An ORAFTI Newsletter
Nr. 11 - Winter 2004

Active Food Scientific Monitor

ORAFTI
ACTIVE FOOD INGREDIENTS

Interview
with
Prof. Dr. Nathalie Delzenne

In this issue we present an interview with Prof. Dr. Nathalie Delzenne from the Université Catholique de Louvain in Belgium.

Prof. Dr. Nathalie Delzenne is a lecturer in Nutrition and Biochemistry and is the leader of the research group in Experimental Nutrition in the Unit of Pharmacokinetics, Metabolism, Nutrition and Toxicology at the Université Catholique de Louvain, School of Pharmacy, in Belgium.
After a PhD in Pharmaceutical Sciences obtained in 1991, she performed a post-doctoral research in Paris (INSERM Unit 342) looking at the effect of nutrients on gene expression in the field of obesity. Back at the Université Catholique de Louvain, she has been involved in the experimental approach to assess the nutritional and health benefits of prebiotic nutrients. By working with inulin-type fructans as model prebiotics, her group has shown effects of these ingredients on lipid metabolism and obesity-related disorders and inflammation. The current hypothesis for such effects is the involvement of intestinal peptides in the modulation of food intake and glucose metabolism after ingestion of dietary fructans.
"My work is fortunately a kind of hobby for me as I work quite a lot. Besides that, my principal leisure is walking with my family. Although my children are still quite young, we walk a lot, often in the mountains. It is really a way for me to relax and to free my mind."

Inulin and oligofructose are fermented in the gastro-intestinal tract and have a direct effect on the digestive system. Recently, it emerged that the fermentative process alters gut physiology in such a way that inulin and oligofructose also exert systemic effects in other parts of our body. One of the most interesting metabolic changes recently discovered is the involvement of inulin and oligofructose in the hepatic metabolism of lipids, at least in animals and maybe also in humans. The identification of representative mediators of the systemic effects induced by non-digestible oligosaccharides, is key for determining target functions or dysfunctions, as well as individuals who would benefit from increasing their dietary intake.

Inulin and oligofructose in the management of obesity

It has been shown that inulin-type fructans are capable of improving the gastro-intestinal function through their prebiotic properties, but also that they do exert beneficial systemic effects.

Yes, indeed. In our research we have focused for some years on the effects of inulin and oligofructose on lipid metabolism. We have observed

continued on page 2

P R E F A C E

by Dr. Anne Franck

“Tell me what you eat, and I’ll tell you what you are”. Our dietary habits influence not only our state of health but also how we feel and the mood we are in. Being healthy has become a lot more than only the absence of a disease. In this respect, the health of our digestive system plays a major role in our general health condition and well-being. And it also impacts on our brain and feelings.

Having a 'gut feeling' is much more than just a figure of speech. The gut and the brain indeed are interconnected and they signal towards each other. Entrance of food into the stomach activates the connections to the brain and as a result feelings of satiety and relaxation occur. In contrast, a rumbling, empty stomach could be held responsible for progressive feelings of irritability and lack of concentration. The system also works the other way around. Arousal or fear get processed by the brain and are sent to the gut. Having a meal is more than just taking calories and nutrients to fulfill our energy requirements, it is also a social and emotional event. The food that we choose determines how we feel and inversely our state of mind is very often responsible for our dietary choices.

And this connection even goes much further as there is a real intensive and direct communication between the digestive system and the brain. It is therefore also obvious that how we feed ourselves determines in large part our health status and the way we feel. A well functioning digestive system that allows optimal advantage of nutritious and healthy food thus contributes to maintain a sound mind in a sound body.
In this issue we present information on the gut-brain connection, and how our gut health determines our mental state and may impact on our cognitive performance. The potential role of prebiotic ingredients such as inulin and oligofructose in that respect is highlighted as well.

Continuation of page 1

Inulin en oli

both in animals and in humans that dietary inulin-type fructans decrease blood triglycerides, primarily through the reduction in the number of plasma VLDL particles. As triglycerides are mostly synthesised in the liver, we thus hypothesised that these non-digestible oligosaccharides have an effect on the hepatic synthesis of triglycerides. This proved to be the case. When we isolated hepatocytes from the liver of rats treated with inulin-type fructans, we saw a persistent decrease in fatty acids that are synthesised during a process called lipogenesis, and a very significant decrease in the synthesis and the secretion of triglycerides, through a coordinate reduction of the activity and mRNA of all lipogenic enzymes. This means that fructans exert a persistent metabolic effect on the liver. There are several hypotheses to explain this effect. One key hypothesis is that the short chain fatty acids (SCFA) which are produced in the colon through the fermentation of oligosaccharides are able to enter the portal vein and reach the liver. We know for instance that one of the SCFA, propionate, is able to decrease lipogenic gene expression, at least in vitro, and also to inhibit triglyceride synthesis in the liver. Propionate is thus a putative

gofructose and the management of obesity

mediator candidate. But the mechanism is more complex. Acetate, which is a substrate for lipogenesis, is also produced during fermentation, which means that there are antagonistic actions between the different SCFA. We are now doing research to discover which SCFA is the key factor in this lipid-lowering effect. We already have shown that propionate hinders the entrance of acetate to the hepatic tissue. There is thus clearly an interaction between these two SCFA.

What may be the practical consequences of these findings ?

If these findings are confirmed in humans, and we already have some arguments for the effect of propionate in humans, this will mean that the colon governs the synthesis of triglycerides. Treating the colon with fructans thus could have protective effects on pathologies which are associated with obesity such as cardiovascular disease or type-2 diabetes. The abnormal accumulation of triglycerides in the liver tissue and the consequent inflammation, a complication which is called non-alcoholic steato-hepatitis (NASH), are indeed associated with obesity. NASH is a frequent pathology occurring mainly in overweight and obese people and in patients with diabetes or hyperlipidemia. It is diagnosed in more than 80% of severely obese people and it is of major importance to find a good dietary approach for this debilitating condition. However, for the moment we have only few human data on the effect of inulin-type fructans on lipid metabolism. There is one study done by the team of Michel Beylot from the INSERM in Lyon, France, using the stable isotope technique, proving that lipogenesis is decreased through the administration of inulin to human volunteers. We conducted recently a case-controlled study in humans which showed that the administration of oligofructose in patients with NASH leads to an improvement of some markers of steato-hepatitis. This kind of studies is not easy as there are only few markers for this pathology, and more research has to be done in the future.

Do you also expect to find positive effects on the management of diabetes ?

There are limited data on diabetes until now. Most of the human studies focused on the putative influence of fructans on lipid metabolism. When a decrease in blood lipids was observed, more marked effects were seen on triglycerides than on cholesterol. In my opinion it is important to focus more on obese or severely overweight people. From animal studies we know that there is a control of food intake which may be produced through the fermentation of inulin-type fructans. We have shown for instance that when oligofructose is fed to animals, there is an increase in the production of some gastro-intestinal hormones, such as glucagon-like peptide-1 amide (GLP-1), which participate in the regulation of post-prandial insulin release and have an anorexigenic effect, whereas ghrelin, an orexigenic hormone, is reduced. We now think that the effect of inulin and oligofructose on lipid metabolism in humans may be related to their capacity to promote the secretion of endogenous intestinal peptides having a satietogenic effect and thus are involved in appetite regulation. Moreover, the increase in GLP-1 secretion by dietary oligofructose also correlates with improved glucose homeostasis in diabetic rats and increased pancreatic insulin secretion, which may improve glycaemic control in diabetic patients.

Do you think that the beneficial effects of inulin and oligofructose on lipid metabolism may be more pronounced in hyperlipidemic and obese subjects ?

Yes, in view of our results, an abnormal lipid accumulation inside the liver is necessary to see significant effects on lipid metabolism. I strongly believe that the modulation of the production of intestinal hormones by the fermentation of inulin-type fructans in the gut is a key factor. The increase in the gene expression inside the colon that we have measured, also must have consequences elsewhere. There are not only the SCFA that may play a role as a relay between what happens in the colon and what happens systemically, but also these intestinal hormones and peptides do play a role. This opens quite a lot of perspectives because among these peptides, there is also GLP-2 which has an effect on immunity and cell proliferation. I think this is a very exciting new field of research relative to the systemic effects of dietary inulin and oligofructose, which may help to clarify the physiological and pathological situations in which the functionality of these nutrients will be useful.

The food – mood connection: how gut health determines our mental state and vice versa

'Tell me what you eat, and I'll tell you what you are'. Our eating pattern is rarely determined by the true physiological needs of that moment or the nutritional value of the food chosen. The food we put in our mouth often serves to satisfy the need for a certain preference, be it sweet, salty, spicy, or fat-like. Nobody will deny the direct link between our ingestive behaviour and the mood we are in. A nice dinner with some good friends, comfort food after a hard days work or a quarrel with our beloved ones, a quick snack to keep us going during stressful working days... Eating disturbances such as anorexia or boulemia nervosa are acknowledged as mental illnesses requiring appropriate psychological and medical treatment. In this ageing society, maintenance of mental capacities is of crucial importance. Supported by epidemiological studies, although not in controlled conditions, antioxidants, vitamins and other nutritional supplements are used to prevent or delay age-related cognitive impairment. Impairment of cognitive function is known to result from changes in the diet, whether they are short term (breakfast in the morning) or long term (the intake of fatty acids changing brain structure).

Despite the obvious interaction between our digestive and our neural systems, surprisingly little research has been carried out on this topic. It is only the alarming acknowledgement that obesity is a threat for all body functions and that it is becoming an uncontrollable epidemic that forced research to look for a means to rigorously control food intake. This necessity has opened the door to study the brain and how it influences our appetite and food preferences. In these areas of research, it is not clear whether the concept of biomarkers has the same meaning as in other domains which relate physiological functions to some health endpoint or disease protection. Which biomarkers for complex psychological and behavioural functions could be identified, is still an important domain of investigation.

The need to eat

Basically, it is very simple. One starts to eat because one feels hungry, and terminates this action because one feels satiated. The increased occurrence of obesity in Western societies indicates that the human feeding behaviour is not that straightforward. In recent years, knowledge has advanced rapidly about the signals which indicate the body's energy requirements, the organs involved and the neuronal circuits that can sense and respond appropriately to these signals by effecting changes in food intake and energy expenditure. The body satiety system encompasses multiple aspects of gastrointestinal function, such as gastric distension and emptying, small bowel transit time, the digestion and absorption of nutrients, biochemical messengers reflecting physiologic measures relating to subjectively rated appetite, actual food intake, and the release of orexigenic (appetite-stimulating) or anorexigenic neurotransmitters and peptides in specific brain areas regulating feeding and energy expenditure.

Circulating levels of leptin and insulin are proportional to fat, the body's major energy store, abundantly present in obese people. Leptin is present in white adipose tissue, while insulin is secreted from the pancreas and changes adipose tissue physiology. Both hormones signal fat mass to the brain with the overall effect of inhibiting feeding and increasing energy expenditure by inhibiting the hypothalamic release of neuropeptide Y (NPY). By contrast, ghrelin is expressed mainly in the stomach and its circulating concentrations rise during fasting; it acts to stimulate food intake, in part via stimulation of the hypothalamic NPY neurons. The gut also generates nutritional signals that reach the brain. These include cholecystokinin (CCK), glucagon-like peptide-1 (GLP-1), and PYY(3-36), all peptides released from the gut after feeding to inhibit hunger both centrally and peripherally (except PYY) (de Graaf et al., 2004). Various abnormalities of leptin, insulin and hypothalamic peptides have been identified in dietary-induced obesity in rodents, which is closely analogous to common human obesity (Harrold et al., 2003). These biochemical messengers can serve as physiologic measures relating to subjectively rated appetite, actual food intake, or both. Biomarkers of satiation and satiety may be used as a tool for assessing the satiating efficiency of foods and for understanding the regulation of food intake and energy balance (Jimerson and Wolfe, 2004).

Optimal digestion requires non-digestible food

Dietary fibre has always been acknowledged as an important food constituent inducing satiety. An increase in either soluble or insoluble fibre intake increases post-meal satiety and decreases subsequent hunger. Consumption of an additional 14 g/day fibre for more than 2 days is associated with a 10% decrease in energy intake and a body weight loss of 1.9 kg over 3.8 months. The observed changes in energy intake and body weight occur both when the fibre is from naturally high-fiber foods or when it is from a fibre supplement (Howarth et al., 2001). The means by which dietary fibres influence satiation and satiety are related to their inherent chemical and physical properties, particularly their bulking and viscosity producing capabilities. This affects multiple aspects of gastrointestinal function, such as gastric emptying, small bowel transit time, and the digestion and absorption of nutrients, especially the glycaemic response after a meal. Independently of the latter, the fibre content of food may also affect the secretion of gut hormones that may act as satiety factors, both pre- and post-absorptively. (Delargy et al., 1997; Schneeman and Tietyen, 1994; Vahouny et al., 1988; Duncan et al., 1983; Heaton, 1980). Inulin and oligofructose, being dietary fibres of the soluble type, exert all or most of the physiological effects commonly attributed to fibre (Cherbut, 2002). As for dietary fibre in general, inulin could have the ability to dilute the energy density of the diet and act on the mechanical threshold and sensory mechanisms of food intake regulation by its capacity to form a particle gel network (Franck, 2002). It might lower gastric emptying and small bowel transit, therefore prolonging the intestinal phase of nutrient processing, absorption and the interaction with pre-absorptive mechanisms essential in the induction and maintenance of satiety (Rolls, 1995).

continued on page 6

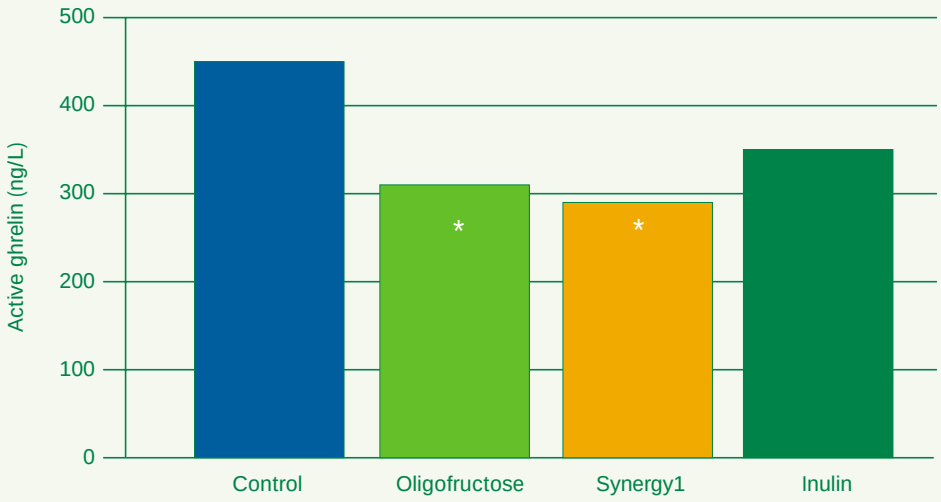
Continuation of page 5

Fibre ≠ Fibre

Unlike other dietary fibres, inulin and oligofructose have a selective fermentation pattern in the colon.

The prebiotic nature of inulin and oligofructose alters the composition and the activity of the gut microflora. The resulting changes in gut physiology and function have consequences that extend beyond the site of fermentation. Several biochemical messengers that serve as signalling molecules for satiety-related processes have demonstrated to be influenced by inulin and oligofructose. In search of the mechanism responsible for the triglyceride-lowering action of inulin and oligofructose (Delzenne et al., 1993; Fiordaliso et al., 1995; Kok et al., 1996a,b) it became apparent that the hormones insulin, GLP-1, GIP and insulin-like growth factor 1 mediate this effect (Kok et al., 1998). Feeding 10% oligofructose (Raftilose®P95) for 30 days to rats did decrease serum triglyceride levels, probably because of the larger pool of GLP-1. This regulator of postprandial insulin release is secreted by the intestinal cells so higher levels could be a consequence of the caecal hypertrophy induced by short chain fatty acids (SCFA) generated from oligofructose fermentation. In the postprandial state after 30 days of oligofructose addition to the diet, serum levels of insulin were significantly reduced, as well as serum and portal blood levels of glucose. The glycaemia induced after an oral glucose load did not differ between the control group and the group fed oligofructose, despite the lower insulin levels. Whether this improved disposal of glucose is caused by a higher insulin sensitivity or by an insulin-independent mechanism such as incretin release (e.g. GLP-1) remains unclear (Kok et al., 1998). The changes in GLP-1 and insulin metabolism suggest that inulin-type fructans could directly modulate gastro-intestinal peptides involved in the control of food intake. This was confirmed in a study in which fructans of different chain length, thus with different fermentation rates and profiles, were added to the diet (10%) of rats for three weeks. The decrease in food intake and the consequent loss of epididymal fat mass could be mediated by an increase in intestinal proglucagon mRNA and GLP-1 levels. Most likely the increase in SCFA production induced the higher portal concentrations of GLP-1 and the lower levels of serum ghrelin (Cani et al., 2004).

Fructans decrease active ghrelin, an inducer of appetite



Plasma active ghrelin (ng/L) of rats fed a control diet, or a diet supplemented with 10% oligofructose (Raftilose®P95), inulin (Raftiline®HP) or a specific mixture of both (Raftilose®Synergy1).
Values are mean ± SEM (n=6), * = significantly different from control, $P<0.05$. (Cani et al., 2004)

Food to boost your mood

Mood and food intake are inextricably linked and mutually influence each other via different biochemical pathways. Palatable foods stimulate endorphin release in the brain, so this is the most likely mechanism to account for the elevation of mood. Absorption of the food ingested plays a crucial role, as deficiency of many vitamins is associated with psychological symptoms: folate deficiency could be associated with depression, as is a low thiamine status. Iron deficiency anaemia is common, particularly in women, and is associated with apathy, depression and rapid fatigue when exercising (Benton and Donohoe, 1999). As is experienced by most of us some of the time, individuals in a negative mood state arising from disorders ranging from tobacco withdrawal to premenstrual symptoms make use of carbohydrate ingestion, especially simple carbohydrates, to provide a

temporary lifting of mood (Wurtman and Wurtman, 1989). While the literature is consistent in demonstrating that carbohydrate consumption can alter a negative mood state, the underlying mechanism mediating this relationship is unknown (Christensen, 1993). A recent major theory was that a meal high in carbohydrate increased the rate that tryptophan enters the brain, leading to an increase in the level of the neurotransmitter serotonin that modulates mood. Although such a mechanism may be important under laboratory conditions it is unlikely to be of significance following the eating of any typical meal.

Flowers for breakfast…

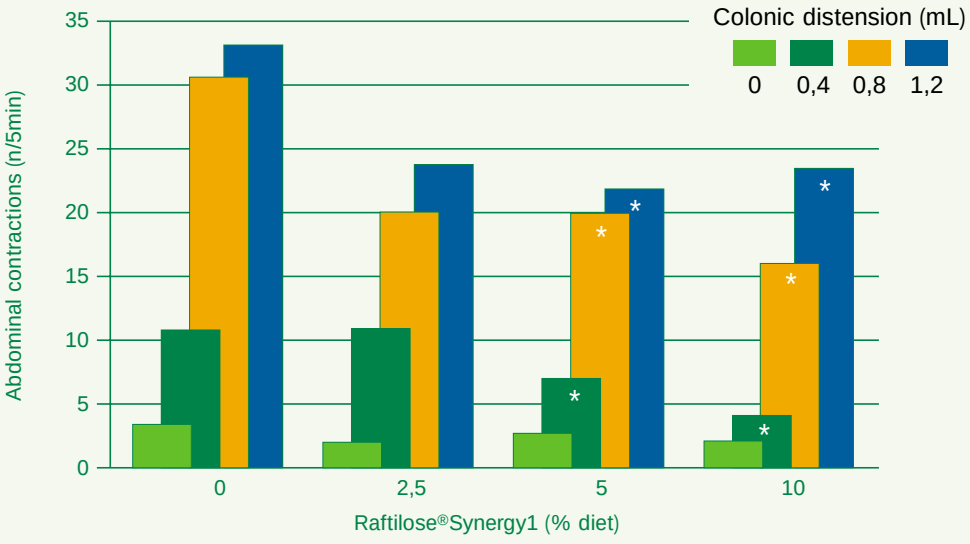
The daily intake of dietary fibre, consumed in the morning as breakfast cereals, ensures less depressed mood, less emotional distress and a lower level of perceived stress compared to individuals that do not eat breakfast every morning (P<0.05). The type of breakfast (high vs low, cereal vs cooked breakfast) has an important influence on mood that cannot be accounted for by other life-style habits such as smoking and alcohol consumption (Smith, 1998 and 1999). The ingestion of simple carbohydrates induces a greater perception of fatigue and a lower satiety compared to a breakfast composed of complex carbohydrates (Pasman et al., 2003). High fibre diets elevate the energy level and reduce the fatigue that is often a consequence of the constipation that many people suffer from (Smith et al., 2001).

… Or inulin, of course

Inulin and oligofructose act on gut physiology and functioning, also causing a relief of constipation and increasing absorption of nutrients, important determinants of a general sense of well-being. In elderly people receiving a synbiotic containing Raftilose®Synergy1, a positive influence could be demonstrated on parameters of well-being that were measured through questionnaires. Whether this was related to or independent from the significant increase in stool frequency (P<0.05) and the improvement of gastro-intestinal quality of life, is not clear (Zunft et al., 2004). The digestive system is of crucial importance for optimal functioning of other systems, a.o. the immune system. Therefore, it does not come as a surprise that inulin and oligofructose could also affect mood state and well-being via indirect mechanisms. Irritable Bowel Syndrome (IBS) is a condition of which the etiology is often associated with psychological distress. In an animal model mimicking IBS, addition of 10% Raftilose®Synergy1 to the diet during 15 days significantly (P<0.05) reduced the hypersensitivity of the animals to colonic distension when they were subjected to a stress factor. In this model, fructans have demonstrated to abolish a physical reaction associated with a stressful event (Lamine et al., 2004). Whether the improvement in mood and well-being is a direct consequence of fermentation in the gut, i.e. improved bowel functioning and relieve of constipation; resulting from more efficient absorption of nutrients, production of vitamins and short chain fatty acids that optimise other organ functions of which one is the brain; or actually originates from the produc-

continued on page 8

Raftilose®Synergy1 decreases pain sensitivity in stress conditions



Effect of a diet enriched with Raftilose®Synergy1 (2.5, 5.0 and 10.0%) versus control on hyperalgesia, measured as the number of abdominal contractions in 5-minute intervals, induced by restraint stress, * = significantly different from the control group, P<0.05. (Lamine et al., 2004)

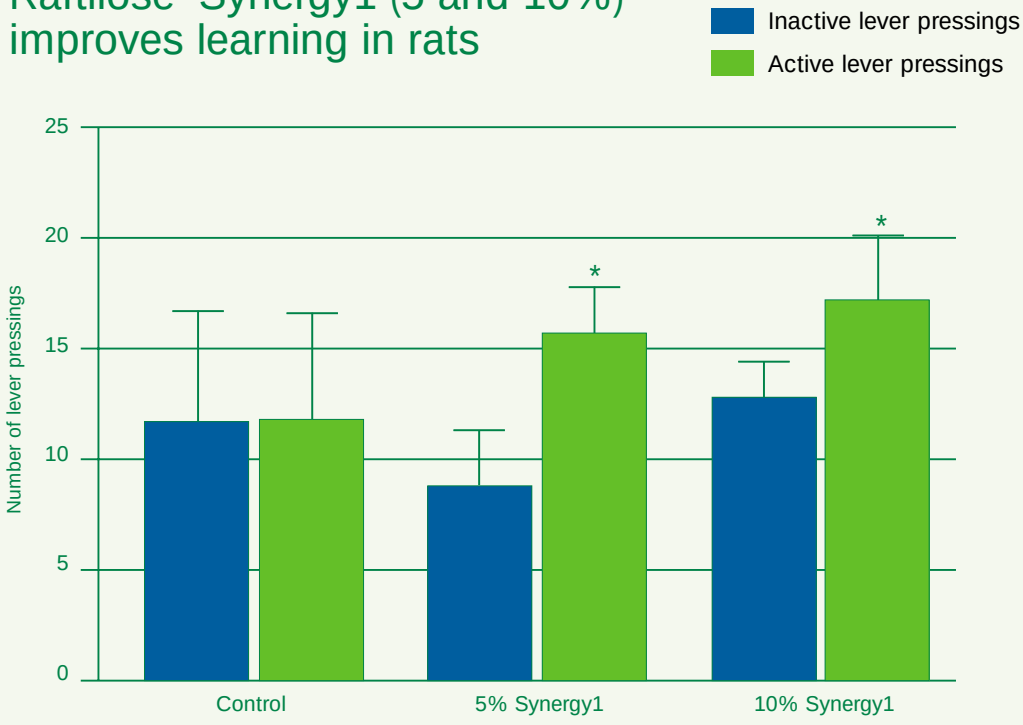
Continuation of page 7

tion of true biochemical messengers that influence neurotransmitter release in the brain, needs further investigation.

Diet in the light of Darwin

It is not easy to demonstrate consistent effects of food on cognitive performance. Because optimal functioning of cognition is crucial for survival, these functions are strongly protected against short-term dietary and physiological disturbances. The biomarkers of cognitive tasks such as memory, attention, speed and accuracy of movement only measure subparts of the complex skills that determine performance. Food and drinks can induce a change in some or all of these components, ultimately affecting the total outcome in a way that is very difficult to predict, let alone measure. Nutrition is considered an important determinant of human mental performance, but most dietary interventions can only demonstrate short-term effects attributable to changes in easy measurable parameters, for instance blood glucose. Long-term outcome requires a multivariate approach and has to focus on maintenance of mental capacities rather than improving them, like in ageing people (Dye and Blundell, 2002). Although difficult to relate due to confounding by other demographic and lifestyle factors, cross sectional analysis demonstrated that in elderly a healthy diet is positively correlated with a better cognitive performance (Huijbregts et al., 1998). The same holds true for a younger population. When considering short-term effects of nutrition on mental capacities, i.e. alertness, it is clear that the presence of dietary fibre in the breakfast is associated with the highest post-breakfast alertness ratings and with the greatest cumulative amount of alertness during the period between breakfast and lunch. In rats, addition of Raftilose®Synergy1 to the diet (5 and 10%) during two weeks, improved their learning abilities. In comparison to the control group, rats receiving the fructan-enriched diet significantly (P<0.05) more often chose to press the lever that was activated to extinct the light from an unpleasantly lit cage instead of the non-active one (Messaoudi et al., 2004). In general, it remains to be established whether the enhanced attention is a direct consequence of satiety, since carbohydrates have a better satiating power than the more palatable high-fat breakfast. Further research is required to determine whether alertness is depending on the type of dietary fibre, as well as carbohydrate (non)digestibility, fermentability, (non)solubility, low or high glycenic index (Holt et al., 1999).

Raftilose®Synergy1 (5 and 10%) improves learning in rats



Number of pressings of a lever, activated or not to extinct an unpleasantly bright light in the cage of rats on a diet enriched with 5 or 10% Raftilose®Synergy1. The number of pressings indicates the ability of the rat to discriminate the active from the inactive lever, reflecting the learning discrimination of the rat to provide relief from the stressful light.
Values are mean ± SEM (n=6), P<0.05. (Messaoudi et al., 2004)

The naked ape with a leaky gut

Food effects are less easy to demonstrate in a population that has a gradual decline in cognitive function compared to a population that has a clear disturbance in cognition. Autism is a life-long developmental disorder but the causes for this profound disorder are largely unknown.

Recent research has uncovered pathology in the gastrointestinal tract of autistic children. The pathology, reported to extend from the oesophagus to the colon, points to a connection between diet and the severity of symptoms expressed in autism. The intestinal permeability is impaired and a leaky gut could develop. The loss of barrier function allows passage of components that might influence brain function (White, 2003). It is suggested that improving the gut condition could ameliorate autistic behaviour, or other cognitive disturbances in developing children (hyperactivity, attention deficit, dyslexia, …) (Mouton).

Conclusion

The presence of an independent enteral nervous system, regulating the digestive functions independently from our central nervous system, is standard knowledge to all clinicians and scientists. The influence of our brain on gut function, for instance in a stress situation, is crucial for the survival of our species and has been studied in detail. The reverse way however, how our gut and digestive system modify and influence the nervous connections in our head, has been neglected. Only recently the large impact of a healthy digestive system on our mental functions is emerging. Inulin and oligofructose, prebiotic functional food ingredients, appear to have a major role to play in the establishment of an optimal food-mood connection.

References

Benton D., Donohoe R.T. (1999) The effects of nutrients on mood. Public Health Nutr. 2(3A):403-409.

Cani P.D., Dewever C., Delzenne N.M. (2004) Inulin-type fructans modulate gastro-intestinal peptides involved in appetite regulation (glucagon-like peptide-1 and ghrelin) in rats. Br. J. Nutr. 92:521-526.

Cherbut C. (2002) Inulin and oligofructose in the dietary fibre concept. Br. J. Nutr. 87(Suppl. 2):S159-S162.

Christensen L. (1993) Effects of eating behavior on mood: a review of the literature. Int J. Eat. Disord. 14(2):171-183.

de Graaf C., Blom W.A., Smeets P.A., Stafleu A., Hendriks H.F. (2004) Biomarkers of satiation and satiety. Am. J. Clin. Nutr. 79(6): 946-961.

Delargy H.J., O'Sullivan K.R., Fletcher R.J., Blundell J.E. (1997) Effects of amount and type of dietary fibre (soluble and insoluble) on short-term control of appetite. Int. J. Food Sci. Nutr. 48(1):67-77.

Delzenne N., Kok N., Fiodaliso M., Deboyser D., Goethals F., Roberfroid M. (1993) Dietary fructo-oligosacccharides modify lipid metabolism in rats. Am. J. Clin. Nutr. 57(Suppl.):820S.

Duncan, K.H., Bacon, J.A. & Weinsier, R.L. (1983) The effects of high and low energy density diets on satiety, energy intake, and eating time of obese and nonobese subjects. Am. J. Clin. Nutr. 37: 763–767.

Dye L., Blundell J. (2002) Functional foods: psychological and behavioural functions. Br. J. Nutr. 88(Suppl.2):S187-S211.

Fiordaliso M., Kok, N. Desager J.P., Goethals F., Deboyser D., Roberfroid M., Delzenne N. (1995) Dietary oligofructose lowers triglycerides, phospholipids and cholesterol in serum and VLDL of rats. Lipids 30:163-167.

Franck A. (2002) Technological functionality of inulin and oligofructose. Br. J. Nutr. 87: S287-S291.

Harrold, J.A.; Williams, G.; Wong, S. (2003) Neuroendocrine targets for the treatment of obesity: physiological roles and unrealized opportunities. Current Medicinal Chemistry: Central Nervous System Agents 3(3):141-155.

Heaton, K.W. (1980) Food intake and regulation by fiber. In: Medical Aspects of Dietary Fiber (Spiller, G. A. & Kay, R. M., eds.), pp. 223–238. New York, NY, USA.

Holt S.H., Delargy H.J., Lawton C.L., Blundell J.E. (1999) The effects of high-carbohydrate vs high-fat breakfasts on feelings of fullness and alertness, and subsequent food intake. Int. J. Food Sci. Nutr. 50(1):13-28.

Howarth N.C., Saltzman E., Roberts S.B. (2001) Dietary fiber and weight regulation. Nutr.Rev. 59(5):129-139.

Huijbregts P.P., Feskens E.J., Rasanen L., Fidanza F., Alberti-Fidanza A., Nissinen A., Giampaoli S., Kromhout D. (1998) Dietary patterns and cognitive function in elderly men in Finland, Italy and The Netherlands. Eur. J. Clin. Nutr. 52(11): 826-831.

Jimerson D.C., Wolfe B.E. (2004) Neuropeptides in eating disorders. CNS Spectr. 9(7): 516-522.

Kok N., Roberfroid M., Delzenne N. (1996a) Dietary oligofructose modifies the impact of fructose on hepatic triacylglycerol metabolism. Metabolism 45: 1547-1550.

Kok N., Roberfroid M., Robert A., Delzenne N. (1996b) Involvement of lipogenesis in the lower VLDL secretion induced by oligofructose in rats. Br. J. Nutr. 76: 880-891.

Kok N.N., Morgan L.M., Williams C.M., Roberfroid M.B., Thissen J.P., Delzenne N.M. (1998) Insulin, glucagon-like peptide 1, glucose-dependent insulinotropicpolypeptide and insulin-like growth factor I as putative mediators of the hypolipidemic effect of oligofructose in rats. J. Nutr. 128:1099-1103.

Lamine F., Franck A., Eutamene H., Wei H., Fioramonti J., Théodorou V. (2004) Effect of the prebiotic Raftilose®Synergy1 on colonic hypersensitivity induced by acute stress in rats. 12th UEGW Congress, September 25-30, 2004, Prague. Abstract.

Messaoudi M., Rozan P., Nejdi A., Hidalgo S., Desor D. (2004) Behavioural and cognitive effects of oligofructose-enriched inulin in rats. Br. J. Nutr. (in press).

Mouton G. La connexion intestins – cerveau dans l'autisme, ou des probiotiques pour soigner le cerveau. Médecine fonctionnelle.

Pasman W.J., Blokdijk V.M., Bertina F.M., Hopman W.P.M., Hendriks H.F.J. (2003) Effect of two breakfasts, different in carbohydrate composition, on hunger and satiety and mood in healthy men. Int. J. Obesity 27:663-668.

Rolls, B J. (1995) Carbohydrates, fats, and satiety. Am. J. Clin. Nutr. 61(Suppl.4):960S-967S.

Sakata, T. (1995) A very low calorie conventional Japanese diet: its implications for prevention of obesity. Obes. Res. 3(Suppl.2): 233S–239S.

Schneeman, B.O. & Tietyen, J. (1994) Dietary fiber. In: Modern Nutrition in Health and Disease, 8th ed. (Shills, M. E., Olson, J. A. & Shike, M., eds.), pp. 89–100. Lea and Febiger, Philadelphia, PA, USA.

Smith A., Bazzoni C., Beale J., Elliott-Smith J., Tiley M. (2001) High fibre breakfast cereals reduce fatigue. Appetite 37:249-250.

Smith A.P. (1998) Breakfast and mental health. Int. J. Food Sci. Nutr. 49:397-402.

Smith A.P. (1999) Breakfast cereal consumption and subjective reports of health. Int. J. Food Sci. Nutr. 50: 445-449.

Vahouny, G.V., Satchithanandam, S., Chen, I., Tepper, S.A., Kritchevsky, D., Lightfoot, F.G. & Cassidy, M.M. (1988) Dietary fiber and intestinal adaptation: effects on lipid absorption and lymphatic transport in the rat. Am. J. Clin. Nutr. 47: 201–206.

White J.F. (2003) Intestinal pathophysiology in autism. Exp. Biol. Med. (Maywood), 228(6):639-649.

Wurtman R.J., Wurtman J.J. (1989) Carbohydrates and depression. Scientific American Jan, 68–75.

Zunft H.J., Hanisch C., Mueller S., Koebnick C., Blaut M., Doré J. (2004) Symbiotic containing Bifidobacterium animalis and inulin increases stool frequency in elderly healthy people. Asia Pac. J. Clin. Nutr. 13(Suppl.):S112.

FREQUENTLY ASKED QUESTIONS

Why adding prebiotics to infant formulae?

Exclusive human breast feeding is the golden standard for infants during the first 4 to 6 months after birth. Breast milk indeed covers all nutritional needs of the child, but if breast milk is not available the alternative is a formula usually based on cow's milk.

The composition of human milk and cow's milk differ at several points, one being the presence of non-digestible oligosaccharides. These are the third largest constituent of human milk, present in many different chemical structures and concentrations, depending on the feeding pattern of the mother and the age of the baby. A constituent that is present in such large quantities in the only food that a baby receives for so many months of crucial importance for its growth and development, probably has an important physiological function. Therefore, it is of great importance to understand the exact role the human milk oligosaccharides play. In order to develop an artificial infant nutrition, based on cow's milk, that resembles human milk as close as possible, it would be wise to add non-digestible oligosaccharides with the same functionality as those found in breast milk. This is especially true as it is impossible to mimic the real composition and the dynamic changes of this optimal biological product. Since an exact copy of human breast milk is not achievable, an infant formula containing ingredients helping to obtain the same biological value as the golden standard is the next option. The main difference between children having breast feeding, and those receiving formula feeding, is the frequency and the consistency of their stool, as well as the composition of their gut flora. Breast-fed babies have regular and soft stools, normally after each meal. This is in contrast with formula-fed children, often having difficulties of hard stools and constipation. Stools produced by breast-fed infants also have a lower pH and a large number of potentially beneficial bifidobacteria and lactobacilli, whereas formula-fed infants have a gut flora with a larger microbiological diversity. Breast-fed infants usually suffer less from episodes of intestinal infections and diarrhoea. Prebiotics such as inulin and oligofructose stimulate selectively the growth of bifidobacteria in the gut, and improve digestion and gut function. Therefore, prebiotics are advisable ingredients to add to infant nutrition formulae in order to obtain stool characteristics and gut microflora that resemble most closely those of babies fed with human milk.

Are there other reasons to enrich infant formulae with prebiotics, besides the bifidogenic and stool-regulating effects ?

Yes, there are. Our current scientific knowledge relates the other advantages of an oligosaccharide-enriched infant formula to the optimisation of the gut microflora composition and activity. A healthy gut ensures a well-developed immune system and a better resistance to pathogens. Prebiotics in the diet improve disease resistance, reducing the number of infections or infectious diarrhoea in children. Dysregulation of the immune system also plays a role in the development of food allergy and atopic dermatitis, often correlated to a disturbed post-natal colonisation pattern and an imbalanced bacterial community in the gut. Stimulation of a beneficial gut microflora decreases the risk for developing allergy in genetically predisposed children. The gut is also an important place for nutrient absorption. The absorption of both nutrients present in food and compounds produced by the gut microflora, such as short chain fatty acids and some vitamins, occur in the gut. Science has only started to discover how early life events have a far-reaching influence throughout our life as an adult. For instance, low or high birth weight is predictive for the risk of developing respectively cardiovascular disease or type-2 diabetes later in life. Furthermore, the effect of specific nutrients at early age on later child development has only started to emerge, with the role of omega-3 fatty acids supporting optimal brain development and vision as the most remarkable example. Only very recently it has become clear that gut health determines in large part our overall health and well-being (see also State of the Art), both at young age and as an adult or elderly. Therefore, the addition of prebiotics such as inulin and oligofructose to infant nutrition could be even more beneficial than supposed from our current scientific knowledge.

MONITOR

Oligofructose is safe for people with intolerance to fructose

Hereditary Fructose Intolerance (HFI) is an important inborn error of fructose metabolism, which results from a deficiency in the fructose aldolase B enzyme. The most frequently observed symptoms include gastrointestinal discomfort, hypoglycaemia, nausea, vomiting, sweating, trembling and convulsions.

Individuals with HFI are typically healthy and asymptomatic if they restrict dietary fructose and sucrose intake.

The potential of fructans, which are increasingly used as functional food ingredients to provide a fructose load in subjects with diagnosed HFI, had not been determined yet.

Furthermore, their use in weaning formulae and infant food necessitates safety evaluation during the presymptomatic period prior to diagnosis of HFI in infancy. Therefore, safety and tolerance of oligofructose was evaluated in five adult subjects and in one infant.

The participants were submitted to a one-week washout period in which their diet was sucrose-free and fructose-restricted. After this week, they received an oral oligofructose (Raftilose®P95) challenge (0.22 g/kg body weight) for two days, of which the effects were followed up for two more days after the last dose. Tolerance was assessed by serum enzyme measurements, clinical examination and a symptom report before and every 12 hours following the oligofructose challenge. Each of the participants tolerated the intake of oligofructose very well and no changes in liver enzymes and blood minerals, glucose, bilirubin or uric acid could be measured. This study demonstrates that oligofructose may be safely given to unselected populations. Adverse effects would not be expected even in individuals with HFI.

Barshop B.A., Nyhan W.L., Steenhout P.H., Endres W., Tolan D.R., Clemens R.A. (2003) Fructo-oligosaccharide tolerance in patients with hereditary fructose intolerance. A preliminary non-randomized open challenge short-term study. Nutr. Res. 23:1003-1011.

Oligofructose improves immune function in healthy and disease conditions

In recent years, the importance of the immune defense mechanisms generated by the gut-associated lymphoid tissue (GALT) has been recognised both in intestinal and systemic disease conditions. Peyer's Patches (PP) are the main inductive site of the GALT and have shown to be extremely sensitive to stress conditions, including pathophysiologic and dietary stresses. The purpose of this study was to investigate whether fructans exert an immunomodulating effect on PP, both in healthy and in endotoxemic animals. Mice were fed a control diet or a diet supplemented with 10% oligofructose (OF) for 16 days. Endotoxemia was induced on day 15 by intraperitoneal injection of lipopolysaccharide (LPS). PP were excised 24 hours post-injection to determine lymphocyte subpopulations, B cells, T-helper and T-suppressor cells (CD4+ and $CD8^{+}$), using flow cytometry. The OF-enriched diet significantly increased the total cell yield and number of B-lymphocytes in healthy and endotoxemic mice ($P<0.001$). In contrast, T-lymphocytes were unaltered in healthy mice but increased in LPS-challenged mice that received the OF-supplemented diet ($P<0.001$). Since the increase of CD4+ cells was more pronounced than that of CD8+ cells, there was a significant increase in the CD4:CD8 ratio ($P<0.01$). This study shows that a diet enriched with OF improves the intestinal immune status by increasing the number of lymphocytes in healthy and endotoxemic animals. Interestingly, there was a distinct effect on the lymphocyte subpopulations during endotoxemia.

Manhart N., Spittler A., Bergmeister H., Mittlböck M., Roth E. (2003) Influence of fructooligosaccharides on Peyer's patch lymphocyte numbers in healthy and endotoxemic mice. Nutrition 19 (7/8): 657-660.

Continued on page 12

References

Aggett P.J., Agostoni C., Axelsson I., Edwards C.A., Goulet O., Hernell O., Koletzko B., Lafeber H.N., Micheli J.-L., Michaelsen K.F., Rigo J., Szajewska H., Weaver L.T. (2003) Non-digestible carbohydrates in the diets of infants and young children: a commentary by the ESPGHAN Committee on Nutrition. J. Ped. Gastroent. Nutr. 36:329-337.

Larque E., Demmelmair H., Koletzko B. (2002) Perinatal supply and metabolism of long-chain polyunsaturated fatty acids: importance for the early development of the nervous system. Ann. N.Y. Acad. Sci. 967:299-310.

Lauren L., Jarvelin M.R., Elliott P., Sovio U., Spellman A., McCarthy M., Emmett P., Rogers I., Hartikainen A.L., Pouta A., Hardy R., Wadsworth M., Helmsdal G., Olsen S., Bakoula C., Lekea V., Millwood I.; EURO-BLCS Study Group. Relationship between birth weight and blood lipid concentrations in later life: evidence from the existing literature. Int. J. Epidemiol. 32(5):862-876.

Levy-Marchal C., Jaquet D., Czernichow P. (2004) Long-term metabolic consequences of being born small for gestational age. Semin. Neonatol. 9(1):67-74.

Miniello V.L., Francavilla R., Straziuso S., Franco C., Gagliardi F., Armenio L. (2004) Infant formula supplemented with prebiotic oligosaccharides : Closer to the reference. AgroFOOD Industry High-Tech, March-April:42-44.

Miniello V.L., Moro G.E., Armenio L. (2003) Prebiotics in infant milk formulas: new perspectives. Act. Paediatr. Suppl. 441:68-76.

Spector S.L., Surette M.E. (2003) Diet and asthma: has the role of dietary lipids been overlooked in the management of asthma? Ann. Allergy Asthma Immunol. 90(4):371-377.

Zadik Z. (2003) Maternal nutrition, foetal weight, body composition and disease in later life. J. Endocrinol. Invest. 26(9):941-945.

continuation of page 11

Fructans could prevent diarrhoea caused by enteral tube feeding

Enteral tube feeding (ETF) is common in both the hospital and community environment, but diarrhoea is a regular and serious complication of ETF. Microflora and the production of short chain fatty acids (SCFA) may protect against diarrhoea, but studies in healthy volunteers have suggested that the composition of currently used ETF formulae may have a negative impact on it.

Recent studies demonstrate that low-residue enteral formulae cause negative alterations to the faecal flora and SCFA production in healthy subjects, which can be partially prevented by fortification with fructans. Conclusive data in patients receiving ETF are not yet available. The authors point out that the current problems with accurate characterisation of faecal output and definition of diarrhoea impede comparison of research studies and standard assessment of therapeutic interventions in clinical practice.

Whelan K., Judd P.A., Preedy V.R., Taylor M.A. (2004) Enteral feeding: the effect on faecal output, the faecal microflora and SCFA concentrations. Proc. Nutr. Soci. 63:105-113.

Bifidobacterium animalis DN-173 010 ferments inulin via an ATP-generating pathway

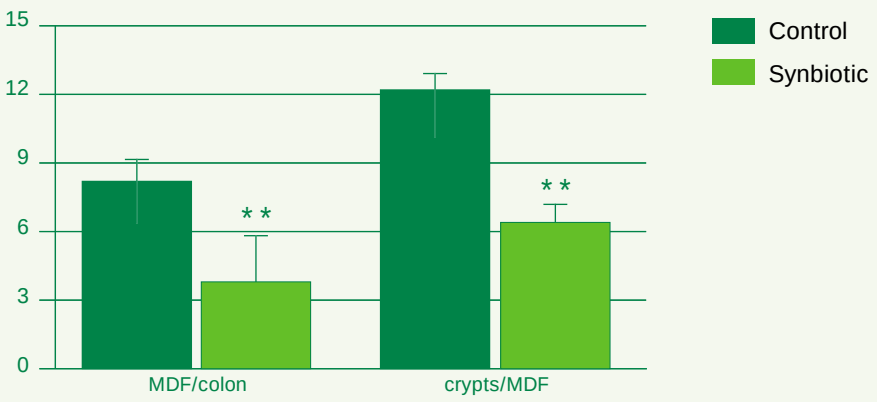
The aim of this study was to examine the growth kinetics of the dairy probiotic Bifidobacterium animalis DN-173 010 strain of commercial importance with different carbohydrates and to obtain quantitative data about the degradation of inulin-type fructans (Raftilose®P95, Raftilose® Synergy1, Raftiline®HP) throughout the fermentation process. The inability of the strain to metabolise glucose is most remarkable, and also fructose and galactose were very poor substrates for this strain. The fact that the oligosaccharides were metabolised faster than their constituting moieties suggests that the strain lacks the necessary uptake mechanisms for the latter.

Quantitative analysis further demonstrated that the selective consumption of the different oligofructose fractions induced changes in growth and metabolite production of the strain throughout the fermentation. It may be assumed that well-fermented sugars stimulate lactic acid production, while less fermentable sugars and hence a low intracellular

A synbiotic containing Raftilose®Synergy1 decreases the number of mucin-depleted foci, a novel biomarker for colon cancer in rats

To study colon cancer, a rat model has been developed in which the administration of the carcinogen azoxymethane (AOM) induces tumours through a multistep process, as in humans. Aberrant crypt foci (ACF) are preneoplastic lesions that are considered to be correlated to the development of tumours, so the determination of ACF in animal models is widely used as a short-term test to predict colon carcinogenesis. Since the correlation between ACF and tumours is not always prominent, an alternative biomarker for colon cancer was proposed. The authors chose to subject the carcinogen-treated rats to a diet containing a synbiotic (10^{10} cfu/g of probiotics and 10% of the prebiotic Raftilose®Synergy1) since its efficacy in the reduction of experimental colon cancer has been demonstrated. Although 31 weeks after injection of the carcinogen both the number and the incidence of intestinal tumours was reduced in rats receiving the synbiotic diet, the number of ACF/colon after 7 and 15 weeks was similar in both groups. The same colon tissue used to detect ACF was restained with a dye to highlight mucin production, since low production is reported as a hallmark of dysplasia. It appeared that these mucin-depleted foci (MDF) were lower in number and multiplicity in the group of rats receiving the synbiotic already at 15 weeks after the administration of AOM. Histological examination elicited that MDF possess dysplastic features similar to those in colon tumours. Although the preliminary characterisation does not permit firm conclusions on the relation between ACF and MDF, this study suggests that MDF are a subgroup of ACF that may predict tumour outcome better than ACF.

Caderni G., Femia A.P., Giannini A., Favuzza A., Luceri C., Salvadori M., Dolara P. (2003) Identification of mucin-depleted foci in the unsectioned colon of azoxymethane-treated rats : correlation with carcinogenesis. Cancer Res. 63:2388-2392.



The number of mucin-depleted foci (MDF) per colon (A) and the number of crypts/MDF (B) in rats fed a control diet or a diet containing synbiotics, 15 weeks after the first azoxymethane treatment (Values are mean ± SEM, n =7, ** = significantly different from control, *P*<0.01). (Caderni et al., 2004)

sugar concentration could stimulate formic acid production to produce extra ATP. The increased production of formic acid may be of interest for the inhibition of intestinal pathogens such as Escherischia coli and Salmonella.

Van der Meulen R., Avonts L., De Vuyst L. (2004) Short fractions of oligofructose are preferentially metabolized by Bifidobacterium animalis DN-173 010. Appl. Environ. Microbiol. 70 (4) :1923-1930.

Fructo-oligosaccharides are completely fermented in the colon of healthy adults

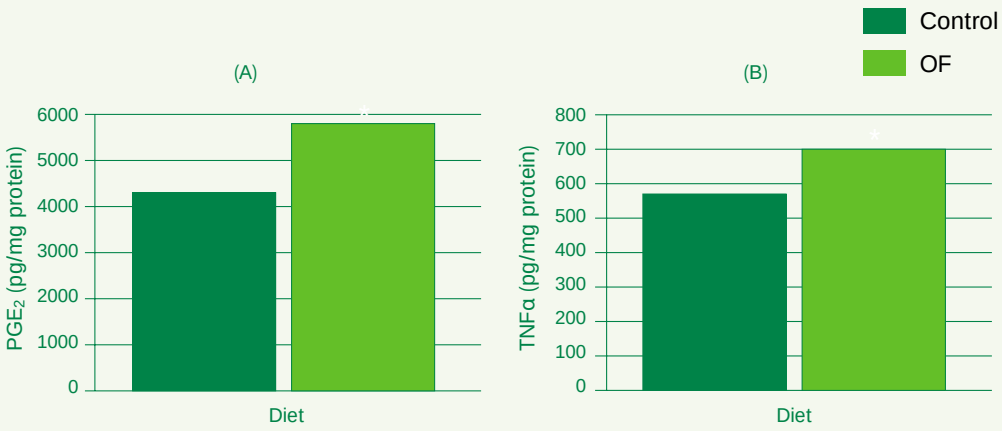
Fructo-oligosaccharides (FOS), galactosyl-sucrose (GS) and isomalto-oligosaccharides (IMO) are used to improve the intestinal microflora upon ingestion. However, experimental data show that the digestibility greatly differs among these oligosaccharides. Breath hydrogen results from fermentation processes in the colon and is widely used to study bacterial overgrowth and carbohydrate malabsorption. In this study, the breath hydrogen test was performed in 38 healthy adults to investigate whether hydrogen excretion is related to the dose of ingested oligosaccharides, in order to determine their utilisation or bioavailability. After screening for hydrogen excretion and tolerance to FOS, the subjects ingested 10 g of FOS, GS, and IMO with increases up to 20 g at one-week intervals. Breath gas was collected at 20 min intervals from 40 to 120 min, and at 30 min intervals from 120 min to 7 h after ingestion of the different test substances. The profiles of breath hydrogen excretion were significantly different between the oligosaccharides tested. Breath hydrogen excretion started earlier for FOS and was more pronounced than for GS, while IMO ingestion did not generate breath hydrogen. FOS and GS breath hydrogen excretion was dose-dependent. A higher dose initiated earlier breath hydrogen excretion probably because a larger amount of material escapes digestion in the small intestine. The results from this study demonstrate that IMO is completely hydrolysed in the small intestine and that FOS are not digested at all, but are fermented in the colon. GS, in which galactose is bound by a ß(1-4) linkage to the glucose part of sucrose, is hydrolysed more slowly by both sucrase and lactase.

Oku T. and Nakamura S. (2003) Comparison of digestibility and breath hydrogen gas excretion of fructo-oligosaccharide, galactosyl-sucrose, and isomalto-oligosaccharide in healthy human subjects. Eur. J. Clin. Nutr. 57:1150-1156.

Oligofructose has a hepatoprotective action in the endotoxemic shock model

Modulation of the immune function by nutrients is an emerging research area in which the intestinal flora plays a crucial role. The link between the gastrointestinal tract and the protection against systemic infections remains hypothetical. The liver and its resident macrophages (Kupffer cells) are the first encountered by pathological agents and endotoxins when entering the systemic circulation. This study investigated whether oligofructose (Raftilose®P95, 10% of the diet for 3 weeks) modulates the response to an endotoxic shock induced by lipopolysaccharide (LPS) administration (10 mg/kg i.p.) and if this is related to the activity of Kupffer cells in the liver. After LPS injection, rats receiving oligofructose had less hepatic injury, demonstrated by smaller and less numerous necrotic foci and a significantly lower serum alanine aminotransferase (ALT) level (P<0.05). The exact immunological events for liver protection still need to be elucidated, both pro-inflammatory tumour necrosis factor alpha (TNFα) and the immunosuppressive mediator prostaglandin E2 (PGE_2) reached higher levels in the oligofructose group after LPS injection compared to controls (P<0.05). In vitro tests showed that oligofructose treatment increased the number of large phagocytotic Kupffer cells and their secretion capacity for immune cell mediators (TNFα and PGE_2). In conclusion, this study demonstrated that oligofructose has a hepatoprotective effect which is probably mediated by PGE_2.

Neyrinck A.M., Alexiou H., Delzenne N.M. (2004) Kupffer cell activity is involved in the hepatoprotective effect of dietary oligofructose in rats with endotoxic shock. J. Nutr. 134(5):1124-1129.



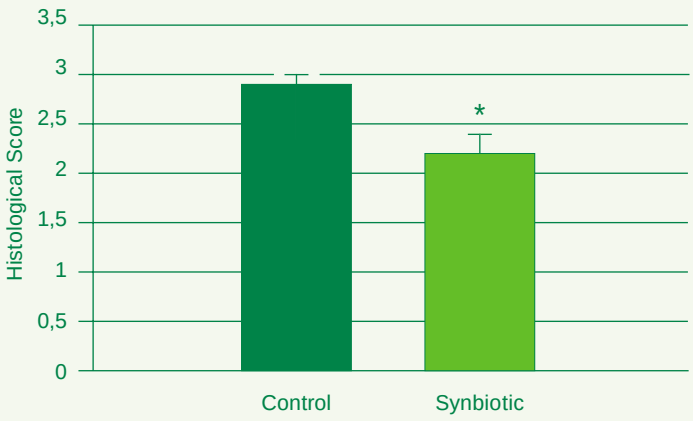
PGE_2 (A) and TNFα (B) secretion by precision-cut liver slices, incubated in the presence of lipopolysaccharide inducing an endotoxemic shock, obtained from rats fed a control diet or a diet supplemented with 10% oligofructose (OF). Values are mean ± SEM (n ≥ 3), * = significant effect of OF treatment, P = 0.05. (Neyrinck et al., 2004)

continued on page 14

continuation of page 13

Inulin effectively reduces inflammation in an animal model of colitis

The precise etiology of inflammatory bowel disease (IBD) is still unknown, but most investigators share the hypothesis that it is the result of an aggressive immune response to the intestinal microflora on a genetically susceptible host background. Alteration of the composition of the gut flora by antibiotics, probiotics and/or prebiotics may influence the course of chronic intestinal inflammation. In this study, the anti-inflammatory and microflora-modulating effect of a synbiotic preparation containing inulin and four bacterial species (2 x 10^9 cfu), administered for 2 months, was investigated in the TG HLA-B27 rat model of spontaneous colitis. At the age of 4 months, these rats demonstrated histological evidence of inflammation (edema, influx of inflammatory cells, mucosal damage, crypt abcesses and ulcerations), which was significantly reduced by prophylactic treatments with the synbiotic (2.2 ± 0.2 vs. 2.9 ± 0.1, $P \leq 0.03$). Characterisation of the caecal microflora revealed an increased diversity in the microflora profile after synbiotic administration, reflecting the poor homeostatic regulation of the bowel ecosystem. The caecal microflora was enriched in the presence of Bifidobacteria animalis, probably reflecting the prebiotic effect of inulin. Since only two of the four bacterial species used in the synbiotic could be cultivated, and neither of these species were detected in the microflora, it is unlikely that these bacteria were important in reducing the severity of colitis. These findings suggest that inulin acted as the primary effective compound to reduce the inflammation in this animal model of spontaneous colitis.



Histological score of inflammation – tissue assessed for edema, inflammatory cells, mucosal damage, ulceration and crypt abcesses – is reduced significantly ($P<0.03$) by 8-week synbiotic treatment in the diet of animals developing spontaneous colitis. Since none of the probiotics of the synbiotic mixture could be recovered in the faeces, the protective effect could be attributed to the prebiotic action of inulin. (Schultz et al., 2004)

Schultz M., Munro K., Tannock G.W., Melchner I., Göttl C., Schwietz H., Schölmerich J., Rath H.C. (2004) Effects of feeding a probiotic preparation (SIM) containing inulin on the severity of colitis and on the composition of the intestinal microflora in HLA-B27 transgenic rats. Clin. Diagn. Lab. Immun. 11 (3):581-587.

Oligofructose improves the gut microflora composition and prevents soy isoflavone breakdown in vitro

The isoflavone genistein, which is thought to possess various potent biological properties, is found predominantly in soyabeans in its glycosidic form genistin. However, studies have shown that genistein is extensively degraded by the human gut microflora with consequent loss of its biological activity. This study was set up to investigate whether a prebiotic could divert the gut bacterial metabolism away from genistein breakdown. In vitro fermentation of soyabean isoflavones (10 g/L) with faecal samples from healthy volunteers degraded 91% of the genistein present. Addition (10 g/L) of glucose or oligofructose (OF) to the fermentation medium prevented genistein breakdown to about 52 and 56%, respectively ($P<0.01$).

At the same time, the presence of OF significantly increased the counts of Bifidobacterium spp. ($P<0.05$) and Lactobacillus spp. ($P<0.01$), while Bacteroides spp. and Clostridium spp. were reduced ($P<0.05$). Fermentation in the three-stage chemostat, with a separate vessel representative for the proximal, transversal and distal part of the colon, generated similar trends. Degradation of genistein by 67, 95 and 93% in vessel 1, 2 and 3 respectively, was reduced to 22, 24 and 26% when OF was present in the fermentation medium. Furthermore, the maintenance of genistein at similar levels suggests that Bifidobacterium spp. and Lactobacillus spp. may be effective deglycosylators, whereas Bacteroides spp. and Clostridium spp. may play a role in degrading the aglycone further. The addition of excess substrate appeared to preserve genistein degradation in vitro, with OF having the extra benefit of selectively increasing beneficial bacterial genera.

Steer T.E., Johnson I.T., Gee J.M., Gibson G.R. (2003) Metabolism of the soyabean isoflavone glycoside genistin in vitro by human gut bacteria and the effect of prebiotics. Br. J. Nutr. 90:635-642.

Synbiotic therapy in patients undergoing surgery

Preservation of the gut barrier function seems to be important to prevent systemic inflammation and septic complications after surgery. Both bacterial translocation from the gut lumen to the lymph nodes and the gastric colonisation with potentially pathogenic bacteria are associated with an increased incidence of postoperative sepsis. In this study, the effect of a combination of the prebiotic oligofructose (16 g/day) and a selection of probiotics (4x10^9 cfu/g) was assessed on bacterial translocation, gastric colonisation, systemic inflammation and septic morbidity in 137 surgical patients (72 on synbiotic, 65 on placebo). The treatment was initiated 2 weeks preoperatively and reintroduced after the surgery until discharge from the hospital. There were no significant differences between the synbiotic and the control groups in bacterial translocation measured at mesenteric lymph nodes and scrapings of the terminal ileum, gastric colonisation measured by a nasogastric aspirate, systemic inflammation measured by serum levels of C reactive protein, interleukin 6 and anti-endotoxin antibodies, or septic complications.

Although the prevention of bacterial adhesion and translocation appears to be important in animal models, it might be possible that in humans other mechanisms act to prevent sepsis, such as immunomodulation. In that regard, the lack of benefit in this study could be due to the short feeding period of the synbiotic, inducing only an immunomodulatory effect too subtle for the magnitude of the surgical insult. Another reason could be the limited sample size, so further research in clinical settings is warranted.

Anderson A.D.G., McNaught C.E., Jain P.K., MacFie J. (2004) Randomised clinical trial of synbiotic therapy in elective surgical patients. Gut 53(2):241-245.

Synbiotic treatment reduces the presence of potential pathogens responsible for septic complications

The pathogenesis of sepsis and multiple organ failure in critical illness remains obscure, but it is generally agreed that the gut plays a pivotal role. The gastro-intestinal flora alters with the use of antibiotics, immunosuppression or changes in intestinal permeability. Since among the resident bacteria potential pathogens are present, these could be a source of sepsis when the gut barrier is functionally or physically breached. The aim of this study was to investigate whether the oral administration of a synbiotic preparation could alter the gut barrier function in critically ill patients (n = 90) and thus reduce sepsis. The synbiotic consisted of a commercial mixture of probiotic bacteria (4 x 10^9 cfu) and oligofructose (Raftilose®P95, 7.5 g), given three times and twice a day respectively. Gastric bacterial colonisation is a surrogate marker of bacterial translocation, so the primary outcome was the incidence and nature of gastric colonisation on day 1 and day 8 of intervention – measuring all gram negative bacteria, Pseudomonas species and Staphylococcus aureus. Other markers included small intestinal permeability, systemic inflammatory response, septic morbidity and mortality. After one week of therapy, patients in the synbiotic group had a significantly lower incidence of potentially pathogenic bacteria (43 vs. 75 %, *P*=0.05) and multiple organisms (39 vs. 75 %, *P*=0.01) compared to those receiving placebo. These results confirm that synbiotics alter the microbial composition of nasogastric aspirates, reducing the carriage of pathogenic bacteria. Since no differences in terms of small intestinal permeability, septic complications or mortality could be detected, the clinical significance of this finding needs to be studied in a larger number of patients.

Prashant K.J., McNaught C.E., Anderson A.D.G., MacFie J., Mitchell C.J. (2004) Influence of synbiotic containing Lactobacillus acidophilus La5, Bifidobacterium lactis Bb 12, Streptococcus thermophilus, Lactobacillus bulgaricus and oligofructose on gut barrier function and sepsis in critically ill patients: a randomised controlled trial. Clin. Nutr. 23:467-475.

Inulin supports probiotics in their protective action on colon cells exposed to genotoxic faecal water

Agents involved in the aetiology of colon cancer are likely to be associated with the aqueous phase of the faecal contents in the gut, the so-called faecal water. Antigenotoxicity of lactic acid bacteria, of prebiotics and of their combination was assessed using faecal water as the genotoxic challenge in a human colon cell line model. Six strains of lactic acid producing bacteria were incubated (10^8 cfu/mL). Certain lactic acid bacteria have the ability to reduce the genotoxic effects of faecal water in human colon cells in culture. Viability of the bacterial cells was a prerequisite and the effect was both dose- and species-dependent, Lactobacillus plantarum and Bifidobacterium Bb12 being most effective. Fermentation of probiotics was particularly effective, especially in combination with inulin. This could be a consequence of different end products of metabolism, providing acetate and butyrate as energy sources to the colon cells.

Burns A.J., Rowland I.R. (2004) Antigenotoxicity of probiotics and prebiotics on faecal water-induced DNA damage in human colon adenocarcinoma cells. Mut. Res. 551: 233-243.

COLOPHON

Active Food Scientific Monitor is published by ORAFTI, a daughter company of RAFFINERIE TIRLEMONTOISE (B), which is part of the SÜDZUCKER Group (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.
Active Food Scientific Monitor appears twice a year and is sent to researchers, nutritionists and health professionals. It will be sent free to anyone else who is interested.

We would be very pleased to receive your suggestions and reactions at the following address:
ORAFTI Active Food Ingredients
Christine Nicolay
Aandorenstraat 1
3300 Tienen - Belgium
tel.: +32 16 80 13 01
fax: +32 16 80 13 08
e-mail: afi@orafti.com
www.ORAFTI.com

Editing, design and coordination
TO.BE www.ornottobe.be

Registered publisher
Anne Franck, Aandorenstraat 1, 3300 Tienen, Belgium

AGENDA

Belgium, Grimbergen

October 16, 2004
Subject: Symposium Pro- and Prebiotica
Content: Prebiotica
Speaker: Douwina Bosscher, ORAFTI
Contact: Prof. Yvan Vandenplas
Tel. +32 2 477 57 81
Email: pedvsy@az.vub.ac.be

Spain, Pamplona

October 15-16, 2004
Subject: Segundo Congreso de la Asociación Española de Dietistas-Nutricionistas
Content: Beneficios nutricionales de la inulina y la oligofructosa y su comunicación a los consumidores (Programa BENEO)
Speaker: Manuel Cirici, ORAFTI
Contact: Dña. Cristina Fernández
Tel. +34 948 42 56 00
Fax + 34 948 42 56 49
Email: dietetica@unav.es
Website: www.aedn.es/IIcongreso/index.htm

Belgium, Leuven

November 26, 2004
Subject: Symposium over de moleculaire mechanismen van het antagonisme tussen Lactobacillus rhamnosus GG en Salmonella typhimurium
Content: Consumer Research & het gebruik van pre-probiotica door de consument.
Speaker: Tim Van der Schraelen, ORAFTI
Contact: Sigrid De Keersmaecker, CMPG, KUL
Tel. +32 16 32 96 92
Fax +32 16 32 19 66
Email: dekeersmaecker@agr.kuleuven.ac.be
Website: www.cmpg.be

Russia, Moscow

November 23-26, 2004
Subject: Ingredients Russia 2004
Forum in the section “Healthy Foods”
Content: Development of functional foods with prebiotic fibers from ORAFTI
Speaker: Maya Perkovets, ORAFTI
Contact: ITE, Mel Vaux
Tel. +44 207 596 5188
Fax +44 207 596 5113
Email: mel.vaux@ite-exhibitions.com
Website: www.ite-exhibitions.com