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Active Food Scientific Monitor

Interview with Professor K.D. Cashman

Nutrition, rugby and …Guinness

In this issue, we present an interview with Professor Kevin D. Cashman, Professor of Food & Health, Department of Food Science and Department of Medicine at University College Cork, Ireland.

Professor Cashman has a BSc in Nutrition. His PhD focused on mineral bioavailability and dietary factors affecting it. "At that time, I was investigating the effect of dietary factors on the absorption of several minerals, including calcium. Bioavailability refers to the process in which a mineral is absorbed across the gut, but also, importantly, how it is then utilised in the body. Therefore, to expand and build upon my work on calcium absorption, I began investigating the effect of calcium and other dietary factors on calcium and bone metabolism, using specific and sensitive serum and urine-based biochemical markers. This gives a better picture of bioavailability. This has been my passion ever since."

Two years ago he was appointed Professor of Food & Health at University College Cork (UCC) in Ireland. This is a joint position between Nutritional Sciences and the Department of Medicine. "My intention is to enhance trans-disciplinary food-health research collaboration and activities in these Departments."

His current research interest is in the role of diet, genetics, and their interaction on bone metabolism and bone health. He is involved in four European Union-funded Framework V shared-cost research projects that investigate the role of diet and nutrition, and their interaction with the human genome, on bone health. Along with his colleague, Professor Albert Flynn in UCC, he co-ordinates one of these projects (entitled OSTEODIET). These projects will provide new information on the role of diet and genetic variability in the development of osteoporosis and on how dietary strategies may be developed for its prevention.

"I am also very interested in the process of intestinal calcium absorption. In recent times, we have been investigating the effect of novel bioactive ingredients on calcium absorption using studies in experimental animals and in human intestinal-like, Caco-2 cells, in culture."

Kevin Cashman is also an avid rugby fan, having played the game since an early age. "I am especially looking forward to the Rugby World Cup in Australia next year, where hopefully we will see Ireland win the tournament." He also enjoys the outdoors, and, especially, a bit of a hike into the Irish countryside. "This does wonders for one's appetite, not only for fine Irish food, but also for a couple of pints of national treasure, i.e. Guinness."

Dietary calcium intake has an important impact on bone metabolism and bone health. Chronic calcium deficiency resulting from inadequate intake or poor intestinal absorption is one of several important causes of reduced bone mass and osteoporosis. It is vital, therefore, that adequate dietary calcium is consumed at all stages of life. Besides the amount of calcium in the diet, the absorption of dietary calcium from foods is a critical factor in determining the availability of calcium for bone development and maintenance. Thus, there is a need to identify food components and/or functional food ingredients that may influence calcium absorption positively in order to ensure that calcium bioavailability from foods can be optimised. Several studies strongly suggest that addition of inulin or oligofructose to food represents an opportunity for increasing the uptake of calcium.

Some functional food ingredients may increase calcium absorption

What are the consequences for bone health of an inadequate intake of calcium ?

A large number of macro- and micronutrients have been proposed as possible determinants of bone health and osteoporosis risk. Of the bone-building nutrients, calcium is the most likely to be inadequate in terms of dietary intake.

Purely from a biochemical or physiological point of view, a short-term inadequate intake or poor intestinal absorption of calcium causes the concentration of circulating ionised calcium to decline acutely, which

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P R E F A C E

by Dr. Anne Franck

Nutritional and Health Benefits of Inulin and Oligofructose

In February 2001 we organised the 3rd ORAFTI Research Conference in London. The proceedings, which were recently published in the British Journal of Nutrition (2002, vol. 87, suppl. 2) review the scientific data concerning inulin and oligofructose that were available at the time of the Conference. They report the view of leading experts from Europe, the United States, Canada and New Zealand in the field of nutrition regarding the technological and mainly the nutritional properties of these food ingredients. They contribute to the scientific data required to scientifically substantiate the classification of inulin and oligofructose as functional food ingredients.

In this issue of the Active Food Scientific Monitor, we present a summary of this publication confirming that inulin and oligofructose are prebiotic dietary fibres. Moreover, a number of animal and human studies are discussed showing that these ingredients induce interesting physiological benefits such as: improved calcium bioavailability; reduction of colon cancer risk; immune-enhancing effects; modulation of lipid metabolism; and even increased sense of well-being.

Scientific data thus exist to substantiate health claims based on enhanced function (e.g. improved gut function, enhanced calcium absorption). Moreover, sound hypotheses and experimental data exist to further justify human studies and long-term intervention trials that might give support to health claims based on disease risk reduction (e.g. reduction of colon cancer risk).

The development of functional food ingredients such as inulin and oligofructose offers a unique opportunity to contribute to the improvement of the quality of our food for better well-being and health.

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triggers an increase in parathyroid hormone (PTH) synthesis and release. PTH acts on three target organs to restore the concentration of circulating calcium to normal. At the kidney, PTH promotes the re-absorption of calcium. PTH affects the intestine indirectly by stimulating the production of the active form of vitamin D, which in turn leads to increased absorption of calcium. PTH induces bone resorption, thereby releasing calcium into the blood. Due to the action of PTH, plasma levels of calcium are restored within minutes to hours. If, on the other hand, there is a chronic deficiency of calcium resulting from a continual inadequate intake or poor intestinal absorption of calcium, the circulating concentration of calcium is maintained largely at the expense of skeletal mass, i.e. from an increased rate of bone resorption. This PTH-mediated increase in bone resorption is one of several important causes of reduced bone mass and osteoporosis. The cumulative effect of calcium depletion on the skeleton over many years contributes to the increasing frequency of osteoporotic fractures with age.

Osteoporosis can be defined as a systemic skeletal disease characterised by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture. Osteoporotic fractures constitute a major public health problem. Currently, in the US alone, 10 million individuals already have osteoporosis, and a further 18 million more have low bone mass, placing them at increased risk for this disorder (National Institutes of Health, 2000). Per annum, one in eight EU citizens

food ingredients may increase calcium absorption

over the age of 50 years will fracture their spine (European Commission, 1998). Of most concern is the projection that the incidence of osteoporosis will increase sharply over the next few decades.

It is particularly worrying that with our understanding of the importance of dietary calcium in bone health, a significant proportion of some population groups fails to achieve the recommended intake of calcium in a number of Western countries. This may have major consequences for bone health.

What can be done to improve the intake of calcium?

The dietary deficiency of calcium identified in some population groups may be addressed in a number of ways. This includes changing eating behaviour at the population level, by increasing the consumption of foods that are naturally rich in calcium (e.g. milk and milk products), calcium fortification of foods consumed by target groups, or increasing calcium intakes from calcium supplements. These may be seen as complementary rather than alternative strategies, and each has advantages and disadvantages. For example, it is notoriously difficult to achieve changes in the diet of entire populations, and thus persuading individuals to consume more dairy products represents a considerable challenge. The use of calcium supplements can be effective in increasing the intake of calcium in individuals who consume them regularly, but it has limited effectiveness at the population level, due to poor compliance with supplements. Calcium-fortified food products could provide additional choices for meeting calcium requirements; however, attention should be paid to the selection of products so that they reach the target groups (i.e. those who have the greatest difficulty in meeting calcium requirements).

Besides the amount of calcium in the diet, the absorption of dietary calcium is a critical factor in determining its availability for bone development and maintenance. Thus, there is a need to identify food components and/or functional food ingredients that may influence calcium absorption positively in order to ensure that the bioavailability of dietary calcium can be optimised.

Why is a better absorption of calcium so important?

Recent studies suggest that when consuming a low-calcium diet, low efficiency of calcium absorption is a problem in the elderly. Moreover, it has been shown that this is an important risk factor for hip fracture. So yes, if we can formulate strategies for enhancing intestinal calcium absorption, then there could be benefits to bone health. Also, at the other end of the age-spectrum, namely children and adolescents, there is a crucial need that calcium be absorbed optimally. This absorbed calcium may then be used for maximal bone mineralisation and development of maximal peak bone mass. Having an optimal peak bone mass reduces future risk of osteoporosis.

Some recent studies suggest that inulin and oligofructose may enhance the absorption of dietary Ca.

Various dietary factors have been evaluated for their potential ability to stimulate calcium absorption. Emerging evidence has shown that certain non-digestible oligosaccharides (NDOs) or prebiotics can improve calcium absorption in adolescents and adults. For example, Coudray et al. (1997) fed nine healthy young men a control diet or the same diet supplemented with 40 g/day of either chicory inulin or sugar-beet fibre for a period of 26 days (2 days of control diet followed by 14 days of progressive increase in amount of inulin and then 12 days at the maximum consumption of inulin) and determined apparent calcium absorption. They found that upon ingestion of inulin, apparent calcium absorption increased significantly ($P<0.01$) from 21.3% to 33.7% (an increase of 58%); but ingestion of sugar-beet fibre had no effect. In a randomised, double blind, cross-over design study, Van den Heuvel et al. (1999) fed 12 healthy male adolescents (aged 14–16 years) either orange juice supplemented with 5 g of oligofructose (Raftilose®P95) or 5 g of sucrose (control treatment) three times daily for 9 days, after which time, they measured true fractional calcium absorption by a dual stable-isotope technique. An increase of 26% in true fractional calcium absorption (47.8% with placebo to 60.1% with oligofructose) was observed upon ingestion of the daily supplement of 15 g of oligofructose.

In an earlier study by the same group, the same daily supplement of 15 g of oligofructose had no effect on calcium absorption in adult healthy men (Van den Heuvel et al., 1998). However, in that study, unlike the latter one, the colonic component of calcium absorption (a putative target for enhancement by prebiotics) was not included because the urine collection was limited to 24 hours after administration of the isotope.

In a recent, randomised, double-blind, cross-over design study, 29 young adolescent girls (11-14 years, consuming a relatively high intake of calcium (1500 mg/day)) received daily either 4 g of enriched inulin(Raftilose®Synergy1) or 4 g of placebo (sucrose) twice daily in a calcium-fortified orange juice for 3 weeks. True calcium absorption was measured using a dual stable-isotope method at the end of each three-week period. A 48-hour urine collection was carried out after administration of the isotope so as to detect any modulatory effect of the enriched inulin on the colonic component of calcium absorption. Consumption of the enriched inulin resulted in an 18% increase in true fractional calcium absorption and in an absolute increase in calcium absorption of 90 mg/day (Griffin et al., 2002).

The findings of the above studies strongly suggest that addition of some prebiotics to food represents an opportunity for increasing the uptake of calcium present in the diet.

As always in nutritional research, more studies would be welcome to further document this effect and to prove that the benefits of these ingredients to calcium absorption can be translated into long-term benefits to bone health.

Nutritional and Health Benefits of Inulin and Oligofructose

At the 3rd ORAFTI Research Conference on "Recent Scientific Research on Inulin and Oligofructose", which took place in London in February 2001, the latest scientific data available on these ingredients were presented and discussed.
The conference was a good opportunity to review and evaluate scientific data concerning the potential health benefits of inulin and oligofructose.
Besides reviews on their properties as dietary fibres and prebiotics, a number of studies on the physiological and nutritional effects of inulin and oligofructose were presented and discussed. These effects relate to, e.g., improved calcium bioavailability, reduction of colon cancer risk and hypotriglyceridemia (Roberfroid, 2002).

Dietary fibre properties

Dietary fibres consist of remnants of edible plant cell-wall saccharides and associated substances resistant to hydrolysis by human alimentary enzymes. They reach the large intestine where they can be fermented by the resident microflora.

Inulin and oligofructose are non-digestible oligo- and polysaccharides found in a number of vegetables, fruits and whole grains. They fit perfectly well into the current concept of dietary fibre, as they resist digestion in the small intestine, are fermented in the large intestine, are less energetic than starch and sucrose, increase stool weight and frequency, and modulate several aspects of intestinal epithelium integrity (Cherbut, 2002; Nyman, 2002).

Prebiotic effect

The prebiotic effect of inulin and oligofructose has been confirmed in numerous laboratory and human

trials and they are therefore being used increasingly in new food product developments (Kolida et al., 2002).

The defining effect of prebiotics is to selectively stimulate the growth of bifidobacteria and lactobacilli in the gut and, thereby, to increase the resistance to invading pathogens. Prebiotics may have additional benefits because of their fermentation in the large intestine, which yields short-chain fatty acids (SCFA). Potentially the most important effect of prebiotic carbohydrates is to strengthen the body's resistance to invading pathogens and, thereby, prevent episodes of diarrhoea (Cummings & Macfarlane, 2002).

There is a great deal of evidence for positive effects of some prebiotics for alleviating constipation. There is experimental evidence suggesting that prebiotics may have promising properties with respect to treatment of inflammatory bowel disease, prevention of cholesterol gallstones, prevention of infections of intestinal origin and reduction of colon cancer risk. These effects need to be further confirmed in well-controlled human studies (Marteau & Boutron-Ruault, 2002).

Immune-enhancing effects

There is increasing evidence that prebiotic fibres can modulate various properties of the immune system, including those of the gut-associated lymphoid tissue (GALT), secondary lymphoid tissues and peripheral circulation (Schley & Field, 2002). Changes in the intestinal microflora that occur with the consumption of prebiotics may mediate immune changes via the direct contact of lactic acid bacteria or bacterial products (cell-wall or cytoplasmic components) with immune cells in the intestine, the production of SCFA from fermentation, or the modulation of mucin production.

Future protocols on the physiological impact of consuming prebiotics should be designed to include assessment of the gut microflora and gut physiology, as well as the function and composition of the various regions of the GALT.

The review by Buddington et al. (2002) examined how fructans influence the defence functions of animals and, thereby, increase resistance to lumenal pathogens and to noxious chemicals in the diet (drugs, pesticides, etc.), and to systemic challenges with pathogens, and whether they accelerate recovery from disturbed gastrointestinal tract (GIT) ecosystems.

Inulin and oligofructose are not considered to be immunogenic and apparently do not induce the expression of various enzyme systems associated with xenobiotic metabolism. Instead, their major influence on defence functions can be attributed directly or indirectly to changes in the population and metabolic characteristics of the bacterial populations present in the GIT. The second line of defence is the multilayered mucosal barrier that acts as selective filter to exclude pathogens, hazardous chemicals and other potential challenges to health. The third line of defence consists of the systemic mechanisms that recognise and eliminate any potentially harmful organisms or chemicals that manage to pass the mucosal barrier.

The review highlighted the importance of the interactions among prebiotics, GIT bacteria and the multiple defence mechanisms of the host.

Improvement of calcium absorption

Dietary calcium intake has an important impact on bone metabolism and bone health. A sufficient intake of calcium and vitamin D can reduce the risk of fractures in post-menopausal women, and it is likely that a low calcium intake may negatively affect peak bone mass. It is vital therefore that adequate dietary calcium is consumed at all stages of life. However, significant proportions of some population groups in Western countries are not consuming the recommended levels of calcium. Cashman (2002) discussed the consequences of this for bone health and osteoporosis risk, and proposed some strategies to enhance the consumption of calcium.

Besides the amount of calcium in the diet, the absorption of dietary calcium is a critical factor in determining its availability for bone development and maintenance. Thus, there is a need to identify food components that may facilitate the absorption of calcium.

Numerous animal studies have shown that inulin and oligofructose stimulate absorption of dietary minerals, mainly calcium and magnesium (Scholz-Ahrens & Schrezenmeir, 2002). Long-term beneficial effects on bone quality have been demonstrated by enhancement of bone mineral content in growing rats or prevention of bone loss in ovariectomised animals. Bone mineral content or density are not necessarily associated with bone health, but some recent experiments have shown that oligofructose prevents the loss of trabecular bone structure induced by oestrogen deficiency. This occurs at different trabecular sites and is correlated with bone strength.

The effects of fructans on mineral metabolism may be based on the enhancement of passive (and active) mineral transport across the intestinal epithelium, mediated by an increase in certain metabolites of the gut microflora and a reduction of the intestinal pH.

Several human studies showed a positive effect of inulin or oligofruc-

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tose on absorption of calcium. Griffin et al. (2002) examined the effect of a relatively modest intake (8g/day) of oligofructose (Raftilose®P95) or a mixture of oligofructose and inulin (Raftilose®Synergy1) during 3 weeks on calcium absorption by 60 girls at or near menarche with intakes of calcium approximating the recommended dietary intake (1200–1300 mg/day). At this daily dose of fructans, absorption of calcium was significantly higher (+18%) in the group receiving Synergy1; no difference was seen between the oligofructose and the placebo groups. This seems to confirm that the chain length distribution of the fructan is an important factor in determining its efficiency with respect to enhanced absorption of minerals.

Modulation of lipid metabolism

Inulin and oligofructose are able to exert "systemic" effects by modifying the hepatic metabolism of lipids in several animal models (Delzenne et al., 2002).

In lean rats and hamsters fed a diet supplemented with inulin or oligofructose, a decrease in serum concentrations of triacylglycerol (TAG) and phospholipid has been reported consistently. A lower hepatic lipogenesis, through a coordinated reduction of the activity of lipogenic enzymes, is a key event in the reduction of very-low-density lipoprotein–TAG secretion. Oligofructose is able to counteract triglyceride metabolism disorders that occur as the result of dietary manipulation in animals, and sometimes independently of lipogenesis modulation. Oligofructose reduces post-prandial triglyceridemia by 50% and avoids the increase in serum level of free cholesterol occurring in rats fed a Western-type, high-fat diet.

Oligofructose also protects rats against accumulation of TAG in the liver (steatosis) induced by fructose, or occuring in obese Zucker fa/fa rats. This would be interesting if confirmed in human studies, since steatosis constitutes one of the most frequent liver disorders, occurring together with syndrome X, in overweight and obese people.

Delzenne et al. (2002) examined the possible relationship between modifications of the level of glucose and/or insulin after ingestion of inulin or oligofructose and de novo lipogenesis, the role of metabolites produced in the ceco-colon by fermentation of fructan in the regulation of lipid metabolism, and the potential importance of glucose-dependent insulin tropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) with regard to the systemic effects of dietary oligofructose. The identification of the mediators of the systemic effects of inulin and oligofructose is indeed the key to identifying target functions or dysfunctions, and finally individuals who would benefit from increasing their intake of fructans.

In humans, attempts to reproduce similar lipid-lowering effects have generated less consistent results. Out of a total of nine human studies, three have observed no effect of inulin or oligofructose on blood levels of cholesterol or triacylglycerol, three have shown significant reductions in TAG, and four have shown reductions in total and LDL cholesterol. These studies have been conducted in both normo- and moderately hyperlipidaemic subjects (Williams & Jackson, 2002).

Because the inhibition of hepatic fatty acid synthesis has been identified as the major site of action for the TAG-lowering effects of inulin and oligofructose, and because this pathway is relatively inactive in man unless a high-carbohydrate diet is fed, variability in response may be a reflection of differences in the background diet (Parks, 2002). Therefore, future studies in humans should use subjects consuming a background diet rather high in carbohydrates. Investigations conducted in subjects with NIDDM or those with a dyslipidemia characteristic of insulin resistance would be of particular value (Williams & Jackson, 2002).

Anticancer properties

A multitude of preclinical and epidemiological studies provide evidence linking various nutrients and cancer. However, a number of studies question the role of diet in the cancer process and have raised concerns about what is physiologically important and the circumstances that may dictate the overall response.

Complementary and overlapping mechanisms appear to account for the response to bioactive food components. Therefore, Milner (2002) pleaded for a greater focus on research to address how nutrients influence genetic pathways associated with cancer and vice versa. Inulin and oligofructose represent intriguing dietary fibres that may have an impact on cancer risk.

Pool-Zobel et al. (2002) reviewed recent research in experimental animal models revealing that inulin and oligofructose added to the diet in concentrations of 5% to 15% prevent formation of azoxymethane-induced aberrant crypt foci and tumours in the colon. Studies in transgenic min mice (having a nonsense mutation in the murine APC gene) have shown that inulin and oligofructose may modulate the occurrence of colon tumours that are not chemically induced. They concluded that in order to confirm the experimental data in humans and to obtain more insight into the effects of fructans in the human colon, human dietary intervention studies relating biomarkers of reduced risk to inulin consumption are needed. The EU is now funding such a human dietary intervention study with synbiotics (the SYNCAN project).

On the other hand, Taper & Roberfroid (2002), reviewing a number of animal studies, showed that addition of inulin or oligofructose to the basal diet reduced the incidence of breast tumours induced by methylnitrosourea (MNU) in female rats, inhibited the growth of transplantable tumours in mice (transplantable liver tumour TLT and mammary mouse carcinoma EMT6) and decreased the incidence of lung metastases of a tumour transplanted intramuscularly (TLT tumour). Furthermore, the dietary treatment of mice having transplanted ascitic tumours with inulin or oligofructose potentiated the effects of six different cytotoxic drugs commonly utilised in human cancer therapy. Preliminary results of studies with radiotherapy seem to confirm a similar effect.

There is some evidence that prebiotics may inactivate carcinogens in the colon by modification of detoxifying enzymes, such as GST. Also, fermentation products, including the SCFA butyrate, could contribute to the protective effect. Butyrate inhibits cell proliferation, it may induce apoptosis of already transformed cells and it modulates GST/GSH expression. It may increase secretion of mucin, a barrier that can deactivate carcinogens and thus protect the epithelial cells.

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FREQUENTLY ASKED QUESTIONS

Do inulin and oligofructose contain GMO?

Inulin and oligofructose produced by ORAFTI are totally GMO-free.
ORAFTI and its partners only work with seeds that are controlled and approved by the appropriate government agencies. In 2001, an audit of the seed suppliers who are testing GMO seeds confirmed that all legal procedures are punctiliously met in order to avoid any contamination. Furthermore, all our processing aids, including the endo-inulinase enzyme that we use for producing oligofructose, are GMO-free.

ORAFTI takes a neutral position in the GMO debate. GMO may be an additional method to improve the quality of food products that may offer further possibilities to enhance human health and well-being. But, as long as we do not have GMO chicory seeds that have been evaluated scientifically and have been approved officially, and as long as there is no public consensus on GMO, ORAFTI will not use GMO seeds or chicory roots for its productions.

Can inulin and oligofructose be consumed by diabetics?

Both inulin and oligofructose are non-digestible fibres. They are not hydrolysed nor are they absorbed during their passage through the human mouth, stomach and small intestine. As a consequence, inulin and oligofructose have no direct effect on postprandial blood glucose level nor on insulin or glucagon secretion, when ingested orally. This has been confirmed in several animal and human studies.
Rumessen et al. (1990), for example, studied inulin in humans with respect to intestinal handling and influence on blood glucose, insulin response, breath hydrogen and oro-cecal transit time. The potential use of inulin as a safe and beneficial food for diabetics has been recognised since the beginning of the 20th century. Lewis (1912), referring to Persia (1905), recommended inulin to diabetics and stated that the product is well digested and assimilated by those people in large doses and through long periods of time. Strauss (1911) reported the feeding of inulin to be very beneficial for the patient. This was confirmed by Root et al. (1925) and by Wise et al. (1931). Since then, many applications for diabetics have been described, including inulin-based diabetic bread and pastry (Beringer & Wegner, 1955; Kuppers-Sonnenberg, 1971) and inulin-based diabetic jam (Birch & Soon, 1973).
In conclusion, diabetics can consume inulin and oligofructose safely, providing they take into account the fact that food products may, of course, contain other carbohydrates.

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MONITOR

Selective stimulation of fecal bifidobacteria by probiotics, prebiotics and synbiotics

Influence of fructan-type oligosaccharides on growth and acidifying activity of bifidobacterium strains was studied in vitro. The selected pairs of bifidobacteria strains and oligosaccharides enhancing their growth were also studied in vivo in Wistar rats to determine the effect of pro-, pre- and synbiotics on the microecology of the gut.

In vitro studies showed that the majority of bifidobacterium species utilised oligofructose and inulin. Incorporation of 5% oligofructose in the diet of rats increased the counts of fecal bifidobacteria by 1.6 log cfu/g. Administration of bifidobacteria together with the prebiotic as synbiotics improved the bifidogenic effect (by 1.4 log cfu/g of feces). Supplementation of the diet had almost no effect on the other groups of gut microflora.

These results confirm the selective stimulation of fecal bifidobacteria by prebiotics and synbiotics.

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Inulin improves distal colitis

The aim of this study was to test the hypothesis that oral inulin prevents colonic mucosal inflammation. Rats with distal colitis induced by dextran sodium sulfate (DSS) received inulin either orally or by enema. Fecal water obtained from inulin-fed rats was administered by enema to rats with colitis and compared with fecal water from control rats. Finally, rats with colitis received daily enemas of either butyrate or placebo.

The daily administration of inulin produced an anti-inflammatory effect. Both inflammatory activity and morphological damage to the mucosa were reduced.

Topical administration of inulin by enema had no effect, which leads to the conclusion that changes in the intracolonic milieu, i.e. the intracolonic generation of butyrate and the growth of lactic acid bacteria, induced by oral inulin, carry the anti-inflammatory action.

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Oligofructose and inulin protect from enteric and systemic pathogens in mice

In this study, mice were fed for 6 weeks a control diet with 100g/kg of cellulose or one of two experimental diets with the cellulose replaced entirely by oligofructose (RAFTILOSE®P95) or inulin (RAFTILINE®HP). From each diet, 25 mice were challenged by a promotor of colorectal cancer (1,2-dimethylhydrazine) or were infected enterically with Candida albicans or systemically with Listeria monocytogenes or Salmonella typhimurium.

The incidence of aberrant crypt foci in the distal colon after exposure to dimethylhydrazine was lower for mice fed inulin (53%) or oligofructose (54%) than in control animals (76%). The fructan-fed mice also had 50% lower densities of C. albicans in the small intestine. Infection with L. monocytogenes caused nearly 30% mortality among control mice, but none of the mice fed inulin died, with survival intermediate for mice fed oligofructose. With S. typhimurium, infection caused 80% mortality in the control mice, 60% in the inulin-fed animals and intermediate values in the oligofructose-fed group.

These results provide the first evidence that resistance against both intestinal and systemic infections caused by pathogenic bacteria can be increased by feeding diets that encourage the proliferation of specific bacteria already in the gastro-intestinal tract (GIT). Although the mechanisms responsible for the improved resistance to Salmonella and Listeria conferred by oligofructose and inulin were not determined, recovery from infections is known to be dependent, in part, on sensitisation of T-cells, which activate and enhance bactericidal activity of lymphocytes.

These findings validate the contention that inulin and oligofructose can be considered as antimutagens and probably act by beneficially modulating the composition of bacteria in the GIT. This study further indicates that the GIT bacteria remain responsive to long-term feeding of prebiotics.

Buddington K.K., Donahoo J.B., Buddington R.K. (2001), Dietary Oligofructose and Inulin Protect Mice from Enteric and Systemic Pathogens and Tumor Inducers, J. Nutr., 132, 472-477.

Continuation of page 9

Prebiotics modulate immune functions affecting the GALT

This study investigated the effects of probiotics, prebiotics and a combination of both on the gut-associated lymphoid tissue (GALT) of rats treated orally with the carcinogen azoxymethane (AOM). Male rats received a high fat (40%) diet supplemented with probiotics (Bifidobacterium lactis and Lactobacillus rhamnosus), prebiotics (10% RAFTILOSE®Synergy1), or a combination of both, for 32 weeks.

The prebiotic supplementation enhanced natural killer (NK) cell activity, IL-10 secretion, IFN-secretion and lymphocyte proliferation. Supplementation of a pro- and a prebiotic combination increased NK cell activity and IL-10 secretion, while lymphocyte proliferation was decreased.

In conclusion, the supplementation of AOM-treated rats on a high-fat diet with prebiotics or synbiotics modulates immune functions primarily affecting the GALT.

Roller M., Caderni G., Rechkemmer G. and Watzl B. (2002), Long-term treatment with a prebiotic modulates the gut-associated immune system of azoxymethane-treated F344 rats, Paper presented at the SKLM Symposium "Functional Food: Safety Aspects", May 5-7 2002, Karlsruhe, Federal Research Centre for Nutrition, Germany.

Oligofructose modulates mucin distribution and mucus gel thickness

This study aimed to determine the effect of a diet containing a butyrate-producing fibre (oligofructose) on the colon mucus in mice. Two groups of mice, 36 animals per group, were fed a semi-synthetic diet supplemented with 4% oligofructose or 4% sucrose (placebo), during 30 days.

Oligofructose (OFS) added to the diet increased the concentration of total short-chain fatty acids in the cecal contents and in the colon contents significantly. On the other hand, OFS increased the number of mucin-containing cells significantly without modifying the distribution of neutral, acid and sulphated mucins. The mucus gel covering the distal colon was thicker in the mice fed the OFS-containing diet.

This modulation of colonic mucin and mucus layer could contribute to the beneficial effect of oligofructose on mucosal integrity and intestinal protection.

Hoebler C., Michel C., Meslin J-C., Vabre S. and Cherbut C. (2002), Effect of the fermentation of oligofructose on the mucin distribution and mucus gel thickness, Paper presented at the Vahouny Symposium, May 27-30, 2002, Royal College of Physicians, Edinburgh, United Kingdom.

Effects of oligofructose on lipid metabolism

A number of animal studies have shown that the addition of fructans (e.g. oligofructose) to the diet of rats can decrease lipogenesis in the liver by lowering the activity of key lipogenic enzymes regulated only through modification of gene expression. The mechanism by which such non-digestible carbohydrates modify hepatic metabolism remains to be clarified.

Postprandial concentrations of insulin and glucose are low in the serum of oligofructose-fed animals, which could explain, partially, its metabolic effect. Other mechanisms involved in the antilipogenic effect of this fructan may be: the production of propionate or incretins (glucose-dependent insulinotropic peptide and glucagon-like peptide-1) or the modification of the availability of digestible carbohydrates.

Several human studies showed a hypotriglyceridemic effect of dietary inulin, whereas other studies did not show significant effects. Factors to be accounted for in the interpretation of these studies include duration of the treatment, dietary intake of carbohydrates and lipids as well as the serum lipid composition at the beginning of the treatment. Studies need to be performed in hyperglyceridemic patients, in whom lipogenic homeostatis could be disturbed, to determine the relevancy of fructans in decreasing lipogenesis in humans.

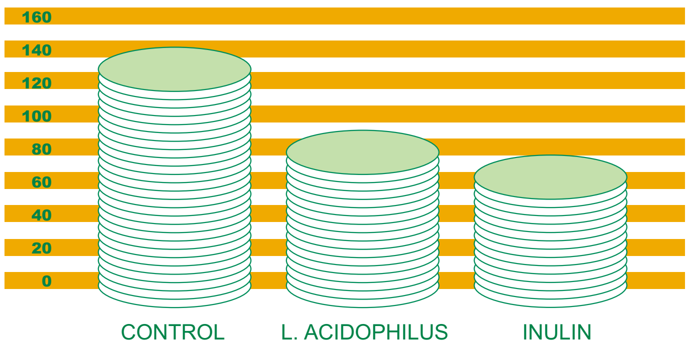
Delzenne N.M. & Kok N. (2001), Effects of fructan-type prebiotics on lipid metabolism, Am. J. Clin. Nutr., 73 (suppl.), 456S-458S.

Inulin protects against colon carcinogenesis in rats

Bolognani et al. (2001) investigated the effect of lactic acid-producing bacteria (Bifidobacterium longum, Lactobacillus casei and Lactobacillus acidophilus) or inulin on the induction by carcinogens (methyl-N-nitrosourea, 1,2-dimethylhydrazine, azoxy-methane) of aberrant crypt foci (ACF) in the colon, which are considered to be early precursor lesions of neoplasia.

No consistent significant change in ACF numbers was detected in the experiments with a purified, high-starch diet. When the basal diet was changed to one containing a higher level of fat, typical of a Western diet, a significant decrease in AOM-induced colonic ACF was seen in rats given L. acidophilus or inulin.

Number of aberrant crypt foci in the colon



The results indicate that the type of diet fed can influence the detection of protective effects of probiotics or inulin, and suggest a protective effect toward colon cancer of L. acidophilus and inulin when added to a typical Western diet.

Bolognani F., Rumney C.J., Pool-Zobel B., Rowland I.R. (2001), Effect of lactobacilli, bifidobacteria and inulin on the formation of aberrant crypt foci in rats, Eur. J. Nutr., 40 (6), 293-300.

Fructans increase bone mineralisation in rats

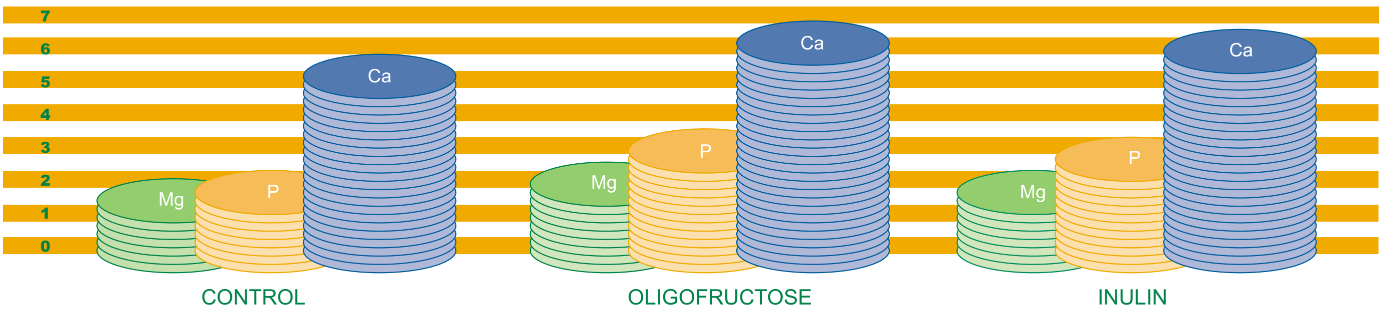
This study examined the effects of feeding diets containing 10% oligofructose (RAFTILOSE®P95) or inulin (RAFTILINE®HP) on bone mineralisation in male rats.

Bone calcium and magnesium levels were significantly higher in the rats fed inulin and oligofructose versus control animals.

These results confirm that fructans that are fermented selectively by the microflora in the large bowel may increase Ca and Mg absorption in the colon and increase bone mineralisation.

Richardson J.E., Walker L.T., Bonsi I.A., Howard C., Shackelford L. & Chawan C.B. (2002), Effects of prebiotics on bone mineralization in Fisher 344 male weanling rats, Paper presented at IFT 2002, June 16-19, Anaheim, USA.

Effect of Dietary Fructans on Bone Minerals



The potential role of fructans in the management of lipid disorders associated with obesity

In humans, hepatic lipogenesis and triglyceride synthesis, assessed in vivo by the use of stable isotopes, was promoted by a high-carbohydrate diet in non-obese subjects and in non-alcoholic steatotic patients, but was not modified in the adipose tissue of obese subjects.

Non-digestible fermentable carbohydrates such as fructans were shown to decrease hepatic lipogenesis in non-obese rats, and to lessen hepatic steatosis and body-weight in obese Zucker rats after 10 weeks of treatment. It seems that fermentation of non-digestible carbohydrates and the production of short-chain fatty acids such as propionate is a prerequisite to observe a decrease in fat mass and fat accumulation in the liver tissue.

The data obtained in humans suggest that the contribution of lipogenesis in the adipose tissue itself seems to be minor in the development of obesity. However, they do not preclude an involvement of de novo hepatic lipogenesis, due to consumption of digestible carbohydrates and to the development of metabolic disorder associated with syndrome X, namely steatosis. If the results obtained in obese Zucker rats are confirmed in obese patients, dietary fructans could be proposed as functional nutrients in the management of lipid disorders associated with obesity.

Delzenne N., Ferre P., Beylot M., Daubioul C., Declercq B., Diraison F., Dugail I., Foufelle F., Foretz M., Mace K., Reimer R., Palmer G., Rutter G., Tavare J., Van Loo J. and Vidal H. (2001), Study of the regulation by nutrients of the expression of genes involved in lipogenesis and obesity in humans and animals, Nutr. Metab. Cardivasc. Dis., 11 (suppl.), 118-121.

Inulin from A to Z

This review article describes the chemical structure and natural occurrence of inulin and its industrial production from chicory roots.

Furthermore, the functional and nutritional properties are summarised. Finally, the food and non-food applications, and perspectives for the future are discussed and a list of patents is given.

Chicory is the main crop used for the industrial production of inulin. Because of its physico-chemical properties, inulin is used for fat replacement, for body, mouthfeel and texture improvement, for foam and emulsion stabilisation, and in synergy with gelling agents.

Inulin has been shown to have several interesting nutritional properties: non-digestibility, low caloric value, modulation of lipid metabolism, stimulation of gut function, prebiotic effect through the modulation of the gut microflora composition, reduction of colon cancer risk and increase in mineral absorption. It is well tolerated and it is suitable for diabetics.

Inulin has become a key ingredient in many food products for either its nutritional or its technological properties, but often to offer a double benefit: an improved organoleptic quality and a better-balanced nutritional composition. A number of applications are described. Potential non-food applications are discussed. Several techniques available for the analysis of inulin (high-performance liquid chromatography, gas chromatography, high-pressure anion-exchange chromatography, permethylation) are summarised.

Franck A., De Leenheer L. (2002), Biopolymers, vol.6, Editor: A. Steinbuchel, Wiley-VCH, Weinheim, Germany, 439-479.

AGENDA

Leatherhead, United Kingdom

October 29, 2002

Leatherhead Food RA - A Boost for Bone Health

Topics to be discussed include:

- The influence of prebiotics on calcium absorption

Speaker: Wim Caers, ORAFTI

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Internet: www.lfra.co.uk

Amsterdam, The Netherlands

December 9-10, 2002

Nutri-Pack 2002

The 1st International Conference on packaging of nutraceuticals and functional foods & beverages

Topics to be discussed include:

- Consumer research to optimise on-pack communication of the benefits of BENEO, a functional food ingredient.

Speaker: Tim Van der Schraelen, ORAFTI

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Antalya, Turkey

April 2-5, 2003

IV International Nutrition and Dietetics Congress

The subject prebiotics will be discussed at a panel 'New Trends in Food Industry: Functional Foods'.

Info: Prof. Türkan K. Merdol, Head of the Departement of Nutrition and Dietetics, Hacettepe University, Istanbul, Turkey
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COLOPHON

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