

# **Prebiotin Structure/Function Claim: Increased Calcium Absorption and Bone Density**

**Doc No.:** VR001

**Revision:** 1

**AUTHOR:** Dr. Frank Jackson, MD

## **1. PURPOSE/SCOPE**

The purpose of this document is to explain how Prebiotin provides increased calcium absorption and bone density in teenagers and post menopausal females and the clinical literature published in support of this structure/function claim.

This includes studies performed and an evaluation of the relevant scientific literature related to the effect of prebiotin on humans relative to increased calcium absorption and bone mineral density.

## **2. GENERAL DETAILS**

### **2.1 Dietary Supplement Name**

Proprietary Product Name:

Prebiotin

### **2.2 Manufacturer**

Jackson GI Medical  
1714 N. 2<sup>nd</sup> Street  
Harrisburg, PA 17102  
USA

### **2.3 Dietary Supplement Description**

Oligofructose Enriched Inulin

## **3. BACKGROUND**

Prebiotin, a Prebiotic Fiber Supplement offers a full-spectrum prebiotic (Oligofructose-Enriched-Inulin, or OEI). OEI is obtained by combining chicory long-chain inulin and oligofructose. Inulin and oligofructose belong to a class of carbohydrates known as fructans. Because of the beta-configuration of the anomeric C2 in their fructose monomers, inulin -type fructans resist hydrolysis by intestinal digestive enzymes, they classify as 'non-digestible' carbohydrates, and they are dietary fibers.

The main sources of inulin and oligofructose that are used in the food industry are chicory and Jerusalem artichoke. Inulin and oligofructose are considered as functional food ingredients since they affect the physiological and biochemical processes in rats and human beings, resulting in better health.

# Prebiotin Structure/Function Claim: Increased Calcium Absorption and Bone Density

Doc No.: VR001

Revision: 1

Unlike ordinary prebiotics such as Inulin or FOS, OEI ensures that Prebiotin nourishes beneficial bacteria throughout the colon. OEI is also the most-researched prebiotic, used in many university and clinical studies.

A prebiotic has been defined as *'a non-digestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon, and thus improves host health.* Inulin and oligofructose are the best-studied prebiotics so far. They are selectively fermented by the microflora in the human colon leading to a bacterial composition that is dominated by bifidobacteria, a perceived health-promoting genus.

The National Cancer Institute defines OEI as:

A substance that is used to improve the health of the digestive system and bones and is being studied in the prevention of colon cancer. Oligofructose-enriched inulin is made by combining two substances that occur naturally in many plants, including chicory root, wheat, bananas, onion, and garlic. Oligofructose-enriched inulin helps healthy bacteria grow in the intestines and helps the body absorb calcium and magnesium. OEI is also called Raftilose Synergy 1.

Source: (<http://www.cancer.gov/dictionary>)

## 4. PUBLISHED LITERATURE

### 4.1 Literature Search

A literature search was conducted using PubMed and Medline to identify articles that contained studies on prebiotin (oligofructose enriched inulin) related to calcium absorption and bone density.

The articles and/or studies listed in Table 1 are summarized individually.

Table 1 Clinical Literature

	Author	Source/Published	Title of Publication	Year of Publication
1	Abrams SA <sup>1</sup> , Griffin IJ, Hawthorne KM, Liang L, Gunn SK, Darlington G, Ellis KJ.	American Journal Clinical Nutrition 2005 Aug;82(2):471-6.	Abstract: A combination of prebiotic short- and long-chain inulin-type fructans enhances calcium absorption and bone mineralization in young adolescents.	2005
2	Abrams SA <sup>1</sup> , Hawthorne KM, Aliu O, Hicks PD, Chen Z, Griffin IJ.	Journal of Nutrition 2007 Oct;137(10):2208-12.	An inulin-type fructan enhances calcium absorption primarily via an	2007

# Prebiotin Structure/Function Claim: Increased Calcium Absorption and Bone Density

Doc No.: VR001

Revision: 1

	Author	Source/Published	Title of Publication	Year of Publication
			effect on colonic absorption in humans.	
3	Holloway L, Moynihan S, Abrams SA, Kent K, Hsu AR, Friedlander AL.	British Journal of Nutrition 2007 Feb;97(2):365-72.	Effects of oligofructose-enriched inulin on intestinal absorption of calcium and magnesium and bone turnover markers in postmenopausal women.	2007
4	Katharina E. Scholz-Ahrens, Peter Ade, Berit Marten, Petra Weber, Wolfram Timm, Yahya Açil, Claus-C. Glüer, and Jürgen Schrezenmeir	Journal of Nutrition 2007 Mar;137(3 Suppl 2):838S-46S.	Prebiotics, Probiotics, and Synbiotics Affect Mineral Absorption, Bone Mineral Content, and Bone Structure	2007

## Article #1

### **A combination of prebiotic short- and long-chain inulin-type fructans enhances calcium absorption and bone mineralization in young adolescents.**

Abrams SA, Griffin IJ, Hawthorne KM, Liang L, Gunn SK, Darlington G, Ellis KJ.

#### Author information

<sup>1</sup>US Department of Agriculture/Agricultural Research Service, Children's Nutrition Research Center, Department of Pediatrics, Baylor College of Medicine and Texas Children's Hospital, Houston, TX 77030, USA. sabrams@bcm.edu

#### **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.

# **Prebiotin Structure/Function Claim: Increased Calcium Absorption and Bone Density**

**Doc No.:** VR001

**Revision:** 1

## **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 +/- 1.6%; P < 0.001) and at 1 y (difference: 5.9 +/- 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<sup>2</sup>; 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.

<http://www.ncbi.nlm.nih.gov/pubmed/16087995>

## **Article #2**

### **An inulin-type fructan enhances calcium absorption primarily via an effect on colonic absorption in humans.**

Abrams SA<sup>1</sup>, Hawthorne KM, Aliu O, Hicks PD, Chen Z, Griffin IJ.

## **Author information**

## **Prebiotin Structure/Function Claim: Increased Calcium Absorption and Bone Density**

**Doc No.:** VR001

**Revision:** 1

Section of Neonatology, Department of Pediatrics, Baylor College of Medicine, Houston, TX 77030, USA. [sabrams@bcm.edu](mailto:sabrams@bcm.edu)

### **ABSTRACT**

Calcium absorption efficiency and bone mineral mass are increased in adolescents who regularly consume inulin-type fructans (ITF). The mechanism of action in increasing absorption is unknown but may be related to increased colonic calcium absorption. We conducted a study in young adults designed to evaluate these mechanisms with a kinetic technique using (42)Ca orally and (46)Ca dosed i.v. Those who responded to 8 wk of supplementation with 8 g of a mixed short and long degree of polymerization ITF by increasing their calcium absorption had kinetic measurements analyzed to evaluate the time course of absorption. The area under the curve of the oral tracer in the blood during the 26 h after dosing was calculated and the time dependence of increased absorption determined. Eight young adults (of 13 studied), with mean calcium intake approximately 900 mg/d, responded to the ITF with an increased calcium absorption of at least 3%. In responders, absorption increased from 22.7 +/- 11.3% to 31.0 +/- 15.3%. Colonic absorption, defined as absorption that occurred >7 h after oral dosing, represented 69.6 +/- 18.6% of the increase, or 49 +/- 28 mg/d. These findings suggest that, in those who respond to ITF, its effects on calcium absorption occur principally in the colon. This benefit to ITF may be especially important when absorption in the small intestine is impaired for anatomic or physiological reasons.

<http://www.ncbi.nlm.nih.gov/pubmed/17884999>

### **Article #3**

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

Holloway L, Moynihan S, Abrams SA, Kent K, Hsu AR, Friedlander AL.

#### **Author information**

Clinical Studies Unit and Geriatric Research Education and Clinical Center, VA Palo Alto Health Care System, Palo Alto, California, USA.

### **ABSTRACT**

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

## **Prebiotin Structure/Function Claim: Increased Calcium Absorption and Bone Density**

**Doc No.:** VR001

**Revision:** 1

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.

<http://www.ncbi.nlm.nih.gov/pubmed/17298707>

### **Article #4**

#### **Prebiotics, Probiotics, and Synbiotics Affect Mineral Absorption, Bone Mineral Content, and Bone Structure**

Katharina E. Scholz-Ahrens, Peter Ade, Berit Marten, Petra Weber, Wolfram Timm, Yahya Açil, Claus-C. Glüer, and Jürgen Schrezenmeir

#### **ABSTRACT**

Several studies in animals and humans have shown positive effects of nondigestible oligosaccharides (NDO) on mineral absorption and metabolism and bone composition and architecture. These include inulin, oligofructose, fructooligosaccharides, galactooligosaccharides, soybean oligosaccharide, and also resistant starches, sugar alcohols, and difructose anhydride. A positive outcome of dietary prebiotics is promoted by a high dietary calcium content up to a threshold level and an optimum amount and composition of supplemented prebiotics. There might be an optimum composition of fructooligosaccharides with different chain lengths (synergy products). The efficacy of dietary prebiotics depends on chronological age, physiological age, menopausal status, and calcium absorption capacity. There is evidence for an independent probiotic effect on facilitating mineral absorption. Synbiotics, i.e., a combination of probiotics and prebiotics, can induce additional effects. Whether a low content of habitual NDO would augment the effect of dietary prebiotics or synbiotics remains to be studied. The underlying mechanisms are manifold: increased solubility of minerals because of increased bacterial production of short-chain fatty acids, which is promoted by the greater supply of substrate; an enlargement of the absorption surface by promoting proliferation of enterocytes mediated by bacterial fermentation products, predominantly

# Prebiotin Structure/Function Claim: Increased Calcium Absorption and Bone Density

Doc No.: VR001

Revision: 1

lactate and butyrate; increased expression of calcium-binding proteins; improvement of gut health; degradation of mineral complexing phytic acid; release of bone-modulating factors such as phytoestrogens from foods; stabilization of the intestinal flora and ecology, also in the presence of antibiotics; stabilization of the intestinal mucus; and impact of modulating growth factors such as polyamines. In conclusion, prebiotics are the most promising but also best investigated substances with respect to a bone-health-promoting potential, compared with probiotics and synbiotics. The results are more prominent in animal models, where more studies have been performed, than in human studies, where experimental conditions are more difficult to control.

<http://www.ncbi.nlm.nih.gov/pubmed/17311984>

## 5. DATA SUMMARY – CLINICAL LITERATURE

Based on the clinical literature and research presented, prebiotin, oligofructose-enriched inulin has been proven to increase calcium absorption and bone density in a diverse population.

## 6. ATTACHMENTS

6.1 Clinical Literature referenced is maintained in the Structure/Function Technical File for Calcium Absorption and Bone Density.

### APPROVALS:

CEO: \_\_\_\_\_ Date \_\_\_\_\_

COO: \_\_\_\_\_ Date \_\_\_\_\_

QUALITY/REGULATORY: \_\_\_\_\_ Date \_\_\_\_\_