

Nutritional and Health Benefits of Inulin and Oligofructose

Concepts in Functional Foods: The Case of Inulin and Oligofructose¹

Marcel B. Roberfroid

Université Catholique de Louvain, Department of Pharmaceutical Sciences, B-1200 Brussels, Belgium

ABSTRACT Recent advances in biosciences support the hypothesis that diet modulates various body functions. Diet may maintain well-being and reduce the risk of some diseases. Such discoveries have led to the concept of “functional food” and the development of the new discipline, i.e., “functional food science.” A practical and simple definition of a “functional food” is a food for which a claim has been authorized. The food components to be discussed as potential “functional food ingredients” are the inulin-type fructans, i.e., chicory inulin and oligofructose. The targets for their effects are the colonic microflora, the gastrointestinal physiology, the immune functions, the bioavailability of minerals, the metabolism of lipids and colonic carcinogenesis. Potential health benefits include reduction of risk of colonic diseases, noninsulin-dependent diabetes, obesity, osteoporosis and cancer. The documentation of such benefits requires scientific evidence that must be evaluated in terms of “health claims.” Previous assessments have concluded that, in terms of “functional claims,” strong evidence exists for a prebiotic effect and improved bowel habit. The evidence for calcium bioavailability is promising, and positive modulation of triglyceride metabolism is undergoing preliminary evaluation. Scientific research still must be done to support any “disease risk reduction claim,” but sound hypotheses do already exist for designing the relevant human nutrition trials. *J. Nutr.* 129: 1398S–1401S, 1999.

KEY WORDS: • functional food • inulin • prebiotic • calcium bioavailability

Today, the industrialized countries are facing, among others, three major challenges:

- to control the cost of health care
- to offer to their aging population a real opportunity to live, not only longer, but also better
- to provide to more and more “busy” consumers, a choice of healthy processed or ready-to-eat foods

At the same time, progress in the biosciences supports the hypothesis that, beyond providing nutrition, diet also may modulate various functions in the body that are relevant to health. The concepts in nutrition are changing from a past emphasis on the absence of adverse effects to an emphasis on the promising use of foods to promote a state of well-being, better health and reduction of the risk of diseases. These concepts have recently become popular with consumers. Indeed, although there are still many people who know little about nutrition itself, consumer awareness of the subject and its relationship to health is nevertheless growing appreciably. Finally, advances in food science and technology are providing the food industry with increasingly effective techniques to control and improve the physical structure and the chemical composition of food products. There is also a growing awareness of the additional benefits and market potential for functional foods. Over the last decade, primarily in Japan and in

the United States, these challenges together with these new concepts in nutrition have justified the development of “functional foods.”

Functional foods

A food can be said to be “functional” if it meets one of the following criteria: 1) [it] contains a food component (being a nutrient or not) which affects one or a limited number of function(s) in the body in a targeted way so as to have positive effects (Bellisle et al. 1998); 2) [it] has physiological or psychological effect beyond the traditional nutritional effect (Clydesdale 1997). Collectively, a functional food should have a relevant effect on well-being and health or result in a reduction in disease risk.

The component that makes the food “functional” can be either an essential macronutrient if it has specific physiologic effects [such as resistant starch or (n-3) fatty acids], or an essential micronutrient if its intake is over and above the daily recommendations. Additionally, it could be a food component even though some of its nutritive value is not listed as “essential” (e.g., some oligosaccharides) or it is even of nonnutritive value (e.g., live microorganisms or plant chemicals).

The production of functional foods

A natural food product can be genuinely “functional” if it contains food component(s) that modulate(s) function(s) in the body that is (are) relevant to health. A food product can be made functional in the following ways:

¹ Presented at the conference Nutritional and Health Benefits of Inulin and Oligofructose held May 18–19, 1998 in Bethesda, MD. This symposium was supported in part by educational grants from the National Institutes of Health Office of Dietary Supplements, the U.S. Department of Agriculture and Oraft Technical Service. Published as a supplement to *The Journal of Nutrition*. Guest editors for the symposium publication were John A. Milner, The Pennsylvania State University, and Marcel Roberfroid, Louvain University, Brussels, Belgium.

1. By increasing the concentration of a natural component to reach a concentration that is more likely to induce the expected effects [e.g., fortification with a micronutrient to reach a daily intake higher than the recommended daily intake but compatible with the dietary guidelines for disease prevention Block (1993)] or by increasing the concentration of a nonnutritive component for which data that demonstrate beneficial effects are available.
2. By adding a component that is not normally present in most foods, but for which beneficial effects have been demonstrated (e.g., non-vitamin antioxidants or prebiotic fructans).
3. By replacing a component, usually a macronutrient whose intake is usually excessive and thus has deleterious effects (e.g., fats) with a component for which beneficial effects have been demonstrated, e.g., chicory inulin as Rafticreme (Franck-Fripiat 1993).
4. By improving the bioavailability of food components for which beneficial effects have been demonstrated.

However, the demonstration of such beneficial effects requires a strict scientific approach for which a strategy can be proposed. This strategy must refer to a functional food science aimed at stimulating research and development of functional foods based on a "function-driven" approach, which is considered more universal than a product-driven approach.

The functional food science

The positive effects of a functional food can be either maintenance and/or improvement of a state of well-being and health, or reduction of the risk of a disease. The design and development of functional foods is a key issue as well as a scientific challenge that should rely on the following:

1. Basic scientific knowledge relevant to functions that are sensitive to modulation by food components; pivotal to maintenance of well-being and health; linked, when altered, to a change in the risk of a disease.
2. The exploitation of this knowledge in the development of markers that can be shown to be relevant to the key functions.
3. A new generation of hypothesis-driven human intervention studies that will include the use of these validated, relevant markers and allow the establishment of effective and safe intakes.
4. The development of advanced techniques for human studies that are minimally invasive and applicable on a large scale.

The initial step in research and development of a functional food is thus the identification of a specific and potentially beneficial interaction between one or more components of the food and a genomic, cellular, biochemical or physiologic function in the organism. This step belongs to fundamental research and must lead to one or more proposals for hypothetical mechanisms of the identified interaction. On such a basis, a functional effect can then be defined and demonstrated in relevant models. The conclusion of these experiments is a new hypothesis with regard to the relevance of the functional effect to human health, tested in strictly designed nutritional studies involving appropriate volunteers. The demonstration of these effects must also include a safety assessment. This evaluation is an absolute prerequisite for functional food development.

A functional food will be of limited value in terms of health benefit if it is not part of the diet. This is the opinion of G. Pascal, who, in his presentation at the 1st East West Perspectives Conference on Functional Foods (Pascal 1996), stated

clearly that: *functional foods must remain foods; they are not pills or capsules but components of a diet or part of a food pattern recognized as being beneficial for well being and health.* It would probably be more appropriate to speak of functional diet or even optimum nutrition rather than functional food.

Among the miscellaneous functions that are relevant to the potential functional effects of inulin and oligofructose are the following:

1. The gastrointestinal functions, especially those associated with a balanced colonic microflora, those mediated by the endocrine activity of this organ, and those that depend on its immune activity, control nutrient (in particular ions) bioavailability, or control stool production, transit time and intestinal motility (Roberfroid 1996 and 1998).
2. The hormonal modulation, via the balance insulin/glucagon or the production of gastrointestinal peptides, or the metabolism of the macronutrients (especially carbohydrates and fatty acids) with, as objective, reduced risk of syndrome X as well as cardiovascular diseases. One example is the reduced hepatic lipogenesis induced by chicory fructans (Fiordaliso et al. 1995, Kok et al. 1996).

Communication to the public

The science base generated by the research and development in the field of functional foods will serve to establish "health claims," which can then be translated into messages for consumers. According to Clydesdale (1997), a "health claim" refers to a positive correlation (i.e., reduction in risk and/or lessening of an adverse physiologic or psychological condition) between a food substance in a diet and a disease or other health-related condition. By reference to the strategy for research and development presented above, these claims will refer to either functional effects or disease risk reduction.

A functional effect refers to the positive consequence(s) of the interaction(s) between a food component and specific genomic, biochemical, cellular or physiologic function(s) without direct reference to any health benefit or reduction of risk of a disease. For example, inulin and oligofructose rebalance metabolic activities (e.g., lipid homeostasis), strengthen immune functions (immunostimulation), restore or stabilize colonic microflora (e.g., selective stimulation of bifidobacteria) and improve bioavailability of nutrients (Roberfroid 1998). Functional claims have already and will in the future lead to new concepts in nutrition. Examples of such new concepts are the prebiotics and synbitotics, colonic foods and bifidogenic factors (Gibson and Roberfroid 1995).

A disease risk reduction refers to the reduction of the risk of a disease by consuming a specific component or ingredient or a mixture of food component(s) or food ingredient(s). Examples include the reduction of risk of cardiovascular disease, infections (e.g., intestinal infections), atherosclerosis, liver diseases, diarrhea, constipation, osteoporosis and syndrome X (e.g., noninsulin-dependent diabetes or obesity). Even though it will depend on the particular disease risk to be reduced, the demonstration of such health effects remains a very difficult task and will require long-term experiments whose final results are difficult to predict.

Both functional effects and disease risk reduction require the demonstration of an effect in humans based on nutritional studies designed according to protocols and evaluation criteria, which are not necessarily these presently used in clinical studies for drug development. Indeed, the target populations of these nutritional studies are, in most cases, "healthy persons" or "persons supposedly healthy" for whom the "usual" diet will

be modified in order to demonstrate a statistically, but also and perhaps more importantly, biologically significant change in parameters/markers indicative of a state of "well-being and good health." In the vast majority of cases, these parameters/(bio)markers are yet to be discovered and, certainly, validated.

The case of inulin and oligofructose

Inulin-type fructans are composed of β -D-fructofuranoses attached by β -2-1 linkages. The first monomer of the chain is either a β -D-glucopyranosyl or β -D-fructopyranosyl residue. They constitute a group of oligosaccharides derived from sucrose that are isolated from natural vegetable sources. Generally, the product with a degree of polymerization (DP) from 2 to 60+ is labeled as inulin (Raftiline), whereas oligofructose, which is produced by partial enzymatic hydrolysis of inulin, is defined as DP < 10 (Raftilose). The inulin from which the small molecular weight oligomers have been eliminated is called inulin high performance (Raftiline HP).

The objective of the Inulin and Oligofructose Conference, 1998, was to review the science base concerning the nutritional and health benefits of inulin and oligofructose. Two major questions were proposed to the participants to stimulate discussions. These questions were discussed extensively in a recent review on "Dietary Fructans" (Roberfroid and Delzenne 1998).

- I. *Does sufficient scientific evidence exist for functional claims for inulin and oligofructose?* The topics to be addressed are as follows:
 - A. The classification of inulin and oligofructose as dietary fiber based on their resistance to digestion, followed by fermentation in the colon leading to improvement of colonic functions (especially fecal bulking), (Gibson et al. 1995, Roberfroid et al. 1993), as well as some systemic physiologic effects (Roberfroid 1993).
 - B. The selective stimulation of bifidobacteria growth in the colonic microbiota to support their classification as prebiotic. Of particular interest is the question of the dose-effect relationship in a complex ecosystem such as colonic microbiota because it may depend on other factors such as the initial number of bifidobacteria (Roberfroid et al. 1998). This may lead to the conclusion that, at the population level, the question of the dose is of low relevance and that, on an average base, taking into account the variability in the number of bifidobacteria in the human colonic flora, doses of a 4-5g/d are efficient in stimulating the growth of these bacteria classified as potentially beneficial for health (Gibson and Roberfroid 1995). Further, as to the classification as prebiotic, questions that remain to be answered are the following:
 1. the long-term persistence of the "bifidogenic" effect both when continuing to consume an inulin/oligofructose-rich diet and after stopping;
 2. the interest, in term of functional effects, of the so-called "synbiotic" approach, which combines both inulin or oligofructose as prebiotic and a probiotic strain (Gibson and Roberfroid 1995); and most importantly,
 3. the health benefits of having a colonic flora in which bifidobacteria predominate (see below for a discussion on possible disease risk reduction claims).

- C. The increased bioavailability of minerals, in particular, calcium.
 - D. The stimulation of the immune system.
 - E. The effects on lipid metabolism. Experimental data support the hypothesis that oligofructose inhibits hepatic lipogenesis in rats and, consequently, induces a significant hypotriglyceridemic effect. Because a metabolic link has recently been demonstrated between insulin resistance and the associated risk factors for atherosclerotic cardiovascular disease, especially hypertriglyceridemia, and because hypertriglyceridemia itself may be a risk factor in atherogenesis, these potential functional effects should be studied carefully in humans, especially in conditions known to be associated with hyperinsulinemia and hypertriglyceridemia (Aarsland et al. 1996, Carlson et al. 1979, Castelli 1986, Taskinen 1993).
- II. *Does scientific evidence support disease-risk-reduction claims for inulin-type fructans?* For inulin and oligofructose, "disease risk reduction claims" are, based on presently available scientific information, which is only tentative; further research is required to support and validate these claims. The most promising areas for the development of such claims are the following:
 - A. Constipation relief due to fecal bulking and possible effects on intestinal motility (Kleessen et al. 1997).
 - B. Inhibition of diarrhea, especially when it is associated with intestinal infections. This may be related directly to the possible inhibitory effect of bifidobacteria on both gram-positive and gram-negative bacteria, which has been reported by Wang and Gibson (Gibson and Wang 1994, Wang 1993).
 - C. Reduction of risk of osteoporosis if the improvement of the bioavailability of Ca, by inulin and oligofructose, is followed by a more physiologic change in bone mineral density and peak bone mass.
 - D. Reduction of the risk of atherosclerotic cardiovascular disease associated with dyslipidemia, especially hypertriglyceridemia, and insulin resistance, which, in particular, is known to be associated with hypercaloric high carbohydrate feeding regimens (Aarsland et al. 1996).
 - E. Reduction of the risk of colon carcinogenesis via an inhibition of the development of aberrant crypt foci and other surrogate markers (Gallaher et al. 1996, Koo and Rao 1991, Reddy et al. 1997, Rowland et al. 1998) and/or reduction in the growth rate of tumors (Taper et al. 1997). In the strategy for functional food development described above, these cancer-inhibitory effects in experimental animals could correspond to the first step, i.e., identification of effects. Because of their implications in health, these effects will have to be evaluated carefully in relevant human studies.

CONCLUSION

The development of functional foods is a unique opportunity to contribute to the improvement of the quality of food and consumer health and well-being. In that context, inulin and oligofructose are natural products that may become classified in the future as functional food ingredients for which validated health claims may become authorized. Only a rigorous scientific approach that yields sound and reliable data will justify any claim. Collectively, this information is clearly a

challenge for both the scientific community and the food industries. The major challenge to these partners is to give the consumers the guarantee that these new food products are not just a new opportunity for more profits, but genuine progress toward allowing them better control of their health. This conference is about the "Nutritional and Health Benefits of Inulin and Oligofructose" and provides a unique opportunity to evaluate present knowledge and propel the science forward.

LITERATURE CITED

- Aarsland, A., Chinkes, D. & Wolfe, R. R. (1996) Contributions of de novo synthesis of fatty acids to total VLDL-triglyceride secretion during prolonged hyperglycemia/hyperinsulinemia in normal man. *J. Clin. Investig.* 98: 2008–2017.
- Bellisle, F., Diplock, A. T., Hornstra, G., Koletzkos, B., Roberfroid, M., Salminen, S. & Saris, W.H.M. (1998) Functional food science in Europe. *Br. J. Nutr.* 80: S1–S193.
- Block, G. (1993) Micronutrients and cancer: time for actions? *J. Natl. Cancer Inst.* 85: 846–848.
- Carlson, L. A., Bottiger, L. E. & Ahfeldt, P. E. (1979) Risk factors for myocardial infarction in the Stockholm prospective study: a 14 year follow-up focussing on the role of plasma triglycerides and cholesterol. *Acta Med. Scand.* 206: 351–360.
- Castelli, W. P. (1986) The triglyceride issue: a view from Framingham. *Am. Heart J.* 112: 432–437.
- Clydesdale, F. (1997) A proposal for the establishment of scientific criteria for health claims for functional foods. *Nutr. Rev.* 55: 413–422.
- Fiordaliso, M. F., Kok, N., Desager, J. P., Goethals, F., Deboyser, D., Roberfroid, M. B. & Delzenne, N. (1995) Dietary oligofructose lowers triglycerides, phospholipids, and cholesterol in serum and very low density lipoproteins of rats. *Lipids* 30: 163–167.
- Franck-Frippiat, A. (1993) Rafticreaming: the new process allowing to turn fat into dietary fiber. *FIE '92: Conference Proceedings*, pp. 193–197. Maarssen Expoconsult Publ., The Netherlands.
- Gallaher, D. D., Stallings, W. H., Blessing, L., Busta, F. F. & Brady, L. J. (1996) Probiotics, cecal microflora, and aberrant crypts in the rat colon. *J. Nutr.* 126: 1362–1371.
- Gibson, G.R., Beatty, E. R., Wang, X. & Cummings, J. H. (1995) Selective stimulation of Bifidobacteria in the human colon by oligofructose and inulin. *Gastroenterology* 108: 975–982.
- Gibson G.R. & Roberfroid M.B. (1995) Dietary modulation of the human colonic microflora: introducing the concept of prebiotics. *J. Nutr.* 125: 1401–1412.
- Gibson, G. R. & Wang, X. (1994) Inhibitory effects of bifidobacteria on other colonic bacteria. *J. Appl. Bactriol.* 65: 103–111.
- Klessen, B., Sykura, B., Zunft, H. J. & Blaut, M. (1997) Effects of inulin and lactose on faecal microflora, microbial activity, and bowel habit in elderly constipated persons. *Am. J. Clin. Nutr.* 65: 1397–1402.
- Kok, N., Roberfroid, M., Robert, A. & Delzenne N. (1996) Involvement of lipogenesis in the lower VLDL secretion induced by oligofructose in the rat. *Br. J. Nutr.* 76: 881–890.
- Koo, M. & Rao, V. (1991) Long term effect of bifidobacteria and neosugar on precursor lesions of colonic cancer in mice. *Nutr. Cancer* 16: 249–257.
- Pascal, G. (1996) Functional foods in the European Union. *Nutr. Rev.* 54: S29–S32.
- Reddy, B. S., Hamid, R. & Rao, C. V. (1997) Evaluation of oligosaccharides for potential chemopreventive properties in colon carcinogenesis using aberrant crypt foci. *Carcinogenesis* 18: 1371–1374.
- Roberfroid, M. (1993) Dietary fiber, inulin and oligofructose: a review comparing their physiological effects. *Crit. Rev. Food Sci. Nutr.* 33: 103–148.
- Roberfroid, M. B. (1996) Functional effects of food components on the gastrointestinal system. *Nutr. Rev.* 54: S38–S42.
- Roberfroid, M. B. (1998) Background paper for a workshop on the role of intestinal flora and nutrient bioavailability. *BIOAVAILABILITY 97: Wageningen, The Netherlands, 25–28 May, 1997.*
- Roberfroid, M. B. & Delzenne, N. (1998) Dietary fructans. *Annu. Rev. Nutr.* 18: 117–143.
- Roberfroid, M. B., Gibson, G. R. & Delzenne, N. (1993) Biochemistry of oligofructose, a non-digestible fructo-oligosaccharide: an approach to estimate its caloric value. *Nutr. Rev.* 51: 137–146.
- Roberfroid, M. B., Van Loo, J.A.E. & Gibson G.R. (1998) The bifidogenic nature of chicory inulin and its hydrolysis products. *J. Nutr.* 128: 11–19.
- Rowland, I. R., Rummey, C. J., Coutts, J. T. & Lievens, L. C. (1998) Effect of *Bifidobacterium longum* and inulin on gut bacterial metabolism and carcinogen-induced crypt foci in rats. *Carcinogenesis* 19: 281–285.
- Taper, H., Delzenne, N. & Roberfroid, M. B. (1997) Growth inhibition of transplantable mouse tumors by non digestible carbohydrates. *Int. J. Cancer* 71: 1109–1112.
- Taskinen, M. R. (1993) Hyperinsulinism and dyslipidemias as coronary heart disease risk factors in NIDDM. *Adv. Exp. Med. Biol.* 334: 295–300.
- Wang, X. (1993) Comparative Aspects of Carbohydrate Fermentation by Colonic Bacteria. Doctoral thesis, University of Cambridge, Cambridge, UK.