Effects of prebiotics on mineral metabolism[1–3]

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ABSTRACT Nondigestible oligosaccharides (NDOs) have been found to stimulate absorption of several minerals and to improve mineralization of bone. Hence, these substances are potential ingredients for "functional foods." In addition to a nutritional effect, functional foods have physiologic and psychological benefits that result in improved health or reduced risk of chronic disease. Most of the scientific evidence for the functional effects of NDOs is based on animal experiments in which NDOs increased the availability of calcium, magnesium, zinc, and iron. This stimulatory effect of some NDOs is assumed to be mainly due to their prebiotic character. A prebiotic is defined as a substrate or food ingredient that is nondigestible for the host but is fermented selectively by some of the intestinal microflora. Thus, it stimulates the growth and activity of bacteria with beneficial consequences for the host's health. Recently, these findings were confirmed in human studies for some NDOs. The effects seem to be specific for the type of carbohydrate and are likely related to the rate of fermentation by the intestinal flora and appear to depend on the ingested dose. Contradictory results of the effect of prebiotics in literature may be due to the experimental design because the effect of NDOs depends on the dose, the time of administration, the content of calcium in the diet, the part of the skeleton investigated, and the age of the subjects studied. *Am J Clin Nutr* 2001;73(suppl): 459S–64S.

KEY WORDS Prebiotic, oligosaccharides, oligofructose, mineral absorption, calcium metabolism, bone structure, humans, rats

INTRODUCTION

Osteoporosis is one of the predominant osteopathies with severe epidemiologic relevance. One of the risk factors is inadequate intake of calcium. Excess intake of dietary compounds that reduce absorbability of minerals should be avoided. Ingredients that stimulate mineral absorption and bone mineralization may support bone health. It was shown by many researchers that nondigestible oligosaccharides (NDOs), such as oligofructose and inulin or lactulose, effectively stimulate mineral absorption. However, conflicting results have been reported as well. This discrepancy may be explained in part by different study designs. In this review, the importance of the experimental design and its effect on mineral metabolism and bone health are discussed.

EXPERIMENTS IN ANIMAL MODELS

Mineral balance

Calcium, phosphorus, and magnesium

The stimulation of calcium absorption by NDOs was shown in young, growing (1, 2), 5-wk-old ovariectomized (3), magnesium-deficient (4), iron-deficient (5), and postgastrectomy-anemic animals (6). Additionally, calcium absorption from the cecum, colon, and rectum was stimulated by dietary oligofructose in normal growing rats (1).

In a study of rats that had undergone ovariectomy at the age of 5 mo (K Scholz-Ahrens, J Schrezenmeir, unpublished observation, 1999), animals were fed a semisynthetic diet containing 0.5% Ca plus 0, 25, 50, or 100 g oligofructose/kg diet, or diets containing 1.0% Ca plus 0 or 50 g oligofructose/kg diet for 16 wk. There was a positive trend for increased calcium retention with oligofructose consumption after 4, 8, and 16 wk despite significantly increased calcium excretion in urine.

Ohta et al (4) did not observe an effect of 1% or 5% dietary oligofructose on phosphorus balance in young magnesium-deficient rats. The same was true for rats fed a diet containing 7.5% oligofructose after a sham operation or gastrectomy (7). In adult ovariectomized rats, urinary excretion of phosphorus was reduced when the diet contained 0.5% Ca and >5% oligofructose. If the diet contained 1.0% Ca, urinary phosphorus was lower in those rats fed 5% oligofructose than in a control group not fed oligofructose. Phosphorus absorption and retention were unaffected by oligofructose at 0.5% or 1% dietary Ca, irrespective of the dose of oligofructose (K Scholz-Ahrens, J Schrezenmeir, unpublished observation, 1999).

Feeding oligofructose to young rats improved magnesium retention significantly, whether it was added to a normal (2) or magnesium-deficient diet (4) or provided to iron-deficient, anemic animals (5). Moreover, oligofructose increased magnesium absorption and retention in cecum-cannulated rats, irrespective of whether magnesium was given orally or infused into the cecum (8). The stimulating effect of oligofructose on the absorption

of magnesium and calcium was 5 times stronger than that of lactulose (1, 9). Like calcium, magnesium was absorbed from cecum, colon, and rectum (1).

Iron and zinc

Ten percent dietary oligofructose stimulated iron retention in growing rats (2). Additionally, oligofructose improved recovery from diet-induced anemia (5). In another study, postgastrectomy anemia was prevented very efficiently by oligofructose and the apparent absorption ratio of iron was significantly increased after the first and second week of oligofructose feeding. Ohta et al (6) observed a transient but significant rise in hematocrit, hemoglobin concentration, and hemoglobin regeneration efficiency. However, these effects did not reach values that could be achieved by refortification of the diet with iron. No effect was seen on serum iron concentration, unsaturated or total-iron-binding capacity, or absorbed iron (6). Apparent retention of zinc was significantly higher in rats consuming a diet that was supplemented with oligofructose, although the effect was less pronounced than for iron, calcium, or, especially, magnesium (2).

Effects on bone

Bone density and mineral content

Bone mineral density measured by dual-energy X-ray absorptiometry (DXA) was significantly higher in femur and tibia both in gastrectomized and to a lesser extent in sham-operated rats (6, 7). The calcium content of the femur was significantly higher after gastrectomized and sham-operated rats consumed diets containing 7.5% oligofructose, whereas the effect of oligofructose on the phosphorus content of the femur and tibia was only visible after gastrectomy (7). The calcium content of the femur and tibia was ≈10% higher after ovariectomized rats had consumed a diet that contained 5% galactooligosaccharide in exchange for sucrose for 4 wk (3). In intact, growing rats, mean (±SEM) femur calcium increased from 0.89 ± 0.05 to 1.07 ± 0.06 mmol/bone when 5% oligofructose was incorporated into the diet at the expense of sucrose (10). An experimental diet low in magnesium and with excess calcium (1.0%) and phosphorus (1.2%) induced magnesium deficiency and heart and kidney calcification in rats. After the experimental diet was supplemented with 5% galactooligosaccharide, there was a trend toward prevention of magnesium deficiency and organ calcification (11). When aged, ovariectomized rats were fed oligofructose added to a diet with 1% Ca for 8 wk, femur calcium was significantly higher. Mean (±SEM) values were 88.2 ± 2.4 mg Ca/femur without oligofructose and 97.2 ± 1.4 mg Ca/femur after 50 g oligofructose/kg diet was exchanged for cornstarch (12).

Bone structure

Scholz-Ahrens et al (12) showed that oligofructose improved bone mineral content in aged, ovariectomized rats. However, stability of bone depends on the structure of the trabecular network rather than on bone mineral content. Therefore, the trabecular network of distal tibiae was also analyzed by using microradiography combined with computer-supported image analysis (13). Rats were fed semipurified diets with different amounts of dietary calcium and oligofructose. The following 7 groups were studied: *1)* sham-operated for ovariectomy, *2)* ovariectomy with 0.5% Ca and without oligofructose, *3)* ovariectomy with 0.5% Ca plus 2.5% oligofructose, *4)* ovariectomy with 0.5% Ca plus 5% oligofructose, *5)* ovariectomy with 0.5% Ca plus 10% oligofructose, *6)* ovariectomy with 1.0% Ca without oligofructose, and *7)* ovariectomy with 1.0% Ca plus 5% oligofructose. Oligofructose prevented ovariectomy-induced loss of trabecular bone (13). This effect was almost significant in animals receiving a diet containing 0.5% Ca (group 2 compared with 3) and was significant ($P < 0.01$) for those receiving diets containing 1.0% dietary Ca (group 6 compared with 7). Mean (±SEM) percentage of trabecular bone area of tissue area (Tb Ar/T.Ar) were $10.6 \pm 0.82\%$ (group 1), 7.7 ± 0.76 (group 2), 10.4 ± 0.88 (group 3), 10.3 ± 0.85 (group 4), 10.1 ± 0.85 (group 5), 10.1 ± 0.77 (group 6), and 13.3 ± 0.77 mg Ca/bone (group 7).

Dietary calcium

The stimulating effect of inulin on fecal fermentation with a shift from acetate toward a higher production of propionate was affected by the amount of dietary calcium (14). There was a significant drop in pH in the cecal lumen, which was less pronounced when diets contained 0.8% than 0.3% Ca. The rise in dietary calcium from 0.3% to 0.8% increased slightly the concentration of soluble calcium in the fiber-free diet, but did so significantly in the presence of inulin. Mean (±SEM) calcium was 9.0 ± 1.0 and 11.1 ± 0.9 mmol soluble Ca/L cecal content without inulin and 13.0 ± 1.3 and 20.0 ± 1.5 mmol soluble Ca/L cecal content with inulin at 0.3% and 0.8% dietary Ca, respectively ($P < 0.05$). Thus, it was shown that the concentration of soluble calcium in the cecum was highest if inulin was added to a diet with a high content of calcium. This effect was highly correlated with the amount of calcium absorbed from the cecum. Similar results were reported by Chonan et al (11). They found a stimulatory effect of galactooligosaccharide on calcium absorption and calcium content in femur and tibia with supplementation with 0.5% Ca but not with 0.05% Ca (15). It was observed that the effect of oligofructose on metabolic calcium balance (K Scholz-Ahrens, J Schrezenmeir, unpublished observations, 1999), calcium content of bone, and the prevention of ovariectomy-induced loss of trabecular structure became more prominent when dietary calcium was high (12, 13). Lactulose, another nondigestible carbohydrate, significantly increased calcium absorption, but only if the diet contained >0.3% Ca (16). Magnesium absorption from the cecum was affected by inulin but not by the background amount of dietary calcium (14).

Dose dependency

Raising the oligofructose content from 1% to 5% in the diet had no effect on absorption of calcium, phosphorus, or magnesium in magnesium-deficient rats after 1 wk (4). After 3 wk, magnesium absorption increased from 2.10 ± 0.29 to 3.01 ± 0.35 mg/d (4). Comparison of dietary concentrations of 0%, 5%, 10%, and 20% inulin revealed a dose-dependent decrease in cecal pH and a rise in cecum weight, cecal wall weight, cecal pool of total short-chain fatty acids (SCFAs), and absorption of magnesium and calcium. A dose-dependent rise in cecal concentrations of SCFAs was observed for inulin concentrations ≤10%. Decreased concentrations of SCFAs and magnesium were found if 20% inulin was given. No further increase in cecal concentration of calcium or phosphorus occurred with greater inulin concentrations (17). In 7- and 9-mo-old ovariectomized rats consuming a diet with 0.5% Ca, ovariectomy-induced loss of bone mass and bone structure was prevented independent of the dose, which was 2.5–10% of the diet (12, 13). In human volunteers, a significant linear trend was detected between the dose of lactulose and its positive effect on calcium absorption (18).

One may suppose that a dose-dependent effect of prebiotics on absorption of some minerals may be linked to the bifidobacteria-stimulating capacity of the substrate. In human volunteers, an intake of 20 g inulin/d for 1 wk significantly stimulated mean (±SD) fecal counts of bifidobacteria from 7.9 ± 0.4 to $8.8 \pm 0.8 \log_{10}/g$. No further rise in bifidobacteria counts were found after 40 g inulin/d was consumed for the following 10 d (19). Roberfroid et al (20) summarized human studies on the effect of different doses of inulin and oligofructose on the counts of bifidobacteria. They concluded that there was no dose-effect relation within the range of ≥4–20 g. At present, it is not clear whether a dose-dependent effect of prebiotics on mineral absorption is associated with a dose-dependent effect on growth of bifidobacteria.

Persistence

The duration of most mineral retention experiments with NDOs was short (14–28 d). Repeated balance studies showed that the stimulating effect of oligofructose on mineral retention was measurable in the first and second week of the experiment but lost significance after 2 or 3 wk. This was true for magnesium in sham-operated and cecectomized rats after 1 wk and for calcium in sham-operated rats after 3 wk (21). In gastrectomized rats, apparent calcium absorption was still higher after 4 wk, whereas no effect was seen in sham-operated rats (7). In a recent experiment with aged rats that had been ovariectomized at the age of 5 mo, the persistence of the effect on bone mineralization mediated by oligofructose depended on the part of the skeleton measured. In femur, prevention of demineralization was more pronounced after 8 wk and lost significance after 16 wk, whereas in lumbar vertebra, the difference between treated and untreated rats became more obvious with time. When calcium retention was measured by metabolic balance, the difference between treated and untreated rats in absolute terms became more pronounced with time, although the effect was not significant. After 4, 8, and 16 wk of diets containing 1% Ca and no oligofructose, mean (±SE) retention was 14.6 ± 4.4, 53.2 ± 10.8, and 71.2 ± 5.0 mg/7 d. After 5% oligofructose was given in place of cornstarch, retention was 19.9 ± 4.4, 63.8 ± 10.8, and 83.0 ± 5.0 mg/7 d (K Scholz-Ahrens, J Schrezenmeir, unpublished observations, 1999). Increased retention values with time may be due to adaptation to ovariectomy-induced estrogen deficiency.

Age

Animals were very young in most studies (1, 3–5, 11, 15, 21, 22). Only a few studies were done in aged rats to account for the different calcium and bone metabolism of adults. In a long-term experiment, oligofructose improved bone calcium content in 7- and 9-mo-old ovariectomized rats after the animals had been consuming the diets for 8 or 16 wk. Furthermore, oligofructose effectively prevented ovariectomy-induced loss of trabecular structure in those rats, especially when dietary calcium was high (12, 13).

Animal model—coprophagy

The rat is a coprophaging rodent. There may be limitations in using this animal model for extrapolation to humans. This may particularly be the case if mechanisms of NDO-mediated changes in mineral absorption from the hindgut are investigated. Experiments in rats have shown that preventing coprophagy reduced iron availability from foods such as peas, spinach, and bran cereal, in which the mineral is present in complexed form. No significant effect was seen if corn meal or $FeSO_4$ was the iron source (23). Prevention of coprophagy in oligofructose-fed animals did not alter cecal pH or the positive effect on calcium and magnesium retention. However, fecal excretion of acetate and propionate was reduced whereas magnesium absorption was increased (10).

STUDIES IN HUMANS

Nondigestible oligosaccharides in general

As indicated in the previous section, much research in experimental animals has shown positive effects of NDOs on calcium, magnesium, iron, and zinc absorption. The mechanism underlying these positive effects is most likely related to increased solubility of these minerals in the cecum and the colon as a consequence of increased microbial fermentation and lower luminal pH. In patients with ileal pouch–anal anastomosis, it was shown that oligofructose was fermented up to 83%, in contrast with resistant starch, which was fermented only up to 46% (24). At a dose of 10 g/d, transgalactooligosaccharides given in a diet for 21 d decreased breath-hydrogen excretion and increased fecal bifidobacteria without affecting enterobacteria or fecal pH in 20–32-y-old volunteers (25). Similar results were reported in 76-y-old subjects after consumption of 20–40 g lactose or inulin for 19 d. Inulin increased mean (±SEM) fecal counts of bifidobacteria from 7.9 ± 0.4 to $9.2 \pm 0.5 \log_{10}$ counts/g dry feces without affecting pH, the concentration of SCFAs (μmol/g dry feces), or the percentage of acetate, propionate, or butyrate (19).

Lactose

NDOs escape digestion in the small intestine in humans. Similarly, lactose will escape digestion in lactase deficiency or in rats after the weaning period. Lactose is known to increase the non-vitamin D–dependent passive calcium absorption in the intestine, at least in rats (26, 27).

Studies on the effect of lactose on calcium absorption in humans have yielded inconsistent results. One explanation could be that in adults who are in calcium balance, lactose-stimulated passive calcium transport may depress vitamin D–mediated active calcium transport via parathyroid hormone so that a net effect on calcium absorption becomes unobservable. Another explanation is that any positive effect of lactose on calcium absorption depends on a low intestinal β-galactosidase activity, which allows the lactose to reach the terminal ileum and colon, where it can be fermented by the intestinal microflora. In this regard, Griessen et al (28) investigated calcium absorption in 7 lactase-deficient subjects and 8 subjects with normal lactase activity using a dual-labeling technique with radioactive calcium tracers. They found that lactose, compared with glucose, only favors calcium absorption in lactase-deficient subjects.

Lactulose

Lactulose is known as a fermentable substrate. It has gained high popularity in the treatment of constipation and chronic hepatic encephalopathy. van den Heuvel et al (18) investigated the effect of 2 doses of lactulose (5 and 10 g/d compared with 0 g/d) on calcium absorption in a crossover design with 12 healthy postmenopausal women. Lactulose was given at breakfast for 9 d. True intestinal calcium absorption was measured by using the dual-calcium-labeling technique, which allowed the measurement of late colonic calcium absorption. The breakfast contained 162 mg

Ca. Mean (±SD) calcium absorption values during control treatment (without lactulose) and during the treatments with 5 and 10 g lactulose were 27.7 ± 7.7%, 30.0 ± 7.6%, and 32.2 ± 7.0%, respectively. The difference in absorption between the reference and the 10-g lactulose dose was significant ($P < 0.01$).

Effects of prebiotics in particular

Coudray et al (29) investigated the effect of inulin (≤40 g/d) on absorption and balance of calcium, magnesium, iron, and zinc in 9 healthy adults by using the classic balance approach in a crossover study with 28-d dietary treatment periods. They found that inulin increased calcium absorption and balance and had no effect on the metabolism of the other minerals. van den Heuvel et al (30) investigated the effect on calcium and iron absorption of inulin, oligofructose, and galactooligosaccharides at a much lower dose (15 g/d) in a 21-d crossover study with 12 healthy, young adult subjects. They used dual-stable-isotope-labeling techniques. Neither inulin nor the fructo- or galactooligosaccharides increased calcium or iron absorption. In a second study, the same authors investigated the effect of oligofructose compared with sucrose on calcium absorption in a crossover experiment in 12 healthy, 14–16-y-old boys (31). The treatment periods lasted 9 d. The investigators used a slightly modified dual-labeling technique that allowed the measurement of late colonic effects on calcium absorption. Oligofructose significantly increased true fractional calcium absorption from a breakfast with 200 mg Ca (47.8 ± 16.4% after sucrose and 60.1 ± 17.2% after oligofructose; $P < 0.05$). In their consensus paper, the group of the European Project on Non-digestible Oligosaccharides (ENDO) claimed that these results are promising evidence of a positive effect of NDOs on mineral absorption in humans (32). Ongoing studies may soon confirm this.

It has been discussed that at least part of the stimulating effect of oligofructose on mineral absorption might be attributed to SCFA production (1). In humans, a strong effect of oligofructose or inulin on fecal pH and concentration or ratio of SCFAs was not found (19, 25). This may partly explain the less pronounced stimulation of mineral absorption by these substances in humans than in animals. Another explanation may be the short duration of the human studies. It is impossible to extrapolate from short-term effects of NDOs on mineral absorption to effects on skeletal development or bone health. Therefore, long-term studies in humans are required.

MECHANISM

Substrate dependency

It has been speculated that the stimulatory effects of NDOs on mineral absorption was mainly due to their prebiotic character, ie, that a nondigestible substrate or food ingredient is fermented selectively by specific colonic microbes with health-promoting consequences for the host (20, 33).

Until now, there has been a lack of evidence showing that the stimulating effect of prebiotics on mineral absorption is mainly due to increased growth of specific bacterial strains, which have a beneficial effect for the host. It could be postulated that the main effect of prebiotics responsible for the higher mineral absorption is related to their effect as "colonic food." Colonic food serves as a substrate for the intestinal flora in a nonspecific way but could stimulate the fermentation rate, production of SCFAs, and luminal acidification. In addition to inulin (29), oligofructose (1, 2), and galactooligosaccharide (3), lactulose (16, 34) stimulated magnesium, calcium, and phosphorus absorption in intact rats and reduced luminal pH (34). Another soluble but nondigestible carbohydrate, guar gum hydrolysate, effectively stimulated calcium and magnesium absorption in rats (35). It was shown that bifidobacteria were found in rats fed guar gum but not in those fed pectin (36) and that the growth of bifidobacteria was stimulated in rats fed a diet containing 2 types of resistant starch but not in the control animals fed maize starch (37).

Contribution of metabolites

The fermentation of NDOs increased fecal bifidobacteria (25, 38, 39), raised SCFA concentrations (14, 39), reduced the intraluminal pH (14, 21, 39), and increased the weight of cecal contents as well as cecal wall weight (3, 39), cecal crypt height, numbers of epithelial cells per crypt, and cecal vein blood flow (39). There is not full agreement on whether lactate production is increased or which SCFAs are mainly stimulated by different NDOs. Inulin and oligofructose are metabolized almost equally extensively and produce similar growth rates in different strains of bifidobacteria. Fermentation, however, is slower for inulin, which has a degree of polymerization >10, than for fractions of oligofructose with a degree of polymerization <5 (20). In one study, gnotobiotic rats were inoculated with human feces and fed diets containing 40 g/kg of glucooligosaccharides, oligofructose, or galactooligosaccharides. The number of bifidobacteria increased significantly with the oligofructose and galactooligosaccharide diets. Mean (±SEM) bacterial counts were 7.4 ± 0.4 $\log_{10}$/g feces after the diet containing sucrose, 7.0 ± 0.2 with glucooligosaccharides, 9.2 ± 0.2 with oligofructose, and 9.6 ± 0.2 $\log_{10}$/g feces with galactooligosccharide (40). The presence of SCFAs was a prerequisite for stimulation of calcium absorption in the human colon (41).

Thus, it seems that there is no final or clear definition of what prebiotics induce, how they are characterized, and which groups of NDOs are included under that term. It has not been clarified satisfactorily *1*) whether prebiotics cause effects going beyond those of other nondigestible carbohydrates or *2*) whether microorganisms selectively enhanced by prebiotics cause effects on calcium metabolism exceeding those of other carbohydrate-fermenting organisms. The definition of a prebiotic has to undergo permanent evaluation according to scientific progress. Possible mechanisms involved in the stimulation of mineral absorption by NDOs are shown in **Figure 1**.

Organ contribution

The increased absorption of minerals after NDO consumption takes place in the cecum and colon but not in the small bowel. It is known that minerals such as calcium, phosphorus, and magnesium are also absorbed effectively from the cecum and colon in rats and humans (22, 42–44). After cecectomy, the stimulatory effect of oligofructose on magnesium but not calcium absorption was reduced (21). Guar gum did not stimulate calcium and magnesium absorption if rats were cecectomized (35). In weanling pigs fitted with a T-cannula at the distal ileum, no effects of NDOs on pH, SCFA concentration, or bacterial population in ileal digesta of galactooligosaccharide-, glucooligosaccharide-, or lactitol-fed animals were observed (45). The concentration of NDOs was low (0.2% of the diet or 0.1 g/kg body wt). In
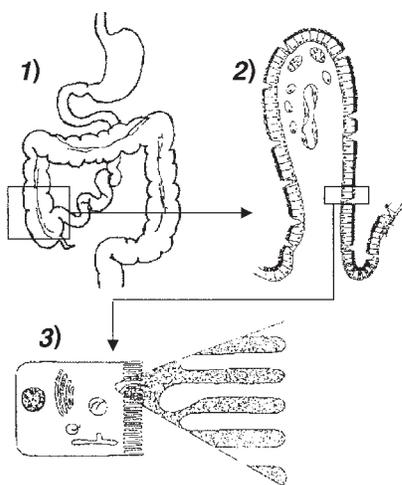
FIGURE 1. Possible mechanisms involved in the stimulation of mineral absorption by nondigestible oligosaccharides:

1) At the gastrointestinal level: the nondigestible substrate passes through the small intestine and reaches the cecum and colon, where selective fermentation by specific colonic microbes occurs. Thereupon, the number of mainly bifidobacteria and the production of short-chain fatty acids increases with a resulting decrease in pH. Finally, the weight of the cecal contents and the cecal wall and the solubilization of minerals are increased.

2) At the villus level: the villus crypt height, number of epithelial cells per crypt, cecal vein flow, and mucosal-to-serosal calcium fluxes (passive calcium transport route) are all increased by nondigestible oligosaccharides.

3) At the cellular level: the expression of calbindin-D9k is stimulated and thereby the active calcium transport route.

ileostomy subjects, excretion into the colon of calcium, magnesium, zinc, and iron was also not affected by intake of inulin or oligofructose, despite the 2.5-fold higher supply per kg body weight compared with the study in pigs (17 g/d, equivalent to 0.25 g/kg body wt) (46).

Contribution of mineral binding proteins

Not only passive diffusion plays a role in large-intestinal mineral absorption. Vitamin D treatment stimulated the activity of calcium binding protein in the colon and cecum in rats. Irrespective of the vitamin D treatment, the content of this protein was higher in the cecum than in the colon. The increase in calcium binding protein was associated with significantly higher calcium fluxes from the mucosal to serosal side in the colon but not in the cecum. Hence, an active transport route for calcium comparable with that in the duodenum was shown (47). Accordingly, this active route may be partly responsible for the higher mineral absorption after consumption of dietary NDOs, besides the mediation through the cascade of effects on the large bowel (increased fermentation activity, morphologic changes of gut epithelial cells, lowered pH, and increased solubility of luminal calcium). Some authors showed that oligofructose-stimulated absorption of calcium may be mediated by stimulated expression of calcium binding proteins, such as calbindin-D9k (48). The stimulatory effect of oligofructose on iron absorption may partly be mediated by its ability to contribute to the modification of intestinal mucins and their content of iron binding proteins (6, 49). How this process could be mediated is not clear at present.

CONCLUSIONS

Prebiotics such as inulin, oligofructose, glucooligosaccharide, and galactooligosaccharide have been found to stimulate absorption and retention of several minerals, particularly magnesium, calcium, and iron. Most of these findings were obtained in rats. Although the number of studies on the effect of nondigestible oligosaccharides on mineral metabolism in humans is limited, so far, positive effects on calcium absorption seem to occur under conditions of increased calcium requirements (eg, adolescence and postmenopause).

The extent of the effect seems to be specific for the type of carbohydrate. The effects are likely related to the fermentation of carbohydrates by the intestinal flora and may depend on the ingested dose within a limited range. Contradictory results on the effect of prebiotics in the literature may be due to differences in the experimental design. Several experimental conditions promoted the stimulation of calcium absorption and retention by NDOs, such as high dietary calcium, an optimum dose of prebiotics, sufficient duration of administration, and the age of subjects. The effect of NDOs on bone mineralization in rats depended on the skeletal site investigated. To date, no evidence of any adverse effects of NDOs on mineral metabolism was reported, provided the limits of tolerance are not exceeded.

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