens in a single-assay run. Human osteocalcin in serum was measured using a commercially available two-site immunoradiometric assay (Diagnostic Systems Laboratories, Inc., Webster, TX, USA). Urinary deoxyypyridinoline cross-links were measured using a competitive enzyme immunoassay kit (Quidel Corp., San Diego, CA, USA) and corrected for urine creatinine. Urine creatinine was measured with a quantitative, colorimetric assay (Quidel Corp). Serum intact PTH was measured using an immunoradiometric assay (Diagnostic Systems Laboratories, Inc.). Serum 25(OH) vitamin D concentrations were measured following extraction with NaOH and acetonitrile using an RIA (IDS Ltd, Boldon, Tyne & Wear, UK).

#### Statistics

Data were analysed using Statview II (Abacus Concepts, Berkeley, CA, USA). Values are presented as mean and their standard errors except where noted. Changes from baseline were calculated for treatment and placebo interventions, and comparisons between interventions were analysed using paired *t* tests. For multiple time points, ANOVA with repeat measures (treatment  $\times$  time) were used. When appropriate, *post hoc* tests for significance were made using Fisher's least significant difference test. Significance was set at  $P < 0.05$ .

## Results

#### Subjects

Fifteen subjects successfully completed the study. One subject was, however, excluded from the analysis owing to non-compliance with the urine collection protocol during the active-phase measurement period. In addition, bone turnover markers and markers of the PTH–vitamin D axis were not measured in an additional subject owing to logistical issues. The baseline characteristics of the subjects are presented in Table 1. There were no significant differences in any

measured variable at baseline visits between the active and the placebo treatment period. All subjects were determined to be vitamin D replete as measured by 25(OH) vitamin D concentration using currently accepted reference ranges.

#### Calcium and magnesium absorption

True absorption of Ca demonstrated a significant increase after treatment with SYN1 (Table 2). In addition, the change in absorption in the active compared with the placebo group was greater for both Ca (+5.1 (SE 2.1) % *v.*  $-3.3$  (SE 2.2);  $P < 0.05$ ) and Mg (+5.2 (SE 2.9) % *v.*  $-4.3$  (SE 3.0);  $P < 0.05$ ). Analyses of starting baseline values and changes in the absorption of Ca and Mg for each phase revealed no order effects or carry-over between treatments.

#### Markers of bone turnover

Deoxyypyridinoline cross-links, an index of bone resorption activity, showed an initial transient decrease at 3 weeks in the SYN1 group ( $P = 0.08$ ) but rebounded to levels greater than baseline by 6 weeks of treatment ( $P < 0.05$  *v.* baseline). There was no significant change in the placebo group and no significant difference between treatments (Fig. 1). Levels of serum osteocalcin, a measure of bone formation activity, were increased at 6 weeks of treatment only in the SYN1 group (Fig. 2).

#### Vitamin D–parathyroid axis

Changes in PTH and 25(OH) vitamin D were measured after 3 and 6 weeks of treatment. There was a non-significant decrease in PTH at 6 weeks in the SYN1-treated group (Fig. 3). No change was observed after 6 weeks of placebo. The average baseline concentration of 25(OH) vitamin D was 25 ng/ml and did not change significantly with treatment in either group.

#### Post hoc analysis

*Post hoc* examination of the data showed that there was a difference in the response to SYN1 between the subjects. For both Ca and Mg, approximately two-thirds of the subjects demonstrated an increase in absorption after treatment, whereas the remaining subjects did not (Fig. 4). Differences in response were not a function of initial absorption values as baseline Mg and Ca absorption was no different between

**Table 1.** Baseline characteristics by treatment group (Mean values and standard deviations)

Variable	SYN1		Placebo	
	Mean	SD	Mean	SD
Age (years)	72.2	6.4	72.2	6.4
Time since menopause (years)	24.7	9.7	24.7	9.7
Body mass index ( $\text{kg}/\text{m}^2$ )	25.1	3.3	25.3	3.2
Ca intake (mg/d)	1086	232	1018	251
Ca supplementation ( <i>n</i> , %)	6, 43%		6, 43%	
Mg intake (mg/d)	298	136	260	98
25 hydroxyvitamin D (ng/ml)	25.0	8.4	24.3	8.0

**Table 2.** Ca and Mg absorption values before and after treatment (Means and their standard errors for fourteen determinations)

True absorption (%)	Baseline		SYN1		Change		Baseline		Placebo		Change	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE
Ca absorption	22.2	2.9	27.3	4.2	5.1	2.1*†	24.1	1.7	20.8	2.4	-3.3	2.2
Mg absorption	51.5	3.0	56.7	3.2	5.2	2.9*	54.6	2.6	50.4	1.7	-4.3	3.0

\* Significantly different from placebo ( $P < 0.05$ ).† Significantly different from baseline ( $P < 0.05$ ).

positive and negative responders. Ca supplementation was also equally distributed between the two groups, and baseline Ca and Mg intake levels did not differ between responder groups. BMD of the lumbar spine was, however, significantly lower in responders compared with non-responders (Fig. 5). Although it is unclear what role normal Mg levels play in bone, it is interesting to note that there was a strong correlation ( $r = 0.777$ ,  $P < 0.001$ ) between baseline bone turnover and response in Mg absorption to treatment with SYN1. In contrast, there was no relationship between baseline bone turnover and the response in Ca absorption ( $r = 0.133$ , NS).

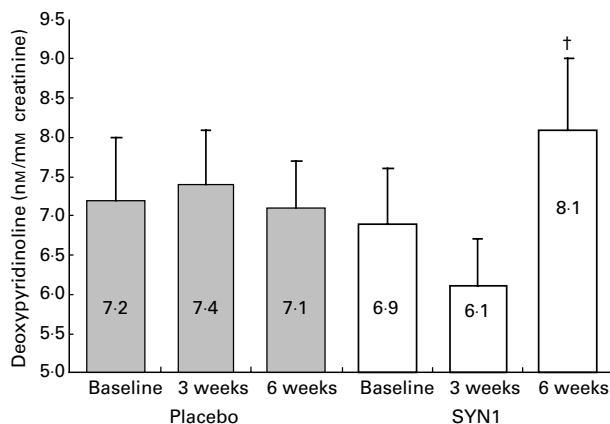
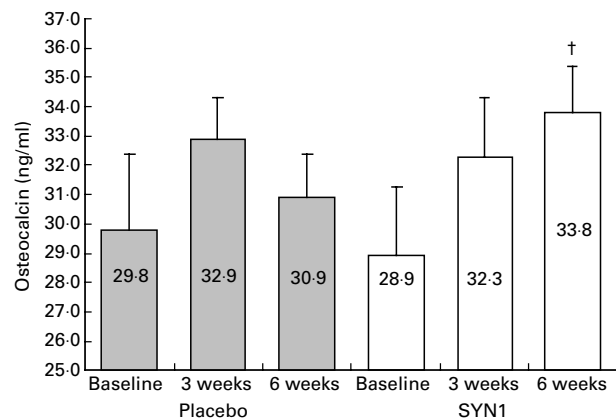
## Discussion

The major finding of this investigation was that 6 weeks of treatment with SYN1 in postmenopausal women resulted in a significant increase in both Ca and Mg absorption relative to the placebo treatment. We hypothesised that the increase in mineral absorption would be followed by a corresponding decrease in bone turnover. Although the bone marker results were not completely clear, a positive balance in formation relative to resorption did seem to be evident at the intermediate 3-week time point. Despite the significant group changes in mineral absorption, there was substantial variability in individual responses to treatment, with the majority of subjects responding by increasing mineral absorption in response to SYN1 treatment, and a subset who did not. Similar patterns have previously been noted in response to oligosaccharide treatment in postmenopausal women (Tahiri *et al.* 2001, 2003). Although reasons for the differences between individuals cannot be definitely

determined from these data, subjects who responded positively to treatment did have lower lumbar spine BMD values than non-responders. A relationship between initial BMD values, bone turnover markers and responsiveness to treatment has previously been described in investigations using some antiresorptive treatments for osteoporosis (Gennari *et al.* 1992).

## Calcium absorption

We observed a significant increase in Ca absorption with non-digestible oligosaccharide treatment in this investigation even though vitamin D status was adequate and Ca intake was good. In rats, it has been demonstrated that treatment with non-digestible fructans successfully increases Ca absorption and results in a corresponding increase in bone mineral (Delzenne *et al.* 1995; Takahara *et al.* 2000; Roberfroid *et al.* 2002; Scholz-Ahrens *et al.* 2002; Coudray *et al.* 2003). Similarly, boys given 15 g chicory oligofructose for 9 d demonstrated increased fractional Ca absorption as measured by a dual-isotope technique (van den Heuvel *et al.* 1999). In young girls, 3 weeks of treatment with either 8 g/d sucrose, oligofructose or SYN1 caused a significant increase in Ca absorption in the group given SYN1 compared with the sucrose group. No significant increase in Ca absorption with oligofructose alone was, however, reported (Griffin *et al.* 2002). The importance of chain length of the chicory fructans on Ca absorption has been demonstrated by Coudray *et al.* (2003). Furthermore, a larger-scale intervention ( $n = 100$ ; placebo and SYN1 8 g/d) for 1 year conducted in prepubescent

**Fig. 1.** Effect of 6 weeks of treatment with SYN1 or placebo on bone resorption as estimated by urinary deoxyypyridinoline cross-link concentration corrected for urinary creatinine. †Significantly different from baseline ( $P < 0.05$ ).**Fig. 2.** Effect of 6 weeks of treatment with SYN1 or placebo on bone formation as estimated by serum osteocalcin concentration. †Significantly different from baseline ( $P < 0.05$ ).

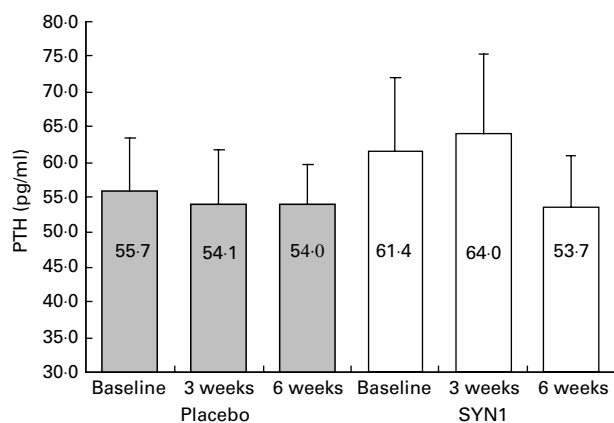


Fig. 3. Effect of 6 weeks of treatment with SYN1 or placebo on parathyroid hormone (PTH).

children demonstrated that the increase in mineral absorption observed after 8 weeks of SYN1 treatment was also evident at 1 year and was associated with enhanced bone mineralisation (Abrams *et al.* 2005).

The presence of oestrogen receptors in the intestine supports the theory that oestrogen may directly increase intestinal Ca absorption (Thomas *et al.* 1993; Prince, 1994). Heaney *et al.* (1989) have estimated that the combined effect of ageing and oestrogen withdrawal at menopause produces a decline in absorptive performance of 20–25% over a 20-year period. Therefore, postmenopausal women could benefit the most from any agent that increases Ca absorption and the Ca load on the system. Indeed, non-digestible oligosaccharide treatment in postmenopausal women has yielded promising results so far. For example, increased Ca absorption has been reported in postmenopausal women treated with 20 g/d transgalacto-oligosaccharides for 9 d (van den Heuvel *et al.* 2000). Although this study utilised a slightly different non-digestible oligosaccharide, the changes observed were similar to those observed in the current investigation.

In contrast to the above studies, a study by Tahiri *et al.* (2003) reported that postmenopausal women treated with non-digestible fructans for 5 weeks (5 g/d for the first 4 d, 10 g/d for the remainder) showed no increase in Ca absorption. The authors postulate that there was an earlier increase in Ca absorption due to treatment, but that the active pathway was downregulated by a feedback mechanism, effectively decreasing Ca absorption to pretreatment levels in order to maintain serum Ca levels within a narrow range. This feedback mechanism may be mediated by a reduction in 1,25 dihydroxyvitamin D followed by a fall in Ca-binding protein. Although the explanation is feasible, we were able to show a significant effect at 6 weeks. As suggested in the study on young girls (Griffin *et al.* 2002), it is possible that the addition of inulin to the oligofructose (SYN1) helped to augment the response in mineral absorption.

#### Magnesium absorption

Mechanisms exist in the intestine and kidney to regulate Mg homeostasis closely. In the intestine, an active transport

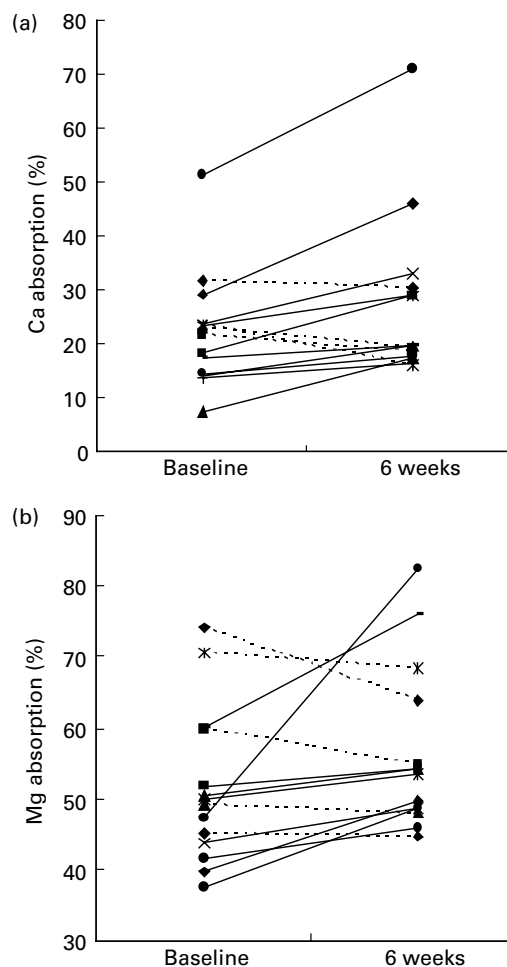
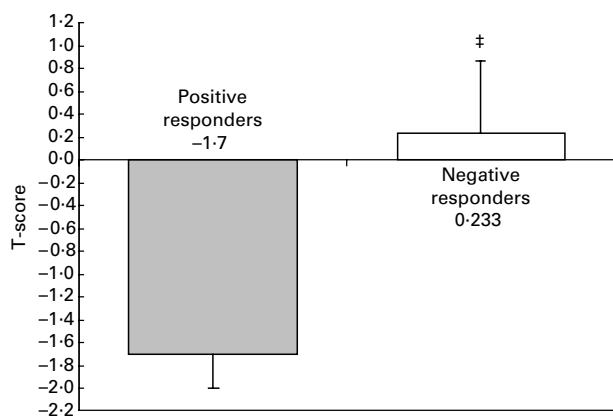


Fig. 4. Individual changes of (a) Ca and (b) Mg absorption in response to active treatment (SYN1).

system increases fractional absorption at low intake levels (Kayne & Lee, 1993). Some studies have indicated that postmenopausal women with osteoporosis have a significant reduction in Mg level in both serum and bone relative to age-matched controls (Cohen, 1988; Reginster *et al.* 1989). Other studies have found no such relationship (Yano *et al.* 1985). Large changes in blood Mg concentration acutely affect PTH secretion in a similar way to Ca (Rude *et al.* 1978). Furthermore, treatment with 1 year of Mg supplements has been reported to increase bone mass in osteoporotic postmenopausal women (Stendig-Lindberg *et al.* 1993). Therefore, Mg availability may be a contributor to bone health. Studies investigating the effect of chicory fructans on Mg absorption have yielded conflicting results. Adolescents (van den Heuvel *et al.* 1999) and young adult men (Coudray *et al.* 1997) showed no increase in Mg absorption when treated for 9 d and 4 weeks, respectively. However, similar to our data, Tahiri *et al.* (2001) reported positive results when treating eleven postmenopausal women with non-digestible fructo-oligosaccharides for 5 weeks, suggesting that postmenopausal



**Fig. 5.** Baseline lumbar spine T-score in responders and non-responders for Ca absorption. ‡Significantly different from positive responders ( $P < 0.05$ ).

women may be more susceptible to the benefits of fructans on Mg absorption than other populations studied.

#### Bone turnover

Consistent with the many studies that show a decrease in bone resorption following an increase in Ca intake (Ginty *et al.* 1998; Scopacasa *et al.* 1998, 2002; Jensen *et al.* 2002), the initial decrease in deoxypyridinoline that was observed with SYN1 treatment was as expected. Similarly, Tahiri *et al.* (2001) demonstrated a non-significant decrease in deoxypyridinoline in postmenopausal women after 5 weeks of treatment with non-digestible fructo-oligosaccharides. More complicated is our observation that resorption values rebounded to a level greater than at baseline by 6 weeks of treatment with SYN1. It may be that the peak rise in Ca absorption occurred earlier than 6 weeks and thus was falling by the 6-week measurement period as previously suggested (Tahiri *et al.* 2003).

In the normal 'coupled' bone system, a decrease in resorption is followed by a decrease in formation (Eastell *et al.* 1993). In our study, it seems that formation became temporarily 'uncoupled' from resorption. Some pharmacological treatments, such as intermittent doses of PTH, owe their anabolic effect to an initial 'uncoupled' increase in bone formation. Anti-resorptive agents slow resorption but also slow formation. If SYN1 temporarily increased formation while at the same time decreasing resorption, a net gain in bone mineral might result. Caution should, however, be used when applying physiological significance to the changes in bone markers observed in this investigation. The changes were small, short term and, based on data by Hannon *et al.* (1998), less than the 'least significant change' value of greater than 25% that was calculated from the within-subject variability of deoxypyridinoline and osteocalcin determined in similar postmenopausal women.

#### Parathyroid hormone

After 6 weeks of SYN1 treatment, we observed a non-significant decrease in PTH. Oral Ca doses of 1 g immediately increase serum ionised Ca and suppress PTH (Herfarth *et al.* 1992; Karkkainen *et al.* 2001) with a duration of effect of

8–10 h (Blumsohn *et al.* 1994). Ca intake at a single meal is generally less than 500 mg, but even smaller Ca doses of 250 mg have been shown to increase ionised Ca and decrease circulating PTH (Karkkainen *et al.* 2001). The timing of Ca intake also appears to be important as it has been shown that dividing a dose of Ca over 6 h prolonged the decrease in serum PTH (Reginster *et al.* 2002). With an average intake of 1000 mg/d, we would expect to see spikes of ionised Ca and a depression of PTH level following each meal. In our study, however, the blood for analysis of PTH was taken after a fast of at least 10 h, minimising our ability to detect the acute effect of Ca intake on circulating PTH level. The timing of our measurement may also explain why there was no significant correlation between change in Ca absorption and change in PTH at 6 weeks.

#### Vitamin D

The response threshold for vitamin D has been described as the serum level of 25(OH) vitamin D at which changes in intake no longer have an effect on the efficiency of Ca absorption. Although the exact threshold level has yet to be determined, it is estimated to be approximately 35 ng/ml, higher than the previously recommended low end of the reference range of 15–20 ng/ml. In a recent study (Heaney *et al.* 2003), Ca absorption efficiency increased by 45–65% when serum levels of 25(OH) vitamin D were augmented from the low end of the current reference range to the mid-range (from 20 ng/ml to 35 ng/ml), suggesting that the reference range should be adjusted. Although all of the women in this study had circulating levels of 25(OH) vitamin D of 15 ng/ml or higher, only two had levels greater than 35 ng/ml. It is therefore possible that, with a larger sample size, the variability in mineral absorption response could be partially explained by the differences in vitamin D status. Further research should be carried out to identify the combined effect of vitamin D and chicory fructans on Ca and Mg absorption.

#### Conclusion

This investigation suggests that 6 weeks of treatment with 10 g/d SYN1 in postmenopausal women can significantly increase Ca and Mg absorption relative to placebo treatment of the same duration. Although the markers of bone turnover did not demonstrate a clear pattern in response to the increased mineral absorption, there was a short-term decrease in the marker of bone resorption. Future investigations focusing on the optimal duration and timing of treatment may help to validate the potential benefits of SYN1 consumption on bone health. This should be investigated in long-term studies in which bone density is the central biomarker.

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