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Interview
with
Prof. Dr. Steven Abrams

In this issue we present an interview with Prof. Dr. Steven Abrams who is Professor of Pediatrics at the Children's Nutrition Research Center in Houston, Texas, USA.

Prof. Steven Abrams was originally trained as an engineer before turning his hand to medicine. After completing his professional qualifications in pediatrics and neonatology, he undertook nutrition training fellowships at both Baylor College of Medicine, and the National Institutes of Health in Bethesda, Maryland. This work looked at bone density and calcium metabolism in preterm infants.

In 1991, Prof. Abrams returned to Baylor College of Medicine where he took up a post as a Faculty member. Most of his time he focuses on global nutritional research and education. This work has extended to participation in numerous international projects on medical education and research. His research activities are primarily focused on mineral bioavailability which has implications for child health in both developed and developing countries.

Prof. Abrams is married and, together with his wife, has co-authored a book on nutrition and religious practices. His main hobby is tennis, and he is currently learning Spanish to enable him to present medical education conferences in Latin America.

Inulin and oligofructose are prebiotics and beneficially affect host health. They are selectively fermented by bifidobacteria and lactobacilli. Their fermentation generates the formation of end products, such as lactic acid and short chain fatty acids. These metabolic changes have been implicated in the way inulin and oligofructose increase calcium and magnesium absorption in the intestines. Calcium is the building block of the skeleton. Therefore, questions rose whether inulin-type fructans have positive effects on bone formation. This issue will deal with these questions. It provides a clear overview of the current data relating to inulin, oligofructose and mineral absorption. In addition, new data will be presented on the long term effects of an oligofructose-enriched inulin on bone health. But let us first ask for the opinion of an expert, Prof. Dr. Steven Abrams.

Inulin and Oligofructose for improving bone health

How did an engineer end up involved in nutrition?

The medical training fellowships stimulated my interest in bone health because, at that time, there were exciting developments in high quality methods for estimating bone mass. The use of isotopes appealed to my engineering background. It has always

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PREFACE

by Dr. Anne Franck

Osteoporosis affects an estimated 75 million people in Europe, USA and Japan according to the International Osteoporosis Foundation. In light of this, the ability to increase calcium and magnesium absorption and bone mineral density would be beneficial to us all. Absorption of an adequate amount of calcium is particularly important during early adolescence in order to achieve an optimal peak bone mass. In doing this, and by further ensuring that the maximum amount of calcium is retained in the bones throughout adulthood, the chances of developing conditions such as osteoporosis later in life can be reduced.

A new year-long intervention study conducted by Prof. Steven Abrams and colleagues from the Texas Children's Hospital in Houston, USA, looked at the effects of the prebiotic Raftilose®Synergy1 on calcium absorption and bone mineralization in 100 young adolescents. A significant increase in true calcium absorption was demonstrated, as already observed during earlier short-term studies, this time both after two months and one year of supplementing the diet with 8 g/day of Synergy1. But the most important result was a significant increase of calcium accretion within the bones of the participants of more than 15% after one year of supplementation with the inulin-type fructans versus the placebo group. Synergy1 did improve both the bone mineral content and the bone mineral density of the volunteers in comparison with the controls. This breakthrough study thus provides an insight into the longer-term effects of Synergy1 and demonstrates that it can be beneficial in increasing bone mineral content and density.

In this issue, we specifically highlight the role inulin and oligofructose play on mineral absorption and bone metabolism, and the way they may contribute to the prevention of osteoporosis.

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Inulin and

been my main research interest to find the best way to optimize the absorption of minerals by children. I use stable isotopes of minerals such as iron, zinc, potassium, magnesium, copper and calcium to find out how they are absorbed under different conditions. The use of stable isotopes as a method to determine mineral absorption is particularly interesting because they allow measuring the actual 'true' absorption, since there is a clear differentiation possible between the mineral taken from the meal which is the labeled one and the mineral pool already present in the body (unlabelled). This differentiation between endogenous and exogenous mineral is not possible with other techniques and therefore estimates of 'apparent' calcium absorption are less reliable. By labeling the minerals taken up from the meal we can follow those throughout the whole body (e.g. by blood drawings and excretion in urine and feces).

Oligofructose for improving bone health

How has being a clinician influenced your nutrition research?

I guess I always want to try and find applications for my research. It's not uncommon in the US for pediatricians to develop a strong interest in nutrition as a major part of our job concerns optimizing growth and development in our patients. Nutrition is an important part of this. Today, pediatricians have to deal with two major health issues. One is the low intake of calcium in children, together with inadequate intakes of vitamin D, zinc and magnesium. Another is rising levels of obesity among children living in Western societies. At first sight it seems remarkable how low micronutrient intakes go together with excess of energy, but the likely explanation is the lack of dietary variety. It's entirely possible to over-consume energy yet fail to obtain enough vitamins and minerals. There is no particular food group to blame as there is a place for treats in the diet. However, children need to be encouraged to make better dietary choices rather than focus on foods which are energy dense but nutrient poor. In the case of calcium, I think more milk consumption would be good and a greater use of fortified foods and beverages, such as juices.

Following on from that, what are the nutritional and health effects of fortifying foods with inulin and oligofructose with respect to calcium absorption and bone health?

I've now been using prebiotics as inulin and oligofructose, particularly Raftilose®Synergy1, in research projects for over 8 years. Our data strongly support a role for Raftilose®Synergy1 in enhancing calcium absorption. Our most recent study on prebiotics looked at calcium absorption and bone mineral content in 11-year olds after supplementation with Synergy1 for 1 year. There was a significant improvement in calcium absorption after 2 months, which persisted after 1 year in the group given Synergy1. Calcium accretion, estimated using bone mineral content, increased by around 30mg per day in the Synergy1 group compared with the control group. It is reasonable to conclude that this might lead to higher levels of bone mineral mass throughout adulthood as well. This may represent a substantial benefit for both growing children and adults since osteoporosis affects a growing number of people throughout the world, mainly due to ageing populations. However, it is most likely that supplementation with inulin-type fructans is beneficial at any age. We cannot yet be sure if certain ages will have more benefit though than others.

In your work you also focus on the effect an individual's genotype may have on his or her response to dietary changes.

Indeed, it is likely that the benefits vary based on one's genetic predisposition for calcium absorption as well as lifestyle characteristics such as exercise and dietary calcium intake. We are still learning how inulin-type fructans affect calcium absorption and bone mineral mass accumulation. It is likely that calcium absorption is a strongly genetic characteristic and that any intervention to increase it, such as Synergy1 supplementation, is affected by the genetic ability to absorb calcium. Our recent study identified a major role for polymorphisms of the Fok1 vitamin D receptor gene. Generally our data suggest that the magnitude of the benefit of enrichment of foods with Synergy1 would be a 20 % increase of the usual calcium absorption which is an important step forward.

Role of Inulin and Oligofructose in the prevention of osteoporosis

Osteoporosis is a serious systemic bone disease affecting increasing numbers of older people. Its prevalence has escalated in recent decades by the improvement in life expectancy in developed countries, leading to a larger proportion of elderly people in society. Osteoporosis is characterized by low bone mass and fragility, resulting in a greater susceptibility to fracture. It is considered to be a multi-factorial condition caused by inadequate calcium intakes, poor mineral absorption, low levels of physical activity and hormonal changes in the post-menopausal period. Current prevention measures include increasing the use of dairy products or calcium enrichment of diets, although these have not been very effective. Improving calcium absorption by the use of prebiotic fibres, such as inulin and oligofructose might be an additional strategy to prevent this growing problem. Since Raftilose®Synergy1, an oligofructose-enriched inulin, is a more potent promoter of calcium absorption than conventional inulin and oligofructose, dietary supplementation with even modest amounts of Raftilose®Synergy1 (8g/d) can improve calcium absorption by 20%. This has important implications for bone health and prevention of onset of osteoporosis at elder age.

While often viewed as a women's condition, osteoporosis affects significant numbers of men. The lifetime risk of an osteoporotic fracture in those aged over 50 years has been estimated as 50% in women and 25% in men. At present, the disease affects 75 million people in Europe, the USA and Japan combined, leading to huge implications for health care expenditure and quality of life. Hospital costs for osteoporotic fractures and related co-morbidities are higher than for other geriatric pathologies. The impact on prognosis and quality of life can be severe with around half of hip fracture patients failing to regain full independence and one in five dying within 6 months. Since the magnitude of the problem is expected to grow by 60%, it is clear that strategies to lower the risk of osteoporosis are urgently needed (Coxam, 2005).

Current preventative measures

Prevention of osteoporosis has so far focused on two aetiological factors; chronically low intakes of calcium (and potentially vitamin D) at various ages, and oestrogen insufficiency in the post-menopausal period. Yet it could be argued that addressing these has not succeeded since rates of osteoporosis remain high in Western countries. Hormone replacement therapy, once viewed as a solution, is now used sparingly due to side effects and a potential impact on cancer risk. In contrast, the theory of calcium supplementation as a means of augmenting peak bone mass is sound and there is much evidence to support its use in practice. Benefits accrue because a sound calcium status maintains the balance between bone-promoting cells (osteoblasts) and bone-resorbing cells (osteoclasts), determining bone mineral density (BMD) and bone mineral content (BMC). This is mediated by parathyroid hormone, 1, 25 dihydroxyvitamin D_3 and calcitonin which work together to maintain calcium homeostasis.

Chan et al. (1995) randomized girls with habitually low calcium intakes to a control or dairy supplementation group for 1 year (n=48; mean age 11y; Tanner stage 2). Calcium intakes increased from 730 mg/d to 1200 mg/d in the dairy group which impacted on total BMC (205 g/y dairy vs. 109 g/y control; P<0.001). Similar results for bone mass accrual were seen in a 48-week supplementation study of pre-pubertal girls (n=149; mean age 8y). The use of calcium-enriched foods increased calcium intakes from 916 mg/d to 1723 mg/d, with girls at the lower baseline levels seeing the greatest benefit (Bonjour et al., 1997). Supplements also seem to work but it depends on habitual calcium intakes. A 1-year study using 500 mg/d calcium carbonate in girls (12-14y, majority at menarcheal stage) found only moderate effects on BMD and BMC. However, habitual intakes were in the region of 1000-1300 mg/d (Molgaard et al., 2004). An 18-month supplementation study used 500 mg/d calcium maleate in girls (n=149; mean age 12y, 65% at menarche), finding benefits for BMD (0.09 g/cm^2 in the supplementation group vs. 0.07 g/cm^2 controls; P<0.05), but not BMC.

The beneficial effect of dietary calcium on bone mineral mass appears to be maintained even after the cessation of supplementation, although the rate of improvement declines. Dodiuk et al. (2005) studied the effects of 1y of calcium carbonate supplementation (1000 mg/d) on long term bone mineral mass in post-menarcheal girls with low habitual calcium intakes (<800 mg/d). At 1y, BMD in the supplemented group had improved more than in the controls (P<0.05). Another follow-up, 3.5y after the intervention had finished, revealed that BMD in the supplemented group had remained constant, although the improvements due to the calcium supplementation had not been lost.

Despite good scientific evidence for the role of dietary calcium in bone health plus widespread nutrition advice and the greater availability of supplements and fortified foods, calcium intakes remain below recommended levels. USA data suggest that 70% of adults have low calcium intakes while, across Europe, low intakes have been reported in a variety of at risk populations including 50% of Irish girls, 75% of French women over 55 years, and 16% of UK 14-34 year olds. In Italy, average calcium intakes are 75% of recommended levels (Coxam et al., 2005). Yet, osteoporosis is not just a problem related to low calcium intakes. Other important factors such as physical activity and calcium bioavailability are involved. It would appear that a multiple approach is warranted. Prebiotics, such as inulin and oligofructose, are emerging as a solution for low calcium bioavailability and absorption.

Calcium and bone development

To understand how prebiotics might improve calcium uptake, it is worth reviewing the normal process of bone accretion from birth. Throughout childhood and early adulthood, dietary and endogenous calcium are taken up by the bone matrix where 98% of total body calcium is stored. Absorption up-regulates to respond to the special demands of the maximum growth periods during early childhood and adolescence. Abrams et al. (2000) found increased calcium absorption, bone calcium deposition rate (calcium gain) and markers of bone metabolism between the late pre-pubertal period and the pubertal age (Tanner stage 2). This corresponded to a mean calcium gain of 135 ± 53 mg/d vs. 110 ± 45 mg/d between the early pre-pubertal and late pre-pubertal stages (P=0.04). The highest rates of calcium gain were around 174 mg/d for boys and 212 mg/d for girls. This lagged 1 to 1½ year behind the peak height velocity which has been estimated at 13.3 years for boys, and 11.4 years for girls (Martin et al., 1997).

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However, if calcium intakes are poor during periods of maximum growth, enhanced absorption may not be enough to safeguard bone health. A rapid expansion of skeletal volume demands an increased supply of calcium. If this is not available, the result is sub-optimal BMD and fragility. Fractures of the distal forearm are relatively common in children, affecting around 1 % of 3 to 15 year olds. The likely cause is skeletal fragility during periods of maximum height velocity when bones are growing at their fastest rate (Parfitt, 1994). Children who experience these types of fractures may also be at risk later in life from osteoporosis. Calcium supplementation during adolescence is an effective means of improving bone density and reducing the risk of fractures. One study reported that an additional 500 mg/d of calcium increased total skeletal calcium by 4% (Lloyd et al., 1993).

Bone accretion is thought to continue until the mid to late twenties when peak bone mass is achieved. A young woman's skeleton has a BMC of around 2200 g, of which 32% or 708 g is elemental calcium. This would have been accumulated over a 20-year period at an average accretion rate of 35 g per year or 97 mg per day, although this estimate obscures the considerable variability in calcium uptake, especially during adolescence. After a decade or so, during which time bone mass remains fairly constant, the calcium content of the bone matrix begins to decline. This process gathers pace with age, accelerating in women in the years immediately following the menopause.

Prebiotics and calcium absorption

Around 90% of dietary calcium absorption usually occurs in the small intestine via one of two transportation methods; transcellular and paracellular. The transcellular system is located in the proximal small bowel and is saturable. Luminal Ca^{2+} is actively transported across the microvillar membrane to the basolateral membrane of the enterocytes. It is then released into the circulation. In contrast, the paracellular system is concentration-driven and enables calcium absorption through the tight junctions between mucosal cells. It is non-saturable, independent of vitamin D and occurs across the whole intestine. In the absence of prebiotics limited calcium absorption usually occurs in the colon, and it is here that prebiotics work partly by enhancing the more flexible paracellular transport system. Evidence for benefit is evident for inulin and oligofructose. By improving the absorption of dietary calcium these ingredients increase peak bone mass and thus help postpone the risk of osteoporosis-induced fractures later in life.

Inulin and oligofructose as prebiotics

Inulin and oligofructose are prebiotic fibres obtained from the chicory root (*Cichorium intybus*) and are composed of ß(2>1) linked fructose units, schematically given as GF_n and F_n (G = glucose, F = fructose and n = number of F- units). Native inulin (Raftiline®ST) encompasses a family of linear structures (GF_n) varying in degree of polymerization (DP) from 3 to 60 (average degree of polymerization, DPav=10). Oligofructose (Raftilose®P95) is obtained by partial enzymatic hydrolysis of inulin and has a small DP ranging from 2 to 8 (DPav=4). Long chain inulin (Raftiline® HP) can be made by selecting only the long chain inulin fractions (DPav=25). Raftilose®Synergy1 is a co-spraydried combination of oligofructose and long chain inulin and therefore has a unique chain length distribution.

Prebiotics are non-digestible food ingredients that beneficially affect host health by selectively stimulating the growth and/or activity of one or a limited number of health promoting bacterial species in the colon (Gibson et al., 2004). Inulin and oligofructose are not digested in the small intestine and reach the colon intact where they are selectively fermented by the microflora, particularly by the endogenous lactic acid bacteria, bifidobacteria and lactobacilli (Menne et al., 2000; Rao, 2001; Gibson et al., 1995: Langlands et al., 2004). End-products of this fermentation are short chain fatty acids and lactic acid whose presence lowers the luminal pH, thus increasing the solubility of minerals such as magnesium and calcium. This could explain the improvements in calcium absorption seen with prebiotic consumption, although other hypotheses include trophic effects across the entire gut or specific impacts on the active calcium uptake transport system. At present research is ongoing to identify likely mechanisms to explain the higher calcium absorption seen with inulin and oligofructose. However, there is certainly a role for colonic bacteria since antibiotic treated rats fed 5 % prebiotics exhibited reduced calcium and magnesium absorption. Thus, improvements in mineral absorption arise from the interactions between the prebiotics and specific colonic bacteria.

Evidence from animal studies

Two key animal models have been used to determine the impact of prebiotics on calcium and magnesium absorption and BMD; (1) young growing animals which represent the adolescent phase in humans, and (2) adult ovariectomized rats, which represent the post-menopausal phase in humans. *Apparent mineral absorption* is then measured by subtracting the faecal mineral content from the actual mineral intakes of the animals.

Over the past 10 years, evidence from animal models has consistently demonstrated that inulin and oligofructose increase calcium and magnesium absorption from the diet. Experiments in growing rats revealed a significantly higher apparent cal-

cium and magnesium absorption after 25 days following addition of 10 % inulin (as Raftiline®ST) or oligofructose (as Raftilose®P95) to the diet compared with placebo. The absorption of calcium was 40 % or 43 % vs. 25 %, respectively ($P < 0.01$). Magnesium absorption was 64 % for both inulin or oligofructose vs. 33 % for the control ($P < 0.01$) (Delzenne et al., 1995). Similar results have been seen in an ovariectomized rat model where it was also shown that bone turnover decreased (Zafar et al., 2004). Data from animal studies show that dietary inulin and oligofructose enhance calcium and magnesium absorption.

It is clear that inulin-type fructans improve calcium absorption but does this translate to advances in bone health? This was evaluated in the two animal models described above. Growing rats were fed either 5 % or 10 % inulin (Raftiline®HP) over 22 weeks. The result was a significant increase in whole body BMC ($P < 0.05$) and whole body BMD ($P < 0.001$) compared with controls (Roberfroid et al., 2002). In this rat model, long-term inulin administration appeared to impact mainly on the trabecular bone network (towards the ends of the bones). In adult ovariectomised rats, addition of 10 % oligofructose (Raftilose®P95) for 16 weeks significantly increased BMC in femur ($P < 0.05$) and lumbar vertebra ($P < 0.05$) compared with controls. This demonstrates that the normal post-menopausal bone losses in the trabecular structures were prevented by supplementation with inulin-type fructans (Scholz-Ahrens et al., 2002).

The combination of oligofructose and long chain inulin does matter

A study on adult rats fed 10 % inulin (Raftiline®HP) and 10 % oligofructose (Raftilose®P95) for 4 weeks found improved calcium and magnesium absorption rates on both diets as expected. However, these rates were further improved with a specific combination of oligofructose and long chain inulin (oligofructose-enriched inulin or Raftilose®Synergy1) as was the calcium and magnesium balance. This suggested a synergistic effect of combining short and long chain inulin-type fructan fractions on mineral absorption (Coudray et al., 2003). The important finding stimulated further research on the impact of Synergy1 on calcium kinetics. Ovariectomized rats were administered ^{45}Ca prior to dietary supplementation with the prebiotic for 21 days. Rats receiving 5 % of Synergy1 significantly increased calcium absorption ($P < 0.005$), bone calcium retention ($P < 0.005$), femoral calcium content ($P < 0.05$) and femoral BMD ($P < 0.05$). Moreover, kinetic data on bone metabolism showed improved bone balance and suppression of bone turnover with Synergy1 supplementation (Zafar et al., 2004). The level of supplementation was less than that used in previous animal experiments with conventional inulin and oligofructose, suggesting that the Synergy1 combination had a more powerful effect.

These experimental data suggest that inulin and oligofructose, particularly Synergy1, not only enhanced calcium and magnesium absorption, but improved bone health during growth and the post-menopausal period. The next step was to repeat these interventions in human subjects which required precise measures of calcium absorption and bone turnover.

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Stable isotopes as the preferential method of investigation

Various experimental methods have been used to investigate the beneficial effects of prebiotics on bone health. These include calcium balance, calcium kinetics, histology, BMD, BMC and biochemical markers. The best method for determining calcium absorption is believed to be stable isotopes as this excludes the confounding variable of endogenous calcium excretion.

A measure of *true calcium absorption* is then provided which cannot be obtained by the balance method. If isotopes are administered as part of a metabolic study, one can also see the individual components of calcium metabolism i.e. absorption, excretion, endogenous secretion, bone formation rates and bone resorption rates (Weaver, 2005).

Evidence from human studies

While there is historic evidence that improving calcium status also improves BMC and BMD, more research on the benefits of inulin and oligofructose is becoming available. A growing number of studies have now been performed in adolescents.

A first study in adolescent boys using the stable isotope technique found a significant increase in calcium absorption with oligofructose (Raftilose®P95) after 9 days of supplementation compared to the controls ($P < 0.05$) (Van den Heuvel et al., 1999). However, a rather high dosage (15 g/d) of oligofructose was used. As a consequence, Griffin et al. (2002) evaluated the effects of Synergy1 at only 8 g/d on calcium absorption during adolescence using dual stable isotopes ($^{46}Ca/^{42}Ca$) and 48 h urine collections. In a double blind cross-over protocol, adolescent girls (n=29; mean age 12y) were randomized to receive either Synergy1 (8 g/d) or a placebo (sucrose) for 3 weeks with a 2-week wash-out in-between. The saccharides were delivered in a calcium-fortified orange juice. The calcium intake of the girls was maintained within recommended levels at 1300-1500 mg/d in each group. True calcium absorption was significantly higher in the group receiving Synergy1 (38.2 ± 9.8 %) than in the placebo group (32.3 ± 9.8 %) ($P = 0.01$). It was clear that in girls with adequate calcium intakes, supplementation with modest amounts of Synergy1 significantly improved their calcium absorption. The most likely destination of the additional calcium was bone since urinary excretion of calcium did not increase.

As the range of responses to Synergy1 was broad with some girls benefiting more than others, a further study was instigated to evaluate which characteristics predicted the most benefit (Griffin et al., 2003).

The new study had a similar protocol to that carried out before in order to merge the two samples. An extra 25 adolescent girls were recruited bringing the overall sample to 54 (mean age 12y) across two centres in Texas and Nebraska . As with the previous study, there was a significant increase in calcium absorption with 8 g/d of Synergy1 compared with the sucrose placebo (36.1 % vs. 33.1 %, respectively). A range of characteristics was studied e.g. age, weight, height, Tanner stage and ethnicity. However, the most consistent determinant of a beneficial effect of Synergy1 on calcium absorption was the fractional calcium absorption during the placebo period. Thus girls with lower baseline levels of calcium absorption responded with the greatest increase when supplemented with Synergy1. Since the subjects all received a similar calcium load from the test meals, the variation cannot be explained by the presence of enhancers or inhibitors of calcium absorption in the diet. Rather, it is likely that the subjects' genotypes governed both their baseline calcium absorption, and their response to Synergy1 consumption.

This has been confirmed by a new long-term trial of Synergy1 which indicated that polymorphisms of the vitamin D-receptor Fok1 gene determine calcium absorption and the magnitude of the response to inulin and oligofructose supplementation (Abrams et al., 2005). However, the main findings from this long-term study, a double-blind controlled trial, related to the impact of Synergy1 on bone accretion over 1 year. Subjects were 100 girls and boys in early puberty (Tanner stage 2 or 3) with a mean age of 11 years. Against a background of normal calcium intakes (900-1000 mg/d), subjects were randomized to receive either 8 g/day of Synergy1 or a placebo (maltodextrin), added to milk or a calcium-fortified orange juice. As Figure 1 shows, 2 months into the intervention, subjects in the Synergy1 group already demonstrated a significantly higher ($P < 0.001$) true calcium absorption compared with controls (38.5 % vs. 30.0 %, respectively). The enhanced calcium absorption was maintained throughout the intervention so that, at 1 year, mean results were 37.7 % for the Synergy1 group and 31.7 % for controls, and were significantly different ($P = 0.048$).

Correspondingly, Synergy1-supplemented subjects had a significantly ($P < 0.05$) greater change in whole body BMC (245 ± 11 g/y) than controls (210 ± 10 g/y) after 1 year (see Figure 2). Assuming that the fraction of calcium in BMC is 32%, these values correspond to a daily skeletal calcium accretion of 218 mg/d for the Synergy1 group and 189 mg/d for the controls ($P < 0.05$). This can be estimated as an additional net accretion of 30 mg/d in the Synergy1 group. The change in whole body BMD was also significantly greater ($P = 0.01$) in the Synergy1 group vs. controls after 1 year (47 mg/cm^2/y vs. 32 mg/cm^2/y) respectively; see Figure 3). This corresponds to an increment in whole body BMD after 1 year of 15 mg/cm^2/y. The interpretation of this study is that Synergy1 increased calcium absorption during pubertal growth which enhanced bone mineralization leading to a greater bone mass during adolescence.

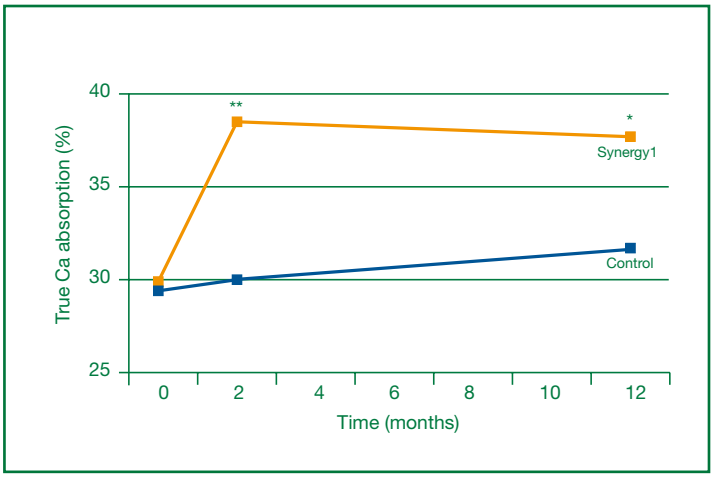

Figure 1: True calcium availability (%) of the subjects (mean ± stdev) after supplementation of the diets with Synergy1 or maltodextrin (control) for 2 months and 1 year.
* Represents a significant difference compared to the controls,
* P < 0.001. ** P = 0.04.

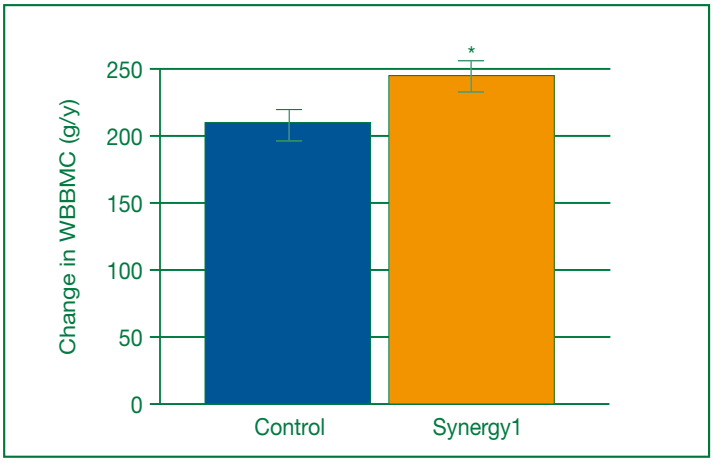

Figure 2: Change in whole body bone mineral content (WBBMC) (g/y) of the subjects (mean ± stdev) after supplementation of the diets with Synergy1 or maltodextrin (control) for 1 year. * Represents a significant difference compared to the controls, P = 0.03.

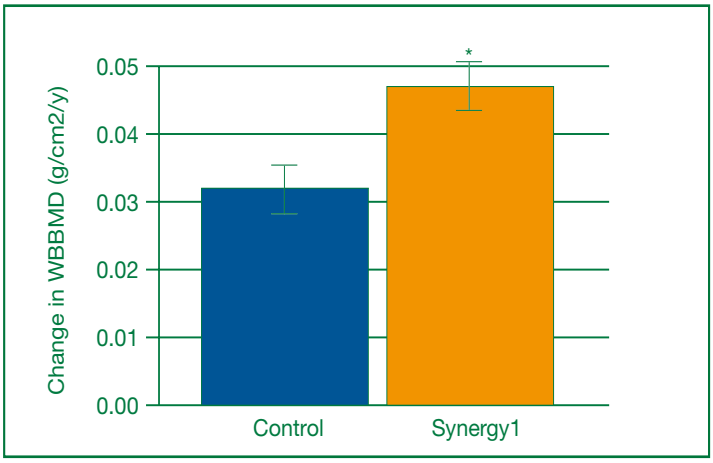

Figure 3: Change in whole body bone mineral density (WBBMD) (g/cm2/y) of the subjects (mean ± stdev) after supplementation of the diets with Synergy1 or maltodextrin (control) for 1 year. * Represents a significant difference compared to the controls, P = 0.01.

An interesting aspect of the study by Abrams et al. (2005) was that subjects were selected for Tanner stage. This increased the likelihood that calcium accretion was at its highest during the study when it would have the capacity to determine bone health at later age. The impact of Synergy1 pushed calcium accretion to maximum levels for girls at normal peak velocity (218 mg/d for Synergy1 compared with 212 mg/d peak velocity) (Martin et al., 1997).

Could Raftilose® Synergy1 help prevent osteoporosis?

There are two windows of opportunity for lowering the risk of osteoporosis. The first is by optimizing peak bone mass in early adulthood, the second is by minimizing bone loss in the stable post-menopausal period. Inulin and oligofructose appear to have a role in both. Improvements in calcium nutrition in early life can account for a 5 to 10% increase in peak bone mass, which could impact on hip fracture rates later in life by around 50 % (Coxam, 2005).

A new study undertaken by Dr. Anne Friedlander and colleagues of the Clinical Studies Unit at Palo Alto VA Health Care System in California, USA, investigated the effect of Synergy1 supplementation on skeletal health after menopause using markers of bone turnover. Post-menopausal women supplemented with Raftilose®Synergy1 (10 g/d) showed significantly (P < 0.05) improved calcium and magnesium uptake after 6 weeks of treatment relative to the placebo (maltodextrin). In response to this increased mineral absorption, Synergy1 increased bone formation by significantly increasing osteocalcin levels (P < 0.05), while at the same time temporary decreasing bone resorption by reducing urinary deoxypyridinoline crosslinks. This may lead to a net gain in bone mineral.

What is the physiological relevance?

It is known that good calcium status in the adolescent period results in a better bone mineralisation and a lower risk of osteoporosis at older ages. However, it appears that during periods of rapid growth, optimal calcium supply might be the major factor limiting bone mineral retention. Thus, the higher calcium absorption and bone mineralisation seen with Raftilose®Synergy1 supplementation compared with non-supplemented controls is of high physiological relevance. It is noteworthy that the efficacy of Raftilose®Synergy1, in relation to calcium gain (e.g. 11 g extra calcium per year during pubertal growth as seen in Abrams et al., 2005), often exceeds that seen in trials of calcium supplementation alone. Reducing skeletal fragility by maximizing peak bone mass during adolescence may be an important strategy in the prevention of osteoporosis.

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In older adults, it is known that BMD at various sites is a good predictor of hip fracture risk (Cummings et al., 1993). Indeed, a population-based cohort study in 7598 elderly women (mean age 75y) found BMD to be a significant predictor of hip fracture (Schott et al., 1998). Although calcium absorption declines with age, it is still possible to minimize bone loss, particularly in the hip region, with calcium supplementation. This translates into reductions in fracture rates of around 30 % by 18 months of treatment (Coxam, 2005).

Prebiotic research in older adults is relatively new. Recently, a new study performed by Dr. Anne Friedlander in post-menopausal women found significantly improved calcium and magnesium absorption when subjects were supplemented with Raftilose®Synergy1 (10 g/d) for 6 weeks. This led to changes in bone kinetics with a lower bone resorption rate and enhanced bone formation .

While it is clear that the use of inulin and oligofructose, especially Raftilose®Synergy1, improves calcium absorption and bone mineralisation, it is not known at present whether these benefits lower the lifetime risk of osteoporosis. Yet the evidence from both adolescents and post-menopausal women suggest that it might. The incorporation of inulin and oligofructose, particularly the oligofructose-enriched inulin (Synergy1), into a wide array of food products offers a new addition to current preventative strategies for osteoporosis.

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FREQUENTLY ASKED QUESTIONS

Do interactions occur between plant bioactive compounds and chicory inulin and oligofructose in the large intestine?

Yes, they occur. Biologically active compounds such as flavonoids, phenolic acids and phytoestrogens occur in plants mainly as glycosylated compounds. Numerous health benefits have been ascribed to these compounds, with respect to their anti-oxidative functions, prevention of cardiovascular diseases and hormone-related diseases such as breast cancer, osteoporosis, and others. However, before these compounds can be absorbed by the human body, they need to be deconjugated by the intestinal microbial flora (e.g. bifidobacteria). Bifidobacteria have ß-glycosidase activities, which liberate the aglycones from their glycosidic linkages and allow these compounds to be absorbed in the body. Chicory inulin and oligofructose are efficient prebiotics that selectively stimulate bifidobacteria growth and activity in the gut. Therefore, inulin and oligofructose indirectly improve the absorption and bioavailability of such plant bioactive compounds.

Inulin and oligofructose can also *potentate* or intensify the potency of bioactive products. One good example is soy, which contains gensitein and daidzein. Both isoflavones are metabolized by intestinal bacteria into secondary metabolites. Daidzein is converted into equol, which has proven to be a more powerful metabolite (e.g. anti-oxidative activity). In this respect, inulin and oligofructose can potentate the health benefits of soy products. This has recently been demonstrated by the maximizing effects inulin-type fructans have on the bone-spearing effects of soy (Mathey et al., 2004) as well as by the improved cholesterol-lowering action of soy when consumed together with inulin and oligofructose compared to the intake of soy alone (Wong et al., 2005).

Mathey, J., Puel, C., Kati-Coulibaly, S., Bennetau-Pelissero, C., Lebecque, P., Horcajada, M.N., Coxam, V. (2004). Fructo-oligosaccharides maximize bone-spearing effects of soy isoflavone-enriched diet in ovariectomized rat. Calcif. Tissue Int., 75, 169-179.

Wong, J.M.W., de Souza, R., Emam, A.; Kendall, C.W.C., Jenkins, D.A. (2005). Effect of colonic microflora enhancement by fructo-oligosaccharides on the hypercholesterolemic action of soy. Experimental Biology, Abstract book (280.1), San Diego, CA.

Can inulin cause an allergic reaction?

Inulin cannot be considered allergenic. About 90% of all allergic reactions are caused by eight items: milk, eggs, peanuts, tree nuts, fish, shellfish, soy and wheat; and about 15 million people in the Eastern world have food allergy. Food allergies involve the immune system and occur when the body mistakenly interprets something in food, usually a protein, as an invader. Inulin is a non-digestible carbohydrate consisting of a mixture of oligo- and polysaccharides composed primarily of fructose units linked by ß(2>1)-linkages. It is found in several edible plants such as vegetables and fruits, and has therefore always been present in certain amounts in the daily diet of the whole population. Only very exceptional cases of allergic reactions to vegetables naturally containing inulin have been reported. Inulin is produced industrially from chicory roots (*Cichorium intybus*). One isolated case of allergic reaction to food containing inulin was reported in 2000 (Gay-Crosier et al., 2000). Based on the fact that polysaccharides are not known to cause allergic reactions, the role of possible protein traces in commercial inulin was hypothesised. More recently a second isolated case of allergic reaction to a food containing inulin was reported in a woman with a past history of allergy to artichoke (Franck et al., 2005). However, in that case, it appeared that the allergic reaction had been triggered by a protein complex formed by heating the inulin-containing food (yoghurt), rather than by the inulin itself. It can thus be accepted that inulin and inulin-protein compounds clearly have an extremely low allergenic potential. Thousands of tons of chicory inulin are used by the food industry every year as it is incorporated in several thousands of consumer food products world-wide, mainly for its beneficial health effects on human metabolism, and every year millions of people consume it.

Gay-Crosier, F., Schreiber, G., Hauser, C. (2000). Anaphylaxis from inulin in vegetables and processed food. N. Engl. J. M., 342, 1372.

Franck, P., Moneret-Vautrin, D.A., Morisset, M., Kanny, G., Megret-Gabeaux, M.L., Olivier, J.L. (2005). Anaphylactic reaction to inulin: first identification of specific IgEs to an inulin protein compound. Int. Arch. All. Immunol., 136, 155-158.

MONITOR

Inulin-type fructans may improve intestinal immunity in rats

As the intestine is the first line of defense from the environment, the ability of the mucosal surfaces to respond vigorously to potential pathogens is a prerequisite against infection. Mucosal production of IgA prevents attachment of micro-organisms and molecular antigens, blocking their harmful effects to the host. The aim of this study was to evaluate the effects of fructo-oligo-saccharides (FOS), chicory inulin (INU) and isomaltooligosaccharides (IMO) on large bowel mass and IgA production in rats. Rats (n=54) were randomly assigned to a control diet or diets supplemented (6%) with one of the oligosaccharides tested for 5 weeks. Caecal and colonic wall weights were significantly higher in FOS and INU groups compared to IMO and controls ($P < 0.05$). Fecal pH and concentrations of acetic acid and total short chain fatty acids (SCFA) were also significantly increased in the FOS and INU vs. IMO and control groups ($P < 0.05$). A trend towards increased levels of IgA in caecum and feces was only seen for FOS and INU-fed groups. FOS and INU thus exerted trophic effects on the large bowel wall, increased the production of SCFA and lowered the pH, which were conditions positively associated with caecal and colonic IgA secretion.

Sung, H-Y., Jeong, H-J., Choi, Y-S. (2004). Effects of fructans and isomaltooligosaccharides on large bowel mass and plasma and fecal immunoglobulin A in rat. Nutr. Sci., 7, 196-200.

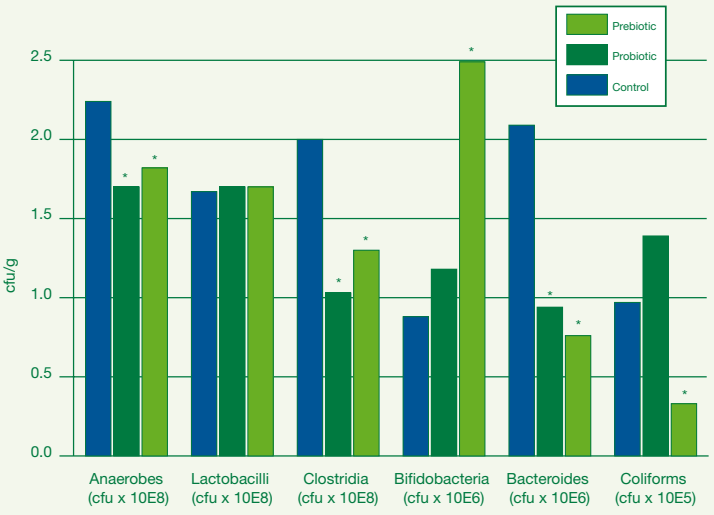
Infant formulas supplemented with oligofructose increase bifidobacteria and decrease pathogens in the caecum of rats

This study examined the effects of infant formulas enriched with prebiotics or probiotics on intestinal microbial changes in rats. The use of rat models has shown its efficacy in numerous studies to monitor diet-induced microbial changes in colon microflora and to evaluate the effect of pre- and probiotics in the prevention of disease (e.g. cancer, distal colitis, and others). Moreover, due to the use of animals, caecal microbial contents can be evaluated rather than examining faeces.

After weaning Wistar rats (n=30) were fed a standard diet (70 %) supplemented with one of three different follow-up infant formulas (30 %): a standard infant formula (control), a prebiotic-supplemented infant formula with 5.7 % (w/w) oligofructose, and a probiotic infant formula enriched with *Bifidobacterium lactis* and *Streptococcus thermophilus*. A significant increment in bifidobacteria levels was detected with the prebiotic infant formula ($P < 0.05$), whereas the *Bifidobacterium*-containing formula had no effect compared to the controls. Moreover, detection of *Bifidobacterium spp.* by DGGE analysis permitted these bacteria to be detected only in caecal contents of prebiotic-fed rats. The pre- and probiotic infant formulas significantly reduced total numbers of anaerobes, *Bacteroides* and clostridia ($P < 0.05$), and only the prebiotic infant formula significantly lowered numbers of coliforms vs. the controls ($P < 0.05$).

To conclude, it appears that both pre- and probiotic infant formulas are capable of reducing numbers of putative pathogens, *Bacteroides spp.* and clostridia, in the caecal contents of rats, whereas the prebiotic formula appears to be more effective, since it also decreased numbers of coliforms and increased *Bifidobacterium spp.*

Montesi, A., Garcia-Albiach, R., Pozuelo, M.J., Pintado, C., Goni, I., Rotger, R. (2005). Molecular and microbiological analysis of caecal microbiota in rats fed with diets supplemented either with prebiotics or probiotics. Int. J. Food Microbiol., 98, 281-289.



Enumeration (cfu per gram of caecal contents) of bacterial groups by plate counts given as means (n=3) from each feeding group: standard infant formula (control), prebiotic infant formula or probiotic infant formula groups. The scale is not the same for all bacterial groups, as indicated in the ordinates legend.
* : Indicates a significant difference from the control group ($P < 0.05$).
(Montesi et al., 2005)

Bifidogenic effects of a synbiotic in the elderly

Gut function changes as people are getting older, and this is often accompanied by an increased incidence of gastrointestinal infections. Among other factors, this may be caused by shifts in the bacterial populations in the large bowel such as decreased bifidobacteria levels and increased numbers of clostridia and enterobacteria. To evaluate whether bacterial changes can be induced in elderly people by consuming a synbiotic, a randomized, double-blind, controlled trial was performed in which subjects received a synbiotic twice a day which contained 6g of oligofructose-enriched inulin (Raftilose®Synergy1), *Bifidobacterium bifidum* and *Bifidobacterium lactis* or placebo (maltooligosaccharides and potato flour). Subjects receiving the synbiotic had significantly higher numbers of total bifidobacteria, *Bifidobacterium bifidum* and *Bifidobacterium lactis* during the feeding (weeks 4 and 5) and the post-feeding (weeks 6 and 8) periods compared to placebo ($P < 0.05$). In some volunteers, levels of *Bifidobacterium adolescentis* and *Bifidobacterium angelatum* even increased by more than 1 (log) order of magnitude. In conclusion, consumption of a Synergy1-based synbiotic supplement by healthy elderly people increased their intestinal bifidobacteria communities, demonstrating that it has potential to be of particular benefit to individuals with more unbalanced gut ecosystems.

Bartosch, S., Woodmansey, E.J., Paterson, J.C.M., McMurdo, E.T., Macfarlane, G.T. (2005). Microbiological effects of consuming a synbiotic containing *Bifidobacterium bifidum, Bifidobacterium lactis,* and oligofructose in elderly persons, determined by real-time polymerase chain reaction and counting of viable bacteria. CID, 40, 28-37.

Oligofructose improves hepatic function

Non-alcoholic steatohepatitis (NASH) is an asymptomatic disease, particularly frequent in patients with obesity, diabetes and hyperlipidemia, and is associated with elevated serum levels of aminotransferases. Steatosis, in some cases, degenerates towards fibrosis, cirrhosis, and ultimately death resulting from liver failure. Previous studies in animal models have shown that oligofructose protects against liver triglyceride (TAG) accumulation and lessens hepatic steatosis. Therefore, a double-blind, cross-over, and placebo-controlled intervention study was performed in patients (n=7) with NASH to asses the effects of 8 weeks ingestion of oligofructose (Raftilose®P95) vs. control (maltodextrin) on serum parameters attesting liver integrity, as well as lipid and glucose homeostasis. Compared to the placebo, oligofructose decreased serum aminotransferases, aspartate aminotransferases

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Inulin as a fat substitute to lower daily energy intake

Strategies to prevent obesity, primarily focusing on decreasing fat content of individual foods, have failed. Poor palatability and the lack of satiating power of these low-fat versions have led to (over) compensation for the reduced energy intake during the rest of the day. The aim of this study was to evaluate whether replacing fat with inulin (INU) or lupin kernel fibre (LKF) influenced palatability, perceptions of satiety, and food intake in 33 healthy men (mean age 52y). On separate occasions, after an overnight fast, participants consumed a breakfast consisting of either a full-fat sausage patty or a reduced-fat patty with one half of the fat replaced by either INU or LPK. All three breakfasts were similar in mass, protein and carbohydrate content. INU en LPK breakfasts were 36 % and 37 % lower in fat and consequently 15 % and 17 % lower in energy density vs. the full-fat counterpart. Mean general acceptability rating of all three sausage patty variants was well above the mid-point of the rating scale, suggesting that consumers sensorially well accepted the low-fat variants. Satiety scores for the INU and full-fat breakfast did not differ, although the INU breakfast provided less energy than the full-fat breakfast. This suggests that inulin did have an impact on early post-meal satiety, but not to the magnitude of the LPK. Energy intakes during the whole day were significantly lower with the INU and LPK breakfasts ($P < 0.05$) compared with the full-fat version, indicating that full compensation for the lower energy content of the INU and LPK breakfasts did not occur. Inulin is well fermentable by the human colonic bacteria, leading to the production of short chain fatty acids (SCFA). Late post-absorption satiety triggers are related to the absorption and metabolism of SCFA, which may explain why inulin influences long-term food intake. INU and LPK are effective fat replacers in the formulation of palatable foods with high satiating power that may be of value in diets designed to reduce long-term fat and energy intake.

Archer, B.J., Johnson, S.K., Devereux, H.M., Baxter, A.L. (2004). Effect of fat replacement by inulin or lupin-kernel on sausage patty acceptability, post-meal perceptions of satiety and food intake in men. Brit. J. Nutr., 91, 591-599.

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($P < 0.05$) and alanine aminotransferase (non-significant), after 8 weeks and decreased insulin levels and C-peptide concentrations after 4 weeks. The results of this pilot study support an improvement of hepatic function with daily oligofructose supplementation in diseases associated with abnormal liver lipid accumulation.

Daubioul, C.A., Horsmans, Y., Lambert, P., Delzenne, N.M. (2005). Effects of oligofructose on glucose and lipid metabolism in patients with nonalcoholic steatohepatitis: results of a pilot study. Eur. J. Clin. Nutr., 59, 723-726.

Addition of prebiotics to formula-fed infants mimics gut flora and metabolic activity of breast-fed infants

Immediately after birth, the intestinal microbial flora develops and the presence or absence of prebiotics in the infants' diets is determinant for the presence of a healthy and well-balanced flora. In breast-fed infants, the flora is dominated by bifidobacteria and lactobacilli, due to the presence of prebiotics in human milk. Previous studies have shown that prebiotics stimulate bifidobacteria growth in formula-fed term and preterm infants, so that their flora resembles more to that of the breast-fed infant. In this study, infants (n=68) of 2 months of age and fed a conventional milk formula were enrolled in a double-blind, placebo-controlled, case-control study. The effects of prebiotics (a combination of galacto-oligosaccharides with long chain inulin) vs. a standard formula (control) were studied on microbial changes and metabolic activity after 6 weeks. A breast feeding group was included too. At the end of the study, the percentage of bifidobacteria was significantly higher in the prebiotic group (59.6 %) vs. the control (49.5 %) ($P = 0.046$). Faecal pH of the infants in the prebiotic group was significantly lower (5.7) vs. the control (6.3) ($P < 0.001$). Lactic acid production, on the contrary, was significantly higher in the prebiotic group (22.2 mmol/kg wet weight of faeces) vs. the control (5.2 mmol/kg) ($P < 0.001$). Proportion of acetate was also significantly higher in the prebiotic group (85.2 %) vs. the control group (77.2 %) ($P < 0.001$). To conclude, this study showed that prebiotics induce bifidogenic effects and changes in the metabolic activity in the gut of infants with an already established microflora, leading to a flora resembling more closely that of breast-fed infants.

Knol, J., Scholtens, P., Kafka, C., Steenbakkers, J., Grob, S., Helm, K.; Klarczyk, M., Schöpfer, H., Böckler, H.-M., Wells, J. (2005). Colon microflora in infant fed formula with galacto-oligosaccharides and fructo-oligosaccharides: more like breast-fed infants. J. Pediatr. Gastroenterol. Nutr., 40, 36-42.

Oligofructose prevents *Clostridium difficile*-associated diarrhoea

Clostridium difficile infection represents one of the most common hospital (nosocomial) infections with high morbidity and mortality. The bacterium is considered a major causative agent of colitis and causes outbreaks of diarrhoea in hospitalized patients. The disease is often triggered by antibiotic therapy, leading to alterations of the intestinal microbial environment into reduced colonization resistance and increased susceptibility to *Clostridium difficile*. Treatment of *Clostridium difficile*-associated diarrhoea involves the use of antibiotics (metronidazole or vancomycin). However, even after successful treatment about 20% of the patients relapse. The aim of this study was to determine whether oligofructose could reduce the rate of relapse from *Clostridium difficile*-associated diarrhoea. Patients (n=142) with *Clostridium difficile* toxin-associated diarrhoea were enrolled in a randomized, double-blind, placebo-controlled study. After cessation of the diarrhoea, patients received oligofructose (12 g/d Raftilose®P95) or placebo (sucrose) for 30 days, in addition to antibiotic treatment. Patients were further followed for another 30 days after the intervention period. Total anaerobes and bifidobacteria levels were significantly higher in the oligofructose group compared to placebo at 30 days ($P = 0.002$ and $P < 0.001$, respectively) and 60 days ($P = 0.001$ and $P = 0.0002$, respectively). Moreover, relapse of diarrhoea was significantly less common in those patients supplemented with oligofructose (8.3 %) compared to placebo (34.3 %) ($P < 0.001$). Patients who relapsed stayed in the hospital longer than those who did not (53 vs. 26 days, $P = 0.021$) and there was a longer period of time from starting metronidazole or vancomycin treatment (6 vs. 3 days, $P = 0.007$). From the results, oligofructose was shown to increase bifidobacteria levels in patients with high risk for relapse from *Clostridium difficile*-associated diarrhoea. In addition, those patients taking oligofructose were less likely to relapse and to further develop diarrhoea.

Lewis, S., Burmeister, S., Brazier, J. (2005). Effect of the prebiotic oligofructose on relapse of *Clostridium difficile*-associated diarrhea: A randomized, controlled study. Clin. Gastroenterol. Hepatol., 3, 442-448.

Fructans increase copper absorption

In this study the effect of fructo-oligosaccharides (FOS) on trace element absorption was investigated. Post-menopausal women (n=11), aged 53-70 years, were randomized in a double-blind, placebo-controlled, cross-over trial. Their diets were supplemented with 10g FOS/d or placebo sucrose for 5 weeks followed by a wash-out period of 3 weeks. At the end of each period, absorption of zinc, selenium and copper was determined by stable isotopes. No modifications of zinc or selenium intestinal absorption were observed after FOS-supplementation. Copper absorption was significantly enhanced ($P = 0.042$) by FOS vs. controls. It appears that fructans increase copper absorption and, thereby, may improve copper status in post-menopausal women.

Ducros, V., Arnaud, J., Tahiri, M., Coudray, C., Bornet, F., Bouteloup-Demange, C., Brouns, F., Rayssiguier, Y., Roussel, A.M. (2005). Influence of short-chain fructo-oligosaccharides (sc-FOS) on absorption of Cu, Zn, and Se in healthy postmenopausal women. J. Am. Coll. Nutr., 24, 30-37.

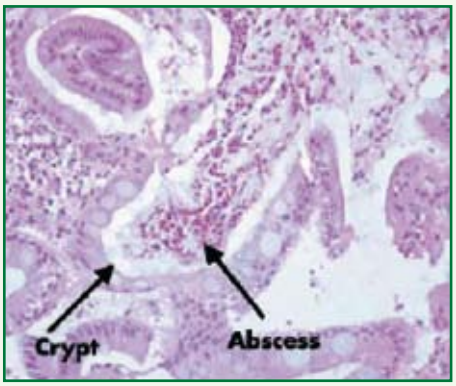
Synbiotic therapy relieves symptoms in ulcerative colitis patients

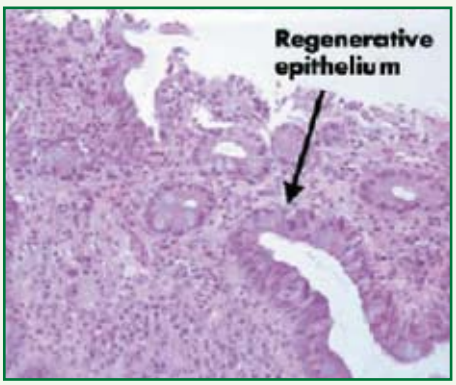
Ulcerative colitis (UC) is a relapsing inflammatory disease of the colon which etiology has not been clarified yet. An altered immune response towards normal commensal organisms may drive the inflammatory process. Patients with UC have also altered bacterial populations in their colon such as lower amounts of bifidobacteria, leading to the hypothesis that synbiotics may be one approach for therapy. Patients (24-67y) with active UC waiting for colonoscopy (n=18), and not taking antibiotics, accepted to be enrolled. Patients were randomized to either a placebo (maltodextrin) or the synbiotic group, ingesting two times 6 g/d for 4 weeks of an oligofructose-enriched inulin (Raftilose®Synergy1) with *Bifidobacterium longum*. Inflammation was assessed by either traditional methods, such as endoscopy and examination of biopsies, and by new sensitive methods, measuring changes in gene expression of antimicrobial peptides called human beta defensins (hBD) and cytokine profiles. hBD are uniquely expressed by epithelial cells. hBD2 and hBD3 are up-regulated in UC and their production is positively correlated with the severity of the active disease, making them excellent targets for assessing inflammatory responses in UC epithelia after therapy. Levels of bifidobacterial specific total rRNA in mucosal biopsies were determined using real-time PCR.

After 4 weeks of treatment, sigmoidoscopy score was markedly reduced in the synbiotic group (-1.3), whereas an increase was observed in the placebo group (+0.58). Histopathology of rectal biopsies showed a similar trend with a reduction in scores for the synbiotic group (-0.6) over 4 weeks and an increase in the placebo goup (+1.0).
Expression levels of inducible hBD2 and hBD3 in synbiotic patients post-treatment were significantly lower vs. pre-treatment ($P < 0.05$). Pro-inflammatory cytokines, TNF-α and IL-1α, were significantly reduced in the post-feeding synbiotic patients compared with the pre-feeding period ($P = 0.018$ and $P = 0.038$, respectively) or the post-feeding control group ($P = 0.018$ and $P = 0.005$, respectively).
Levels of bifidobacterial colonization in mucosa of UC patients was increased by 42-fold after synbiotic administration vs. 4.6-fold in the placebo-group.

In conclusion, synbiotic therapy over four weeks significantly reduced mucosal inflammation markers in active UC. This was concurrent with a reduction in colitis at the macroscopic and microscopic levels and an increase in mucosa-associated bifidobacteria, providing evidence for the potential of synbiotics in therapies for patients suffering form acute UC.

Furrie, E., Macfarlane, S., Kennedy, A., Cummings, J.H., Walsh, S.V., O'Neil, D.A., Macfarlane, G.T. (2005). Synbiotic therapy (*Bifidobacterium longum*/Synergy1) initiates resolution of inflammation in patients with active ulcerative colitis: a randomized controlled pilot trial. Gut, 54, 242-249.





Histopathology of rectal mucosa from a patient with UC pre-synbiotic therapy (up) and post-treatment (below). The figure below shows resolution of the acute inflammatory activity following synbiotic consumption (12 g/d) Raftilose®Synergy1 in combination with *Bifidobacterium longum* for 4 weeks. The crypt abscesses (present in the upper picture) have disappeared and the epithelium shows a more regenerative appearance (picture below). (Furrie et al., 2005)

AGENDA

COLOPHON

Active Food Scientific Monitor is published by ORAFTI, a subsidiary of RAFFINERIE TIRLEMONTOISE (B), and is part of the ORAFTI/ PALATINIT Ingredients Group of SÜDZUCKER (D). ORAFTI produces inulin (Raftiline®), oligofructose (Raftilose®) and fructose syrups (Raftisweet®) from chicory roots. The commercial department of ORAFTI is based in Tienen and operates worldwide in 70 countries through own sales offices and distributors. The production units are located in Belgium and The Netherlands.
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Poland, Krakow

October 6-8, 2005
Subject: European Conference on Probiotics and their Applications
Content: Prebiotics and probiotics in Inflammatory Bowel Disease
Speaker: Dr. Francisco GUARNER
Info: Ms. Sito, Euprobio
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Spain, Barcelona

October 13, 2005
Subject: Prebiotic workshop; EU-project on Early Nutrition Programming for Adult Health (EARNEST)
Content: Topics to be discussed include:
- Prebiotic effect of inulin and oligofructose
- Effects of inulin and oligofructose on calcium absorption and bone health
- Protective effects of inulin and oligofructose against colonic cancer (data from the SYNCAN project)
- Effects of inulin and oligofructose on immune response and prevalence of infection
- Role for inulin and oligofructose as prebiotics in infant foods

Speaker: Experts in the different fields
Info: R. Toboso
Tel. +34 93 487 61 74
Email: ramon.toboso@orafti.com
Website: www.orafti.com

Belgium, Brussels

October 19-20, 2005
Subject: Healthy Foods Summit
Content: Health is the Future of Food
Speaker: Paul COUSSEMENT, ORAFTI
Info: J. Pedersen
Tel. +44 1 628 486038
Email: jpedersen@newhope.com
Website: www.healthyfoodssummit.com