



Review

Health benefit application of functional oligosaccharides

Xu Qiang, Chao YongLie*, Wan QianBing

Department of Prosthodontics, West China College of Stomatology, Sichuan University, Chengdu 610041, PR China

ARTICLE INFO

Article history:

Received 12 April 2007

Received in revised form 8 March 2009

Accepted 10 March 2009

Available online 19 March 2009

Keywords:

Functional oligosaccharides

Hyperlipidemics

Anticarcinogenic

Obesity

Cardiovascular disease

Diabetes

ABSTRACT

There is no doubt that the functional oligosaccharides have positive effects on human health, both in the prevention and in treatment of chronic diseases. Therefore, there is great interest in health benefits of the functional oligosaccharides. The functional oligosaccharides of various origins (viruses, bacteria, plants and fungi) have been used extensively both as pharmacological supplements, food ingredients, in processed food to aid weight control, to regulation of glucose control for diabetic patients and reducing serum lipid levels in hyperlipidemics and other some acute and chronic diseases. Keeping in view, the pharmacological importance of the functional oligosaccharides and its derivatives, this article discusses the potential of the functional oligosaccharides to modulate the gut flora, to affect different gastrointestinal activities and lipid metabolism, to enhance immunity, and to reduce diabetes, obesity and cardiovascular risk for further exploitation of health benefits of the functional oligosaccharides.

© 2009 Elsevier Ltd. All rights reserved.

1. Introduction

Modern consumers are increasingly interested in their personal health, and expect the foods they eat to be – beyond tasty and attractive – also safe and healthy. As interest in the link between diet and health gathers pace, many consumers seek ways to feel well and stay healthy by eating nutritionally designed foods. Non-digestible carbohydrates such as dietary fibers, oligosaccharides, and resistant starch have various physiologic functions (Bird, Brown, & Topping, 2006; Mussatto & Mancilha, 2007a, 2007b; Nabarlatz, Ebringerová, & Montané, 2007; Nacos et al., 2006), and the promotive effects of many non-digestible carbohydrates on wellbeing, better health and reduction of the risk of diseases have been well examined (Hussain, Claussen, Ramachandran, & Williams, 2007; Zhang & Huang, 2005). Among non-digestible carbohydrates, the functional oligosaccharides present important physicochemical and physiological properties beneficial to the health of consumers, and for this reason, their use as food ingredients has increased rapidly. The functional oligosaccharides are intermediate in nature between simple sugars and polysaccharides and are claimed to behave as dietary fibres and prebiotics (Kunz & Rudloff, 2006). These compounds as non-absorbable food ingredients are microbial food supplements and may benefit the host by selectively stimulating salutary bacteria in the large intestine. The best known functional oligosaccharides include fructooligosaccharide, glucooligosaccharides (GOS), isomaltooligosaccharides,

soybean oligosaccharides, xylo-oligosaccharides and maltitol (Chen, Lu, Lin, & Ko, 2000; Muzzarelli, 2009; Reis, Coimbra, Domingues, Ferrer-Correia, & Domingues, 2004). These compounds promote a good balance of intestinal microflora and decrease gastrointestinal infections. The beneficial physiologic functions of the functional oligosaccharides in humans were summarized as follows: (1) they do not stimulate an increase in blood glucose or insulin secretion because they dissolve in the gut to form a viscous gel that lowers the absorption of released glucose; (2) they supply small amounts of energy, approximately 0–3 kcal/g of sugar substitute; (3) they are noncariogenic; (4) they improve the intestinal environment and change the intestinal microbiota so that it is dominated by salutary bacteria as a result of the acidic intestinal environment; (5) they improve and suppress diarrhea and symptoms of diarrhea and (6) they stimulate intestinal absorption of minerals, such as calcium, magnesium and iron (Manning & Gibson, 2004; Monchois, Willemot, & Monsan, 1999; Ngo, Kim, & Kim, 2008). Moreover, consumption of the functional oligosaccharides reduces the risk of civilization diseases such as cardiovascular disease, colon cancer and obesity (Marionneau et al., 2001). Supported by extensive scientific research today, health products continue to stimulate great interest and demonstrate potential for future growth. There is a market for the functional oligosaccharides that assist in constructing a healthy diet, and also for foods directly targeted to certain risk groups. In addition, the functional oligosaccharides are also used in feeds, pharmaceuticals, or cosmetics as stabilizers, bulking agents, immunostimulating agents or prebiotic compounds (Simon, 1996).

The present review summarizes physiological properties of the function oligosaccharides and potential health benefits.

* Corresponding author. Tel.: +86 13708099161; fax: +86 28 85503474.

E-mail address: xuqiang_doctor1998@yahoo.com.cn (C. YongLie).

2. Effect of the functional oligosaccharides on gastrointestinal microorganisms and urogenital infections

The gastrointestinal tract is very heavily populated with bacteria, mainly of strictly anaerobic bacteria. Most of these organisms are benign to the host; however, certain gut species are pathogenic and may be involved in the onset of acute and chronic disorders (Rollo, Luciani, Marota, Olivieri, & Ermini, 2007; Vinderola, Matar, Palacios, & Perdígón, 2007). Due to their chemical structure, the functional oligosaccharides are substrates that can only be consumed by a limited number of bacteria, stimulating thus their growth. Among the group of bacteria present in the gastrointestinal tract, the bifidobacteria and lactobacilli are those that most utilize oligosaccharides being considered as the only microorganisms able to beneficially affect the host's health (Mikkelsen & Jensen, 2004; Vernazza, Gibson, & Rastall, 2005). The reported health benefits of bifidobacteria include stabilizing the gut mucosal barrier, modulation of immune response, modulation of intestinal microbiota, prevention of traveller's diarrhea in children, reduction of necrotizing endocarditis in neonates, alleviation of atopic dermatitis symptoms in children, improvement of constipation, and antibacterial and anticarcinogenic activities (Matamoros Fernández, 2007). Some functional oligosaccharides, such as isomaltooligosaccharide, are reported to increase cecal *Bifidobacterium* population in young broiler chickens (Thitaram et al., 2005). In addition, the functional oligosaccharides can still significantly modify the colonic microflora, because these oligosaccharides serve as substrate for growth and proliferation of anaerobic bacteria, mainly the bifidobacteria, which inhibit the growth of putrefactive and pathogenic bacteria present in the caeco-colon. For example, soybean meal oligosaccharides (SMO) are reported to show promise for use as a product which may promote competitive exclusion of potential pathogens. A bifidus predominance of the intestinal flora of breastfed infants has already been reported by Moro who already concluded that human milk contains some functional oligosaccharides, which act as a growth factor for these microorganisms (Moro, 1900).

Healthy vaginal flora is mainly composed (50–90%) of *Döderlein's* bacilli, which comprise different strains of lactobacilli (Rousseau, Lepargneur, Roques, Remaud-Simeon, & Paul, 2005). Lactobacilli make up a biofilm on the surface of the vaginal mucosa (Rousseau et al., 2005), which is considered to protect the vagina against pathogenic microorganisms through different mechanisms. When lactobacilli are reduced or absent, other microorganisms may grow excessively, thus causing disorders. Indeed, most urogenital infections result from vaginal flora imbalance. Probiotics can be defined as "live microorganisms which when administered

in adequate amounts confer a health benefit on the host" (El-Tahlawy, Gaffar, & El-Rafe, 2006; Qin et al., 2006; Rousseau et al., 2005). One way to operate on the urogenital flora is to provide nutrients that stimulate the growth of lactobacilli to the detriment of pathogens one (Merk, Borelli, & Christian Korting, 2005; Reid, Beuerman, Heinemann, & Bruce, 2001). Among the carbohydrates that are qualified as prebiotics, fructooligosaccharides (FOS) and glucooligosaccharides (GOS) are of interest. These functional oligosaccharides can avoid the urogenital infections against pathogenic microorganisms by promoting proliferation of lactobacilli.

3. Type II diabetes and obesity

Obesity and obesity related type II diabetes are typical diseases of the modern Western society. Current recommendations for the management of type II diabetes and obesity include an increase in dietary fiber intake (Singh, 2007). Dietary fiber's viscose and fibrous structure can control the release of glucose with time in the blood, thus helping in the proper control and management of diabetes mellitus and obesity (Bennett et al., 2006; Huang, Zhang, Cheung, & Tan, 2006). The functional oligosaccharides are often cited as being important dietary fibers in nutritional advice concerning specific disorders associated with the metabolic syndrome (de Alcântara, Martim, Silva, Dietrich, & Buckeridge, 2006; Kim & Rajapakse, 2005; Roth, Ziak, & Zuber, 2003). Commercially produced oligosaccharides are fructooligosaccharides, isomaltooligosaccharides, maltooligosaccharides, arabinoxylan oligosaccharides, glucose-oligosaccharides, galacto-oligosaccharides and so on (Table 1). Glycemic index, a classification of food based on their blood glucose response relative to a starchy food, e.g., white bread, or standard glucose solution, has been proposed as a therapeutic principle for diabetes mellitus by slowing carbohydrate absorption (Kim et al., 2006). On the basis of studies in animals and humans, it has been proposed that intake of the functional oligosaccharides, which are fermented in the caeco-colon, could be interesting way to modulate satiety, glucose or lipid metabolism, and hypertension (Nesselhut et al., 1993). Low glycemic index food, e.g., high functional oligosaccharides food, has been shown to reduce postprandial blood glucose and insulin responses and improve the overall blood glucose and lipid concentrations in normal subjects, and patients with diabetes mellitus (Kawamori, Kadowaki, Onji, Seino, & Akanuma, 2007). Among the functional oligosaccharides, short chain fructooligosaccharides (FOS), given at the dose of 10% in the diet of rats for a few weeks, reduces hepatic triglyceride content, postprandial glycemia and triglyceridemia in normal rats, lessens hepatic steatosis and fat mass development in obese Wistar rats fed a high fat diet. This phenomenon could be partly explained by a satietogenic effect of FOS (Delmée

Table 1
Functional oligosaccharides.

Type	Monosaccharides	Number of monosaccharides	Bonds indicative of functions
IMOS (isomaltooligosaccharides)	Glucose	2–5	α -1,4
SBOS (soybean oligosaccharides)	Fructose, galactose, glucose	2–4	α -1,6
FOS (fructooligosaccharides)	Sucrose, fructose	2–5	β -1,2
XOS (xylo-oligosaccharides)	Xylose	2–7	α -1,4
MOS (maltooligosaccharides)	Mannitose, glucose	2–10	α -1,2, α -1,4
Gentio-oligosaccharides	Glucose	2–10	β -1,6
Glucose-oligosaccharides	Glucose	2–10	α -1,2, β -1,3, β -1,6
Palatinose	Glucose, fructose	2	β -1,6
Malto-oligosaccharides	Glucose	2–8	α -1,2
Lactosucrose	Galactose, fructose	2–3	β -1,4
Clycosylsucrose	Glucose, fructose	3	α -1,2, β -1,4
Galato-oligosaccharides	Galactose	2–5	β -1,2, α -1,4
Lactulose	Galactose, fructose	2	β -1,4
Raffinose	Galactose, fructose, glucose	3	β -1,2, α -1,4
Stachyose	Galactose, fructose, glucose	4	α -1,4

et al., 2006; Li, Fang, & Zhang, 2007). In streptozotocin-treated diabetic rats, FOS feeding during 4–6 weeks improves glucose tolerance, decreases glycemia, and partially restores insulin secretion (Giacco et al., 2004). Moreover, an improvement of glucose/insulin ratio has also been observed in rats receiving FOS added in a high-fructose diet (Giacco et al., 2004). Barshop et al. (2003) investigated the effect of isomaltooligosaccharides (IMOS) and fructooligosaccharides (FOS) on the alteration of cecal microbiota, cecal pH, total cecal weight and serum lipid levels and also evaluated the inhibitory effect on precancerous colon lesions in rats. IMOS and FOS markedly decreased the cecal pH and serum triglyceride concentration, and increased the total cecal weight and bifidobacterial population.

There are indications that the arabinoxylan oligosaccharides (AXOS) have an effect against type II diabetes (Charalampopoulos, Wang, Pandiella, & Webb, 2002; Muzzarelli, 2009). AXOS decrease postprandial glucose levels (Charalampopoulos et al., 2002) and insulin response (Grootaert et al., 2007) and increase postprandial ghrelin, a hormone produced by gastric cells to stimulate food intake, as shown in healthy humans (Rantanen et al., 2007). Ogawa, Takeuchi, and Nakamura (2005) determined whether AXOS improve postprandial glucose and insulin responses in healthy humans. The peak postprandial glucose concentration after meals containing AXOS-rich fiber was significantly lower than that after consumption of a control meal.

Dietary fiber has the ability to bind with bile acids and prevents its reabsorption in the liver thus, inhibit cholesterol synthesis (Mussatto & Mancilha, 2007a,b). The functional oligosaccharides, such as Gum Arabic (a natural carbohydrates exudate from Acacia senegal and Acacia seyal trees in Africa), has a low calorific value of not greater than 2 kcal/g (Sun et al., 2005). Its intrinsic glycaemic index is near zero, and it is not ingested in the small intestine. It has therefore applications to reduce plasma glucose and serum cholesterol (Lekka et al., 2006). In glucose tolerance test in 12 healthy subjects in whom the addition of 20 g acacia gum to a 100 g load of glucose, there was a significant reduction in plasma glucose (16.1%), serum insulin (11.2%) and serum cholesterol (17.2%) after 90 min. A study in five healthy human volunteers taking 25 g/day of acacia gum shows a significant reduction in total serum cholesterol concentrations (Doi et al., 2006). Another study confirms these observations (Sharma, 1985), which showed that in seven non-obese men consuming 15 g/day acacia gum twice a day along with their main meals over 30 days, there was a significant decrease in serum total cholesterol, particularly the LDL and VLDL fractions. It is also assumed that changes in the concentration of serum cholesterol have been related with changes in intestinal microflora. Some strains of *Lactobacillus acidophilus*, whose population can be modulated by the functional oligosaccharides, assimilate the cholesterol present in the medium (Mountzouris et al., 2006), while others appear to inhibit the absorption of cholesterol micellae through the intestinal wall (Mountzouris et al., 2006).

4. Reduction of diarrhea

The functional oligosaccharides also plays a role in ameliorating diarrhea (Mourão et al., 2006), especially when it is associated with intestinal infections. According to Chi, Chen, Wang, Xiong, and Li (2008), this may be directly related to the possible inhibitory effect of bifidobacteria both on Gram+ and Gram– bacteria. It was found that fructooligosaccharides (FOS), such as those derived from chicory, have been used with increasing frequency as food additives, with possible benefits including support of beneficial gastrointestinal flora and reduction of infectious diarrhea (Rhoades, Gibson, Formentin, Beer, & Rastall, 2006; Rivero-Urgell & Santamaria-Orleans, 2001). Shipley, Allen, and Swanson (1983) reported that the raffinose family oligosaccharides (RFOs, or raffinose, stachyose

and verbascose) are of physiological importance since they increase bifidobacteria and relieve diarrhea. Tang et al. (2005) reported that dietary supplementation of 0.12% galacto-mannan oligosaccharide (GMOS) was able to increase growth performance and decrease diarrhea occurrence in piglets.

Some authors also consider that the functional oligosaccharides improve the absorption of water and electrolytes in the small intestine and as a result leads to a reduction in the incidence of diarrhea and its duration. This effect has been demonstrated in animals (Juśkiewicz & Zduńczyk, 2002) and humans (Morrow et al., 2004; Vernazza et al., 2005). For example, 39 adult volunteers with fecal incontinence or watery stool had a decrease in the percentage of incontinent stools compared to a placebo when progressively ingesting 25 g/day of acacia gum supplement over 1 month. It is clear that such problems can be effectively and simply treated, particularly in the elderly (Kaur, Chopra, & Saini, 2002).

5. Constipation relief due to fecal bulking and possibly effects on intestinal microflora

The intestinal microflora plays a considerable role in the metabolism of endogenous and exogenous substances in the diet, and is thought to participate in beneficial and deleterious effects on human health. In human subjects, fructo- and galacto-oligosaccharides are known for their ability to stimulate the growth of *Bifidobacterium* and *Lactobacillus* and to inhibit that of potentially pathogenic bacteria, *Enterobacteria*, *Clostridium* and *Salmonella*. The end products of the functional oligosaccharides fermentation by colonic bacteria, the SCFA, are efficiently absorbed and utilized by the human colonic epithelial cells, stimulating their growth as well as the salt and water absorption, increasing thus the humidity of the fecal bolus through osmotic pressure, and consequently improving the intestinal motility. Moreover, the intestinal tract of mammals harbours a complex bacterial ecosystem, which has not yet been fully characterized. Studies show that constipation can be influenced by the microbiota composition and its metabolic activities (Liebregts et al., 2007). The functional oligosaccharides treatment can inhibit and palliate intestinal disorders. For example, FOS, MOS and GOS are good substrates for bacteria of the types *Bifidobacterium* spp. and *Bacteroides* spp. (Xue, Chen, Lu, & Jin, 2009). These oligosaccharides promote an increase in short chain fatty acids. The production of short chain fatty acids by bifidobacteria stimulates intestinal peristalsis and increases the humidity of the fecal bolus through osmotic pressure (Fernández-Bañares, 2006). It has been observed that rats fed FOS may help to prevent constipation (Colecchia et al., 2006). It has also been found that a controlled administration of GOS in 0.12 g/kg body weight for male Japanese adults may help to restrain the growth of pathogenic bacteria, to retard disorders caused by imbalanced fermentation in colon and to avoid intestinal disorders such as constipation, inflammatory bowel disease. Jigami and Odani (1999) reported that feeding high amounts of mannan oligosaccharides (MOS) could help to palliate any negative effects of increasing fecal consistency, avoiding the colonization of digestive pathogens, and improve feed efficiency of milk replacer.

6. Immunomodulatory activities and anti-tumor

According to various investigations, metabolites from the fermentation of complex carbohydrates can be beneficial to health because they show a protective effect against colon or rectal cancer, decrease infectious intestinal diseases by inhibiting putrefactive and pathogenic bacteria (*Clostridium perfringens*, *Escherichia coli* and *Salmonella*), increase mineral bioavailability such as that of calcium, aid in the decreases of hypercholesterolemia, hyper-

lipoproteinemia, and hyperglycemia, and stimulate the immune system (Chakraborty et al., 2006; Dou et al., 2009). The use of the functional oligosaccharides, as prebiotic functional food ingredients, depends on their ability to escape digestion and absorption in the upper part of the intestine and reach the lower part where they should induce fermentation and selective stimulation of the growth and/or activity of intestinal bacteria associated with health and wellbeing (Arakane, Zhu, Matsumiya, Muthukrishnan, & Kramer, 2003; Kunz & Rudloff, 2006). There is a variety of the functional oligosaccharides produced worldwide, intended for use as functional food ingredients (Tosh, Brummer, Wood, Wang, & Weisz, 2004). The functional oligosaccharides of various origins (viruses, bacteria, plants and fungi) have been shown to exert potent immunomodulatory activities (Surenjav, Zhang, Xu, Zhang, & Zeng, 2006; Yang et al., 2005; Zhang & Huang, 2005; Zhu & Lin, 2006). Studies show that the specific functional oligosaccharides are preferentially utilized by select groups of intestinal microflora. For example, fructooligosaccharides are preferentially utilized by *Bifidobacterium* and have been used to increase intestinal levels of some micro-nutrients, such as vitamin and amino acids by stimulating proliferation of *Bifidobacterium* spp. in humans. The animals fed the glucose-oligosaccharides and Glycosylsucrose diets also showed higher counts of *Bifidobacterium*, demonstrating the bifidogenic effect of these components (Harhangi et al., 2002; Li et al., 2007). Nearly all the vitamins are involved in the functions of the immune system cells: phagocytosis, synthesis of molecules regulating the leucocytic function (interleukins), and production of immunoglobulins (Sikka, Lall, Arora, & Sethi, 2002).

Another mechanism of the functional oligosaccharides improving immunity is assumed that innate defence responses can be activated through the interaction of sugar moieties with innate receptors on the plasma membrane of host cells, in particular in macrophages and dendritic cells (Arnold, Dwek, Rudd, & Sim, 2006; Nezlin & Ghetie, 2004). It has been demonstrated that the synthetic β -(1 \rightarrow 6)-branched β -(1 \rightarrow 3) glucosylsucrose and its analogues, the basic unit of lentinan and other β -glucose-oligosaccharides, has been reported to have immunostimulatory effects. It has been described that β -glucose-oligosaccharides stimulate innate immune reactions by binding to selective receptors (such as dectin-1) mainly expressed on M2 macrophages (Zhang, Cheung, Chiu, Wong, & Ooi, 2006). Xylo-oligosaccharides (XOS) are a new group of oligosaccharides that are gaining importance as functional food ingredients in pharmaceuticals, feed formulations, and agriculture. XOS exhibit excellent physicochemical and physiological properties. They act as prebiotics promoting the growth of beneficial bifidobacteria in the colon, thus reducing the risk of colon cancer (Nabarlatz et al., 2007). Long-chain XOS have hypolipemic activity and improve intestinal function (Kihara & Sakata, 2002). Glucuronic acid-containing XOS show animal growth regulating activity and antimicrobial activity (Kontula, von Wright, & Mattila-Sandholm, 1998). In addition, immunopotentiating and apoptosis induction activities were reported for niger- and agaro-oligosaccharides. Likewise, recent observations indicate that the use of GOS/FOS in dietary products might provide an opportunity to stimulate the adaptive immune response in a Th1-direction and subsequently inhibit infections and Th2-related immune disorders in humans, for instance allergies. In addition to its role in autoimmune disorders, galectin-1 also showed immunosuppressive activity in a murine experimental model of graft versus host disease (GVHD) (Kiss et al., 2007). Galectin-1 treatment *in vivo* resulted in reduced inflammatory infiltrates in target tissues and a selective reduction of Th1 cytokines (Cao et al., 2007).

The functional oligosaccharides has been shown to be effective for prevention of cancers and tumors in man (Chen & Fukuda, 2006). Mechanisms by which the functional oligosaccharides could

act against toxicity and carcinogenesis include the reduction of chemical adsorption in relation with physicochemical capacity to bind chemicals, physiologic and mechanical effects to enhance fecal passage and bulking in the gastrointestinal tract (Gibson, 2004; Roberfroid, 2002). Another potential mechanism involves the role of the functional oligosaccharides as a substrate for bacterial fermentation to increase the production of bioactive volatile fatty acids (Messner et al., 1997). This anticarcinogenic effect appears to be related to an increase in cellular immunity, the components of the cell wall and the extra-cellular components of bifidobacteria. Fecal physiological parameters such as pH, ammonia, *p*-cresol, and indole are considered to be risk factors not only for colon cancer development but also for systemic disorders. Over recent decades, the development and consumption of functional probiotic foods has been increasing alongside awareness of their beneficial effects in promoting gut health as well as in disease prevention and therapy, and this has raised interest in health-promoting foods. The contribution of probiotic bacteria, mainly lactobacilli and bifidobacteria, to maintaining or improving microbial balance in the gut is currently under way into their role in reducing the risk of cancer, influencing immunomodulatory features and preventing food allergies, counteracting hypercholesterolemia, and alleviating the symptoms of lactose intolerance. It has been demonstrated in a human study that the intake of transgalactosylated disaccharides reduces the fecal pH as well as ammonia, *p*-cresol and indole concentrations with an increase in bifidobacteria and lactobacilli and a decrease in *Bacteroidaceae* populations (Manning & Gibson, 2004). These alterations may be considered to be beneficial in reducing the risk of cancer development. A low colonic pH may also aid in the excretion of carcinogens. All the effects above mentioned beneficially affect the host health, and for this reason, the functional oligosaccharides are considered as functional food (Crittenden & Playne, 1996; Manning & Gibson, 2004), which can be defined as “a food ingredient which affects physiological function(s) of the body in a targeted way so as to have positive effect(s) which may, in due course, justify health claims” (Sangeetha, Ramesh, & Prapulla, 2005).

7. Effect of the functional oligosaccharides on absorption of different minerals

Several minerals are recognized as having great importance in keeping fit: zinc, copper, selenium, magnesium and iron (Emmett & Rogers, 1997). The functional oligosaccharides and its some derivatives (chitosan) may influence the availability of minerals, such as iron, calcium and magnesium (Bhattarai, Remant, Aryal, Khil, & Kim, 2007; Petit et al., 2006; Somsook et al., 2005). Animal studies have found that dietary chitosan possibly arrests the absorption of calcium (Liao, Shieh, Chang, & Chien, 2007). Calcium is essential to the body. It is the most common mineral in the body and is required for proper functioning of most organs, such as the heart and brain. It is particularly needed in the normal development of the bones and teeth. Osteoporosis is a bone disease where calcium leaves the bones, causing them to weaken. There are many things that help to cause osteoporosis. Not getting enough calcium in the diet is an important one. Fiber should be part of a healthy diet. Fiber is very helpful to the digestive tract, so it is important to balance the level of calcium intake with the amount and type of fiber in the diet. A diet containing up to 35 g of fiber per day should be adequate for healthy bowel movements, without adversely affecting calcium absorption.

8. The functional oligosaccharides reduce cardiovascular risk

Cardiovascular risk is the major public health concern in many countries and accounts for more deaths than any other disease or group of diseases (Perry et al., 2007). Serum lipid abnormalities re-

sult in increasing vascular risks; hence, aggressive treatment of hyperlipidemia is recommended. Advancing age and hypercholesterolemia have been widely considered cardiovascular risk factors in the elderly. Intervention with lipid management is necessary for people with obesity and vascular risks (Bodí et al., 2007). Functional foods are foods or dietary components that can provide a health benefit beyond basic nutrition. The use of the functional oligosaccharides in diet is a part of the management of dyslipidemia (Perry et al., 2007). Optimal intake of the functional oligosaccharides reduces the risk of obesity, blood pressure and many other cardiovascular diseases (Bodí et al., 2007). Studies show that adding certain the functional oligosaccharides sources to mixed test meals at the level of 4–10 g/meal can, to some extent, reduce the postprandial triglyceridemia and cholesterolemia generated by a mixed meal. Sources of soluble viscous cholesterol-lowering fibers (i.e., oat bran) or those with hypotriglyceridemic properties (i.e., concentrated wheat fiber or wheat germ) have been shown to display such an effect postprandially (Herrmann, Ciechanover, Lerman, & Lerman, 2004). In another study, a high-fiber diet (41 g/day) induced lower plasma glucose and insulin peaks compared with a low-functional-oligosaccharides diet (12.4 g/day) at the end of a day-long follow-up, together with a nonsignificant trend to lower diurnal TG levels (Aprikian et al., 2001). A few of the other studies using other sources of the functional oligosaccharides (oat fiber, pea fiber, soybean fiber and psyllium) have also shown these alterations of postprandial lipid parameters. Senn et al. (1992) pointed to the importance of a combination of dietary ingredients in the optimization of decreasing health risk from a cardiovascular risk perspective. The functional oligosaccharides such as β -glucose-oligosaccharides has been shown to have effects on the glycemic, insulin, and cholesterol responses. In 1997, the FDA approved the claim associating the functional oligosaccharides from certain foods and coronary heart disease risk reduction. Other the functional oligosaccharides sources, such as cistanche deserticola, alginate and konjac, have also been reported to decrease serum total cholesterol and low-density lipoprotein cholesterol concentrations (Herrmann et al., 2004).

9. Conclusion

High dietary fat intake, exacerbating postprandial lipemia, altering the overall lipoprotein and blood glucose pattern, has been established and acknowledged as a diabetes, obesity and cardiovascular risk factor. Conversely, digestible and indigestible carbohydrates have been recommended, while a high intake of sugars is generally thought to be detrimental. Unfortunately, in Western countries the high CVD prevalence is largely attributable to the contemporary lifestyle which is often sedentary, and includes a diet high in saturated fat and sugar, and low in $n-3$ PUFAs, fruit, vegetables and fiber. The functional oligosaccharides possess the potential to modulate the gut flora, to affect different gastrointestinal activities, to influence inflammatory processes and to reduce diabetes, obesity and cardiovascular risks.

In this review, we focus on available knowledge on the interactions of the functional oligosaccharides with lipid, lipoprotein, plasma glucose, serum insulin metabolism and their effect on intestinal microflora, diabetes, obesity and cardiovascular risks. Interactions between the functional oligosaccharides and the process of lipid digestion and absorption have been investigated during the last decades, recent studies have shown that dietary carbohydrate moieties (e.g., glucose) can stimulate both the intestinal uptake of cholesterol and lipid resecretion. Growing evidence also clearly indicates that the functional oligosaccharides and their derivatives can reduce risk factors for CVD. Moreover, some large-scale clinical trials in subjects with advanced atheroma confirm the protective effects of the functional oligosaccharides.

In fact, nowadays, the functional oligosaccharides are recognized as important food ingredients to keep and improve our health, and as many consumers depend on processed foods as the mainstay of their diets, the increased the functional oligosaccharides content of popular foods assist consumers in obtaining recommended levels of unavailable carbohydrate.

In conclusion, the results of these *in vivo* biological assays demonstrate that functional oligosaccharides has antioxidant, antimutagenic, antibacterial properties and other pharmacological activities. The functional oligosaccharides may be a good candidate for use in food and pharmacological applications.

References

- Aprikian, O., Levrat-Verny, M.-A., Besson, C., Busserolles, J., Rémésy, C., & Demigné, C. (2001). Apple favourably affects parameters of cholesterol metabolism and of anti-oxidative protection in cholesterol-fed rats. *Food Chemistry*, 75, 445–452.
- Arakane, Y., Zhu, Q. S., Matsumiya, M., Muthukrishnan, S., & Kramer, K. J. (2003). Properties of catalytic, linker and chitin-binding domains of insect chitinase. *Insect Biochemistry and Molecular Biology*, 33, 631–648.
- Arnold, J. N., Dwek, R. A., Rudd, P. M., & Sim, R. B. (2006). Mannan binding lectin and its interaction with immunoglobulins in health and in disease. *Immunology Letters*, 106, 103–110.
- 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 nonrandomized open challenge short-term study. *Nutrition Research*, 23, 1003–1011.
- Bennett, N., Greco, D. S., Peterson, M. E., Kirk, C., Mathes, M., & Fettman, M. J. (2006). Comparison of a low carbohydrate-low fiber diet and a moderate carbohydrate-high fiber diet in the management of feline diabetes mellitus. *Journal of Feline Medicine & Surgery*, 8, 73–84.
- Bhattacharai, S. R., Remant, B. K. C., Aryal, S., Khil, M. S., & Kim, H. Y. (2007). N-Acylated chitosan stabilized iron oxide nanoparticles as a novel nano-matrix and ceramic modification. *Carbohydrate Polymers*, 69, 467–477.
- Bird, A. R., Brown, I. L., & Topping, D. L. (2006). Low and high amylose maize starches acetylated by a commercial or a laboratory process both deliver acetate to the large bowel of rats. *Food Hydrocolloids*, 20, 1135–1140.
- Bodí, V., Sanchis, J., Lopez-Lereu, M. P., Nunez, J., Mainar, L., Pellicer, M., et al. (2007). Evolution of 5 cardiovascular magnetic resonance-derived viability indexes after reperfused myocardial infarction. *American Heart Journal*, 153, 649–655.
- Cao, E. H., Zang, X. X., Ramagopal, U. A., Mukhopadhyaya, A., Fedorov, A., Fedorov, E., et al. (2007). T cell immunoglobulin mucin-3 crystal structure reveals a galectin-9-independent ligand-binding surface. *Immunity*, 26, 311–321.
- Chakraborty, A. K., de Frietas Sousa, J., Chakraborty, D., Funasaka, Y., Bhattacharya, M., Chatterjee, A., et al. (2006). Gnt-V expression and metastatic phenotypes in macrophage-melanoma fusion hybrids is down-regulated by 5-Aza-dC: Evidence for methylation sensitive, extragenic regulation of Gnt-V transcription. *Gene*, 374, 166–173.
- Charalampopoulos, D., Wang, R., Pandiella, S. S., & Webb, C. (2002). Application of cereals and cereal components in functional foods: A review. *International Journal of Food Microbiology*, 79, 131–141.
- Chen, S. H., & Fukuda, M. (2006). Cell type-specific roles of carbohydrates in tumor metastasis. *Methods in Enzymology*, 416, 371–380.
- Chen, H.-L., Lu, Y.-H., Lin, J., & Ko, L.-Y. (2000). Effects of fructooligosaccharide on bowel function and indicators of nutritional status in constipated elderly men. *Nutrition Research*, 20, 1725–1733.
- Chi, A.-P., Chen, J.-P., Wang, Z.-Z., Xiong, Z.-Y., & Li, Q.-X. (2008). Morphological and structural characterization of a polysaccharide from *Gynostemma pentaphyllum* Makino and its anti-exercise fatigue activity. *Carbohydrate Polymers*, 74, 868–874.
- Colecchia, A., Vestito, A., Larocca, A., Pasqui, F., Brandimarte, G., Nikiforaki, A., et al. (2006). Effect of a symbiotic preparation on the clinical manifestations of irritable bowel syndrome, constipation-variant: Results of a multicenter study. *Digestive and Liver Disease*, 38, S86.
- Crittenden, R. G., & Playne, M. J. (1996). Production, properties and applications of food-grade oligosaccharides. *Trends in Food Science & Technology*, 7, 353–361.
- de Alcántara, P. H. N., Martim, L., Silva, C. O., Dietrich, S. M. C., & Buckeridge, M. S. (2006). Purification of a β -galactosidase from cotyledons of *Hymenaea courbaril* L. (Leguminosae). Enzyme properties and biological function. *Plant Physiology and Biochemistry*, 44, 619–627.
- Delmée, E., Cani, P. D., Gual, G., Knauf, C., Burcelin, R., Maton, N., et al. (2006). Relation between colonic proglucagon expression and metabolic response to oligofructose in high fat diet-fed mice. *Life Sciences*, 79, 1007–1013.
- Doi, Y., Ichihara, T., Hagiwara, A., Imai, N., Tamano, S., Orikoshi, H., et al. (2006). A ninety-day oral toxicity study of a new type of processed gum arabic, from *Acacia senegal* exudates, in F344 rats. *Food and Chemical Toxicology*, 44, 560–566.
- Dou, J. L., Xu, Q. S., Tan, C. Y., Wang, W. X., Du, Y. G., Bai, X. F., et al. (2009). Effects of chitosan oligosaccharides on neutrophils from glycogen-induced peritonitis mice model. *Carbohydrate Polymers*, 75, 119–124.
- El-Tahlawy, K., Gaffar, M. A., & El-Rafie, S. (2006). Novel method for preparation of β -cyclodextrin-grafted chitosan and its application. *Carbohydrate Polymers*, 63, 385–392.

- Emmett, P. M., & Rogers, I. S. (1997). Properties of human milk and their relationship with maternal nutrition. *Early Human Development*, 49, S7–S28.
- Fernández-Bañares, F. (2006). Nutritional care of the patient with constipation. *Best Practice & Research Clinical Gastroenterology*, 20, 575–587.
- Giacco, R., Clemente, G., Luongo, D., Lasorella, G., Fiume, I., Brouns, F., et al. (2004). Effects of short-chain fructo-oligosaccharides on glucose and lipid metabolism in mild hypercholesterolaemic individuals. *Clinical Nutrition*, 23, 331–340.
- Gibson, G. R. (2004). Fibre and effects on probiotics (the prebiotic concept). *Clinical Nutrition Supplements*, 1, 25–31.
- Grootaert, C., Delcour, J. A., Courtin, C. M., Broekaert, W. F., Verstraete, W., & de Wiele, T. V. (2007). Microbial metabolism and prebiotic potency of arabinoxylan oligosaccharides in the human intestine. *Trends in Food Science & Technology*, 18, 64–71.
- Harhangi, H. R., Steenbakkers, P. J. M., Akhmanova, A., Jetten, M. S. M., van der Drift, C., & Op den Camp, H. J. M. (2002). A highly expressed family 1 β -glucosidase with transglycosylation capacity from the anaerobic fungus *Pyromyces* sp. E2. *Biochimica et Biophysica Acta (BBA) – Gene Structure and Expression*, 1574, 293–303.
- Herrmann, J., Ciechanover, A., Lerman, L. O., & Lerman, A. (2004). The ubiquitin-proteasome system in cardiovascular diseases – A hypothesis extended. *Cardiovascular Research*, 61, 11–21.
- Huang, Q. L., Zhang, L. N., Cheung, P. C. K., & Tan, X. T. (2006). Evaluation of sulfated α -glucans from *Poria cocos* mycelia as potential antitumor agent. *Carbohydrate Polymers*, 64, 337–344.
- Hussain, A., Claussen, B., Ramachandran, A., & Williams, R. (2007). Prevention of type 2 diabetes: A review. *Diabetes Research and Clinical Practice*, 76, 317–326.
- Jigami, Y., & Odani, T. (1999). Mannosylphosphate transfer to yeast mannan. *Biochimica et Biophysica Acta (BBA) – General Subjects*, 1426, 335–345.
- Juśkiewicz, J., & Zduńczyk, Z. (2002). Lactulose-induced diarrhoea in rats: Effects on caecal development and activities of microbial enzymes. *Comparative Biochemistry and Physiology – Part A: Molecular & Integrative Physiology*, 133, 411–417.
- Kaur, I. P., Chopra, K., & Saini, A. (2002). Probiotics: Potential pharmaceutical applications. *European Journal of Pharmaceutical Sciences*, 15, 1–9.
- Kawamori, R., Kadowaki, T., Onji, M., Seino, Y., & Akanuma, Y. (2007). Hepatic safety profile and glycemic control of pioglitazone in more than 20,000 patients with type 2 diabetes mellitus: Postmarketing surveillance study in Japan. *Diabetes Research and Clinical Practice*, 76, 229–235.
- Kihara, M., & Sakata, T. (2002). Production of short-chain fatty acids and gas from various oligosaccharides by gut microbes of carp (*Cyprinus carpio* L.) in micro-scale batch culture. *Comparative Biochemistry and Physiology – Part A: Molecular & Integrative Physiology*, 132, 333–340.
- Kim, S. H., Lee, S. J., Kang, E. S., Kang, S., Hur, K. Y., Lee, H. J., et al. (2006). Effects of lifestyle modification on metabolic parameters and carotid intima-media thickness in patients with type 2 diabetes mellitus. *Metabolism*, 55, 1053–1059.
- Kim, S.-K., & Rajapakse, N. (2005). Enzymatic production and biological activities of chitosan oligosaccharides (COS): A review. *Carbohydrate Polymers*, 62, 357–368.
- Kiss, J., Kunstár, A., Fajka-Boja, R., Dudics, V., Tóvári, J., Légrádi, Á., et al. (2007). A novel anti-inflammatory function of human galectin-1: Inhibition of hematopoietic progenitor cell mobilization. *Experimental Hematology*, 35, 305–313.
- Kontula, P., von Wright, A., & Mattila-Sandholm, T. (1998). Oat bran β -gluco- and xylo-oligosaccharides as fermentative substrates for lactic acid bacteria. *International Journal of Food Microbiology*, 45, 163–169.
- Kunz, C., & Rudloff, S. (2006). Health promoting aspects of milk oligosaccharides. *International Dairy Journal*, 16, 1341–1346.
- Lekka, M., Laidler, P., Łabędź, M., Kulik, A. J., Lekki, J., Zajac, W., et al. (2006). Specific detection of glycans on a plasma membrane of living cells with atomic force microscopy. *Chemistry & Biology*, 13, 505–512.
- Li, Y.-Q., Fang, L., & Zhang, K.-C. (2007). Structure and bioactivities of a galactose rich extracellular polysaccharide from submergedly cultured *Ganoderma lucidum*. *Carbohydrate Polymers*, 68, 323–328.
- Liao, F.-H., Shieh, M.-J., Chang, N.-C., & Chien, Y.-W. (2007). Chitosan supplementation lowers serum lipids and maintains normal calcium, magnesium, and iron status in hyperlipidemic patients. *Nutrition Research*, 27, 146–151.
- Liebrechts, T., Adam, B., Bredack, C., Röth, A., Heinzel, S., Lester, S., et al. (2007). Immune activation in patients with irritable bowel syndrome. *Gastroenterology*, 132, 913–920.
- Manning, T. S., & Gibson, G. R. (2004). Probiotics. *Best Practice & Research Clinical Gastroenterology*, 18, 287–298.
- Marionneau, S., Cailleau-Thomas, A., Rocher, J., Moullac-Vaidye, B. L., Ruvoën, N., Clément, M., et al. (2001). ABH and Lewis histo-blood group antigens, a model for the meaning of oligosaccharide diversity in the face of a changing world. *Biochimie*, 83, 565–573.
- Matamoros Fernández, L. E. (2007). Introduction to ion trap mass spectrometry: Application to the structural characterization of plant oligosaccharides. *Carbohydrate Polymers*, 68, 797–807.
- Merk, K., Borelli, C., & Christian Korting, H. (2005). Lactobacilli–bacteria–host interactions with special regard to the urogenital tract. *International Journal of Medical Microbiology*, 295, 9–18.
- Messner, P., Allmaier, G., Schäffer, C., Wugeditsch, T., Lortal, S., König, H., et al. (1997). III. Biochemistry of S-layers. *FEMS Microbiology Reviews*, 20, 25–46.
- Mikkelsen, L. L., & Jensen, B. B. (2004). Effect of fructo-oligosaccharides and transgalacto-oligosaccharides on microbial populations and microbial activity in the gastrointestinal tract of piglets post-weaning. *Animal Feed Science and Technology*, 117, 107–119.
- Monchoix, V., Willemot, R.-M., & Monsan, P. (1999). Glucanases: Mechanism of action and structure–function relationships. *FEMS Microbiology Reviews*, 23, 131–151.
- Moro, E. (1900). Morphologische und bakteriologische untersuchungen über die darmbakterien des säuglings: Die bakteriumflora des normalen frauenmilchstuhls. *Jahrbuch Kinderheilkunde*, 61, 686–734.
- Morrow, A. L., Ruiz-Palacios, G. M., Altaye, M., Jiang, X., Lourdes Guerrero, M., Meinen-Derr, J. K., et al. (2004). Human milk oligosaccharides are associated with protection against diarrhea in breast-fed infants. *The Journal of Pediatrics*, 145, 297–303.
- Mountzouris, K. C., Balaskas, C., Fava, F., Tuohy, K. M., Gibson, G. R., & Fegeros, K. (2006). Profiling of composition and metabolic activities of the colonic microflora of growing pigs fed diets supplemented with prebiotic oligosaccharides. *Anaerobe*, 12, 178–185.
- Mourão, J. L., Pinheiro, V., Alves, A., Guedes, C. M., Pinto, L., Saavedra, M. J., et al. (2006). Effect of mannan oligosaccharides on the performance, intestinal morphology and cecal fermentation of fattening rabbits. *Animal Feed Science and Technology*, 126, 107–120.
- Mussatto, S. I., & Mancilha, I. M. (2007a). Non-digestible oligosaccharides: A review. *Carbohydrate Polymers*, 68, 587–597.
- Mussatto, S. I., & Mancilha, I. M. (2007b). Non-digestible oligosaccharides: A review. *Carbohydrate Polymers*, 68, 587–597.
- Muzzarelli, R. A. A. (2009). Chitins and chitosans for the repair of wounded skin, nerve, cartilage and bone. *Carbohydrate Polymers*, 76, 167–182.
- Nabarlatz, D., Ebringerová, A., & Montané, D. (2007). Autohydrolysis of agricultural by-products for the production of xylo-oligosaccharides. *Carbohydrate Polymers*, 69, 20–28.
- Nacos, M. K., Katapodis, P., Pappas, C., Daferera, D., Tarantilis, P. A., Christakopoulos, P., et al. (2006). Kenaf xylan – A source of biologically active acidic oligosaccharides. *Carbohydrate Polymers*, 66, 126–134.
- Nesselhut, T., Rath, W., Grunow, E., Kaufholz, G., Ostermai, U., Cillien, N., et al. (1993). The relationship between urinary Tamm–Horsfall glycoprotein excretion and urinary activity of glycosidases in normal pregnancy and pre-eclampsia. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, 48, 23–31.
- Nezlin, R., & Ghetie, V. (2004). Interactions of immunoglobulins outside the antigen-combining site. *Advances in Immunology*, 82, 155–215.
- Ngo, D.-N., Kim, M.-M., & Kim, S.-K. (2008). Chitin oligosaccharides inhibit oxidative stress in live cells. *Carbohydrate Polymers*, 74, 228–234.
- Ogawa, K., Takeuchi, M., & Nakamura, N. (2005). Immunological effects of partially hydrolyzed arabinoxylan from corn husk in mice. *Bioscience, Biotechnology, and Biochemistry*, 69, 19–25.
- Perry, J. C., D'Almeida, V., Souza, F. G., Schoorlemmer, G. H. M., Colombari, E., & Tufik, S. (2007). Consequences of subchronic and chronic exposure to intermittent hypoxia and sleep deprivation on cardiovascular risk factors in rats. *Respiratory Physiology & Neurobiology*, 156, 250–258.
- Petit, A.-C., Noiret, N., Sinquin, C., Ratskol, J., Guézennec, J., & Colliet-Jouault, S. (2006). Free-radical depolymerization with metallic catalysts of an exopolysaccharide produced by a bacterium isolated from a deep-sea hydrothermal vent polychaete annelid. *Carbohydrate Polymers*, 64, 597–602.
- Qin, C. Q., Li, H. R., Xiao, Q., Liu, Y., Zhu, J. C., & Du, Y. M. (2006). Water-solubility of chitosan and its antimicrobial activity. *Carbohydrate Polymers*, 63, 367–374.
- Rantanen, H., Virkki, L., Tuomainen, P., Kabel, M., Schols, H., & Tenkanen, M. (2007). Preparation of arabinoxyllobiose from rye xylan using family 10 *Aspergillus aculeatus* endo-1,4- β -D-xylanase. *Carbohydrate Polymers*, 68, 350–359.
- Reid, G., Beuerman, D., Heinemann, C., & Bruce, A. W. (2001). Probiotic *Lactobacillus* dose required to restore and maintain a normal vaginal flora. *FEMS Immunology and Medical Microbiology*, 32, 37–41.
- Reis, A., Coimbra, M. A., Domingues, P., Ferrer-Correia, A. J., & Domingues, M. R. M. (2004). Fragmentation pattern of underivatized xylo-oligosaccharides and their alditol derivatives by electrospray tandem mass spectrometry. *Carbohydrate Polymers*, 55, 401–409.
- Rhoades, J., Gibson, G., Formentin, K., Beer, M., & Rastall, R. (2006). Inhibition of the adhesion of enteropathogenic *Escherichia coli* strains to HT-29 cells in culture by chito-oligosaccharides. *Carbohydrate Polymers*, 64, 57–59.
- Rivero-Urgell, M., & Santamaria-Orleans, A. (2001). Oligosaccharides: Application in infant food. *Early Human Development*, 65, S43–S52.
- Roberfroid, M. (2002). Functional food concept and its application to prebiotics. *Digestive and Liver Disease*, 34, S105–S110.
- Rollo, F., Luciani, S., Marota, I., Olivieri, C., & Ermini, L. (2007). Persistence and decay of the intestinal microbiota's DNA in glacier mummies from the Alps. *Journal of Archaeological Science*, 34, 1294–1305.
- Roth, J., Ziak, M., & Zuber, C. (2003). The role of glucosidase II and endomannosidase in glucose trimming of asparagine-linked oligosaccharides. *Biochimie*, 85, 287–294.
- Rousseau, V., Lepargneur, J. P., Roques, C., Remaud-Simeon, M., & Paul, F. (2005). Prebiotic effects of oligosaccharides on selected vaginal lactobacilli and pathogenic microorganisms. *Anaerobe*, 11, 145–153.
- Sangeetha, P. T., Ramesh, M. N., & Prapulla, S. G. (2005). Recent trends in the microbial production, analysis and application of fructooligosaccharides. *Trends in Food Science & Technology*, 16, 442–457.
- Senn, H.-J., Orth, M., Fitzke, E., Köster, W., Wieland, H., & Gerok, W. (1992). Human serum gangliosides in hypercholesterolemia, before and after extracorporeal elimination of LDL. *Atherosclerosis*, 94, 109–117.
- Sharma, R. D. (1985). Hypocholesterolemic effect of gum acacia in men. *Nutrition Research*, 5, 1321–1326.

- Shipley, P. L., Allen, A. D., & Swanson, T. N. (1983). Cointegrate formation between plasmids carrying virulence factor and antibiotic resistance genes in *E. coli*. *FEMS Microbiology Letters*, 20, 365–368.
- Sikka, P., Lall, D., Arora, U., & Sethi, R. K. (2002). Growth and passive immunity in response to micronutrient supplementation in new-born calves of Murrah buffaloes given fat soluble vitamins during late pregnancy. *Livestock Production Science*, 75, 301–311.
- Simon, P. M. (1996). Pharmaceutical oligosaccharides. *Drug Discovery Today*, 1, 522–528.
- Singh, B. (2007). Psyllium as therapeutic and drug delivery agent. *International Journal of Pharmaceutics*, 334, 1–14.
- Somsook, E., Hinsin, D., Buakhrong, P., Teanchai, R., Mophan, N., Pohmakotr, M., et al. (2005). Interactions between iron(III) and sucrose, dextran, or starch in complexes. *Carbohydrate Polymers*, 61, 281–287.
- Sun, X. F., Xu, F., Sun, R. C., Geng, Z. C., Fowler, P., & Baird, M. S. (2005). Characteristics of degraded hemicellulosic polymers obtained from steam exploded wheat straw. *Carbohydrate Polymers*, 60, 15–26.
- Surenjav, U., Zhang, L. N., Xu, X. J., Zhang, X. F., & Zeng, F. B. (2006). Effects of molecular structure on antitumor activities of (1 → 3)- β -D-glucans from different *Lentinus edodes*. *Carbohydrate Polymers*, 63, 97–104.
- Tang, Z.-R., Yin, Y.-L., Nyachoti, C. M., Huang, R.-L., Li, T.-J., Yang, C. B., et al. (2005). Effect of dietary supplementation of chitosan and galacto-mannan-oligosaccharide on serum parameters and the insulin-like growth factor-I mRNA expression in early-weaned piglets. *Domestic Animal Endocrinology*, 28, 430–441.
- Thitaram, S. N., Chung, C.-H., Day, D. F., Hinton, A., Jr, Bailey, J. S., & Siragusa, G. R. (2005). Isomaltooligosaccharide increases cecal bifidobacteria population in young broiler chickens. *Poultry Science*, 84, 998–1003.
- Tosh, S. M., Brummer, Y., Wood, P. J., Wang, Q., & Weisz, J. (2004). Evaluation of structure in the formation of gels by structurally diverse (1 → 3)(1 → 4)- β -D-glucans from four cereal and one lichen species. *Carbohydrate Polymers*, 57, 249–259.
- Vernazza, C. L., Gibson, G. R., & Rastall, R. A. (2005). In vitro fermentation of chitosan derivatives by mixed cultures of human faecal bacteria. *Carbohydrate Polymers*, 60, 539–545.
- Vinderola, G., Matar, C., Palacios, J., & Perdígón, G. (2007). Mucosal immunomodulation by the non-bacterial fraction of milk fermented by *Lactobacillus helveticus* R389. *International Journal of Food Microbiology*, 115, 180–186.
- Xue, S. X., Chen, X. M., Lu, J. X., & Jin, L. Q. (2009). Protective effect of sulfated *Achyranthes bidentata* polysaccharides on streptozotocin-induced oxidative stress in rats. *Carbohydrate Polymers*, 75, 415–419.
- Yang, J. H., Du, Y. M., Huang, R. H., Sun, L. P., Liu, H., Gao, X. H., et al. (2005). Chemical modification and antitumour activity of Chinese lacquer polysaccharide from lac tree *Rhus vernicifera*. *Carbohydrate Polymers*, 59, 101–107.
- Zhang, M., Cheung, P.-C.-K., Chiu, L.-C.-M., Wong, E.-Y.-L., & Ooi, V.-E.-C. (2006). Cell-cycle arrest and apoptosis induction in human breast carcinoma MCF-7 cells by carboxymethylated β -glucan from the mushroom sclerotia of *Pleurotus tuber-regium*. *Carbohydrate Polymers*, 66, 455–462.
- Zhang, C. X., & Huang, K. X. (2005). Characteristic immunostimulation by MAP, a polysaccharide isolated from the mucus of the loach, *Misgurnus anguillicaudatus*. *Carbohydrate Polymers*, 59, 75–82.
- Zhu, X. L., & Lin, Z. B. (2006). Modulation of cytokines production, granzyme B and perforin in murine CIK cells by *Ganoderma lucidum* polysaccharides. *Carbohydrate Polymers*, 63, 188–197.