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The soluble fiber complex PolyGlycopleX lowers serum triglycerides and reduces hepatic steatosis in high-sucrose-fed rats

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Abstract

Viscous soluble fibers have been shown to reduce risk factors associated with type 2 diabetes and cardiovascular disease. The novel functional fiber, PolyGlycopleX (PGX) (InovoBiologic Inc, Calgary, Alberta, Canada) displays greater viscosity than other currently identified soluble fibers. The objective of this study was to determine if PGX lowers serum and hepatic triglycerides (TGs) in a high-sucrose-fed rat model. In this rodent model, feeding a high-sucrose diet consistently increases serum TGs. We hypothesized that consumption of PGX would attenuate hypertriglyceridemia and reduce hepatic steatosis compared with cellulose in rats fed a high-sucrose background diet. Male Sprague-Dawley rats were fed diets containing 65% sucrose and supplemented with either 5% cellulose (control) or 5% PGX (wt/wt) for 43 weeks. At study termination, serum insulin and TGs, hepatic steatosis, and hepatocellular injury were assessed. Body weight increased over time in both groups, but weight gain was attenuated in rats fed PGX vs cellulose in weeks 2 through 22 ($P < .05$). Serum TGs did not differ from baseline for the first half of the study but consistently increased in the cellulose group thereafter. PolyGlycopleX significantly reduced serum TG to near-baseline levels. At study termination, rats fed PGX had significantly lower hepatic steatosis scores (measured by Sudan black staining) compared with rats fed cellulose. Hepatocellular injury scores did not differ between the groups. In conclusion, PGX reduced serum TG and lipid accumulation in the liver of sucrose-fed rats. Further examination of its potential as a fiber supplement aimed at lessening the burden of hepatic steatosis is warranted.

Keywords: Viscous fiber; Hepatic steatosis; Hypertriglyceridemia; Functional fiber; Rat
Abbreviations: ANOVA, analysis of variance; HbA1c, glycated hemoglobin; NAFLD, nonalcoholic fatty liver disease; PGX, PolyGlycoplex; SCFA, short-chain fatty acids; TG, triglyceride.

1. Introduction

The human food supply has changed drastically over the past 50 to 75 years, including increased processed food consumption and reduced dietary fiber content in many regions [1,2]. Evidence from randomized controlled trials

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supports the inclusion of viscous soluble fiber in diets to reduce hemoglobin A1c, fasting and postprandial glycemia, and cardiovascular risk factors [3]. Viscous or soluble dietary fibers have significant hypocholesterolemic effects, although their impact on serum triglycerides (TGs) is less consistent [4]. In rats fed a cholesterol-free diet containing sugar beet fiber, serum TGs were reduced 58% compared with a control diet [5], whereas a blend of guar gum, psyllium, and pectin lowered serum TGs by 22% in guinea pigs [6]. In humans, soluble fiber-enriched diets based on barley or inulin significantly reduced serum TGs in hypercholesterolemic men and women [7] and healthy young subjects [8], respectively. Psyllium fiber, on the other hand, appears to exert significant hypocholesterolemic effects without changing serum TGs [4].

In addition to solubility, viscosity also contributes to the physiologic effects of dietary fiber via decreases in the diffusion of nutrients. This is accomplished by reduced contact between food and digestive enzymes, altered contractile movements, slowed gastric emptying, and a thickening of the unstirred water layer through which glucose and cholesterol diffuse in the lumen [9]. PolyGlycopleX (PGX) [(α-D-glucurono-α-D-manno-β-D-manno-β-D-gluco), (α-L-gulurono-β-D mannurono), β-D-gluco-β-D-mannan [10,11]; InovoBiologic, Inc, Calgary, Alberta, Canada] is a novel functional fiber complex manufactured by a proprietary process (EnviroSimplex; InovoBiologic Inc., Calgary, AB, Canada) from 3 dietary polysaccharide powders (konjac glucomannan, xanthan gum, and sodium alginate). The resulting product has a level of viscosity that is higher than any currently known polysaccharide and is well tolerated by rodents [12] and man [13]. Recent examination of the rheological characteristics of PGX showed that the interaction between konjac glucomannan-xanthan gum complex and sodium alginate forms a new, ternary complex [10,11] that may explain in part the products high viscosity. Given the growing interest in functional foods and, particularly, in mixed food–grade polysaccharides, the examination of the effects of PGX on aspects of metabolic health is warranted.

Nonalcoholic fatty liver disease (NAFLD), an umbrella term for a spectrum of diseases involving hepatic fat accumulation, is rapidly increasing in prevalence alongside the increased prevalence of obesity worldwide [14]. Treatment options are currently limited, but there is the potential for viscous dietary fiber to reduce the burden of this disease. Experimentally, long-term, high-sucrose feeding in rats has been shown to variably cause weight gain and consistently cause elevated serum TG levels [15-17]. We hypothesize that consumption of PGX will attenuate hypertriglyceridemia and reduce hepatic steatosis compared with cellulose in rats fed a high-sucrose background diet. The specific objective of this study was to determine if the highly viscous, functional fiber PGX reduces body weight, serum TGs, and hepatic lipid accumulation in sucrose-fed Sprague-Dawley rats, a model that consistently displays elevations in serum TGs.

2. Methods and materials

2.1. Experimental design

The study was approved by the Eurofins (Dayton, NJ) institutional animal use and care committee and conformed to the *Guide for the Care and Use of Laboratory Animals*. Twenty male Sprague-Dawley rats were housed in a temperature- and humidity-controlled room with a 12-hour light-dark cycle and fed a basic rat chow (D11725; Research Diets, New Brunswick, NJ) formulated to contain 65% (wt/wt) sucrose (Table 1). The rats were divided into 2 groups that consumed ad libitum the background high-sucrose diet with either cellulose at 5% (wt/wt) or PGX at 5% (wt/wt) (n = 10 per group). PolyGlycopleX is a novel, soluble, highly viscous polysaccharide (functional fiber) complex, whereas cellulose is an insoluble reference fiber (Research Diets). Cellulose is widely used as a control fiber that is insoluble and nonfermentable [20,21]. The diets were formulated to be near isoenergetic with the cellulose diet providing 16.3 kJ/g and the PGX diet providing 16.7 kJ/g [22]. The animals were fed the diets for 43 weeks. Body weight was measured weekly, and food consumption was measured daily by weighing each food cup to the nearest 0.1 g and subtracting this weight from the previously measured weight.

2.2. Serum TGs and insulin and blood glucose

Once each week in the morning, blood was collected via retroorbital bleed in the fasted (overnight) state. Because of the higher volume of blood required to perform the subsequent analysis (approximately 250 μL), retroorbital bleeding was selected over other methods such as serial tail bleeding. A small quantity of blood was immediately analyzed for blood glucose concentration with an Acensia Elite Glucometer, Toronto, ON, Canada. The remainder of the blood was allowed to clot, and the serum was analyzed

Table 1
Experimental diet composition (g/100g)

	PGX diet	Cellulose diet
Casein	20	20
Methionine	0.3	0.3
Sucrose	65	65
Fiber	5 PGX	5 cellulose
Corn oil	5	5
Salt/mineral mix	3.5	3.5
Vitamin mix	1	1
Choline bitartrate	0.2	0.2
Dye	0.1	0.1
Energy density (kcal/g)	3.98	3.90

PolyGlycopleX was shipped to Research Diets (New Brunswick) for incorporation into rat chow (D11725). The macronutrient energy contribution of the diets was 68% for carbohydrate, 21% for protein, and 12% for fat. Energy density of the diets was calculated from typical energy densities of the ingredients provided by Research Diets. Similar to other fermentable fibers, an energy value of 1.5 kcal/g was used for PGX [18]. The vitamin and mineral mixes were those used in the standard AIN-93M diet formulation [19].

for insulin and TG. Serum TG analysis was conducted at IDEXX Laboratories (North Grafton, Mass) using a colorimetric method. Serum insulin was measured with a radioimmunoassay kit from Anilytics, Gaithersburg, Md.

2.3. Terminal measurements

At the end of the study, blood was drawn for glycated hemoglobin (HbA1c), which reflects average plasma glucose concentration over prolonged periods. Glycated hemoglobin measures were performed in-house using the Bayer DCA 2000+ System (Tarrytown, NY). Rats were euthanized via CO_2 inhalation. At necropsy, fat was removed from the abdominal viscera (not including the urogenital viscera) and weighed. One liver lobe was snap frozen and stained for lipid content using 5-μm sections and staining with Sudan black for free fatty acids and TG content. The liver slides were evaluated and graded semiquantitatively for presence of Sudan black–positive vacuoles on a scale of 0 to 5 (Histo-Scientific Research Laboratories, Mt Jackson, Va). Five on the scale indicates greater steatosis. Another liver lobe was fixed in formalin for hematoxylin and eosin staining to determine hepatocellular injury. Injury severity was scored based on a scale of 0 to 5, where 0 indicates the absence of injury and 5 indicates severe injury.

2.4. Statistical analyses

Data with multiple measures over time such as body weight were analyzed using repeated-measures analysis of

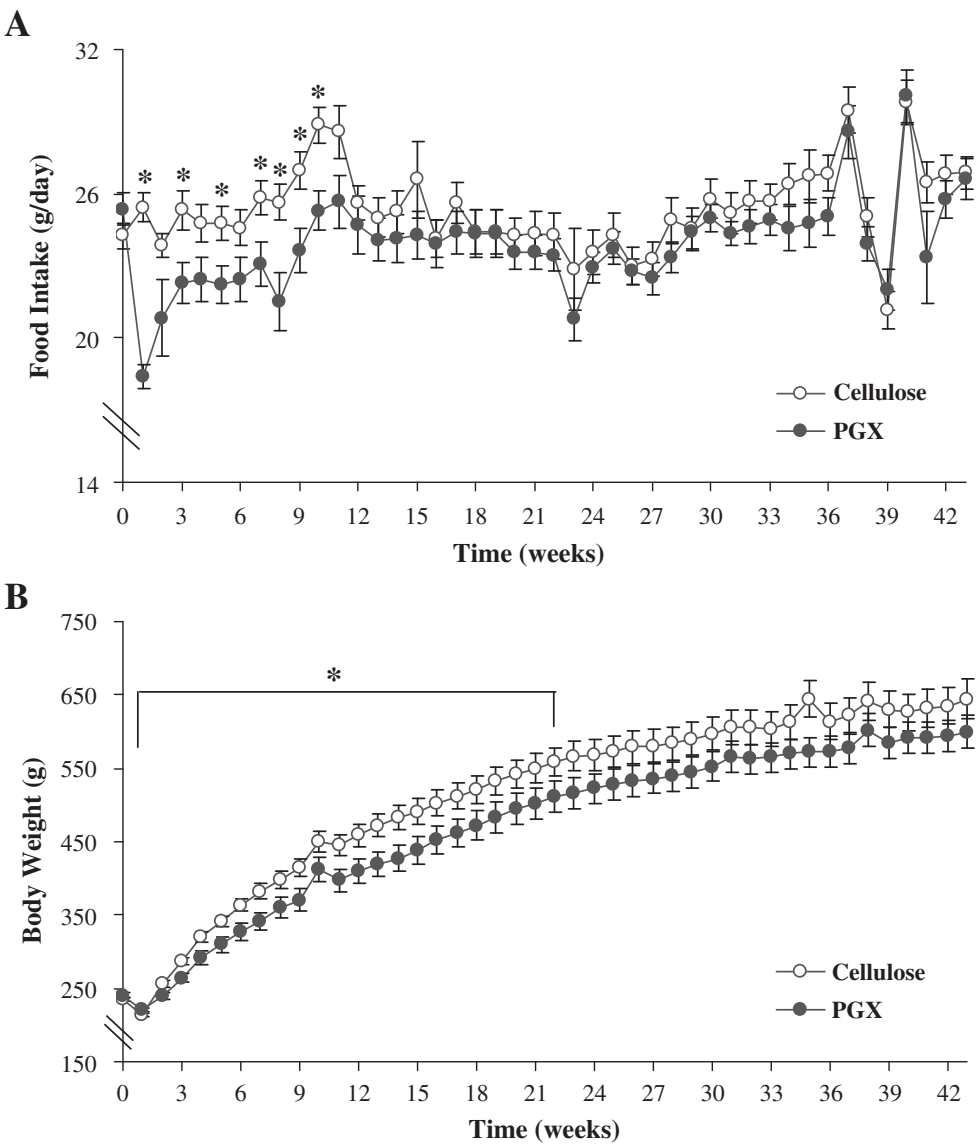

Fig. 1. Longitudinal food consumption and body weight in rats fed the PGX- or cellulose-containing high-sucrose diet for 43 weeks. A, Weekly food consumption. B, Weekly body weight. Data are expressed as mean ± SE; n = 10. The ∗ represents a significant difference between PGX and cellulose (ANOVA, $P < .05$).

Table 2
Glycated hemoglobin, fat mass, and liver effects in rats fed a PGX- or cellulose-containing sucrose diet for 43 weeks

	PGX diet	Cellulose diet
HbA1c (%)	3.35 ± 0.04	3.31 ± 0.05
Visceral fat mass	18.3 ± 2.3	25.4 ± 3.2
Hepatic steatosis	2.7 ± 0.4 [a]	3.9 ± 0.3
Hepatocyte vacuolation (microvesicular)	2.7 ± 0.4	3.5 ± 0.3
Hepatocyte vacuolation (macrovesicular)	0.8 ± 0.3	1.7 ± 0.5

Data are expressed as mean ± SE; n = 10. Measurements were made at study termination. Visceral fat mass did not include genital fat mass.

[a] Represents a significant difference between PGX and cellulose (ANOVA, P <.05).

variance (ANOVA) with time and diet as the main effects. Differences between groups for parameters with single measures were analyzed by 1-way ANOVA. Histology scores were measured using Kruskal-Wallis test for nonparametric data.

3. Results

3.1. Food intake and weight gain

The interaction between time and diet was significant for food consumption (P < .001), wherein rats fed PGX had lower food intake at most time points between weeks 1 and 10 compared with cellulose (P < .05; Fig. 1A). Initial body weight did not differ between the 2 groups (214.7 ± 2.6 and 220.8 ± 3.5 g for cellulose and PGX, respectively). Consumption of the high-sucrose diet was associated with increased body weight in both groups over time; however, weight gain was significantly attenuated in the rats fed PGX compared with cellulose from initiation until week 22 (P < .05) (Fig. 1B). The difference in final body weight between the groups was not significantly different (P = .20; 599.5 ± 22.0 vs 644.8 ± 26.2 g for PGX and cellulose, respectively); nevertheless, the rats fed PGX maintained an approximately 7% lower body weight at study termination. The 28% lower visceral (nongenital) fat mass in PGX-fed rats was not significantly different from cellulose (P = .09; Table 2).

3.2. Blood and serum measures

Serum TG concentrations were stable during the early part of the study but steadily increased with time in the cellulose-treated group (Fig. 2). The group treated with PGX showed significantly lower serum TGs vs the cellulose-fed group at weeks 22 and 38 (P < .01 and P < .05, respectively). At the end of the study, serum TG levels in the PGX-fed group did not differ from their baseline levels. Fasted blood glucose and insulin levels did not differ between the groups throughout the study. Homeostatic model assessment of insulin resistance scores, an indication of the degree of insulin resistance, rose over time (P < .001) but did not differ between diet groups. Glycated hemoglobin values were in the low end of the reference range for rats and did not differ between groups (Table 2).

3.3. Sudan black staining and hepatic damage

Rats fed PGX-containing diet showed less hepatic steatosis (measured by Sudan black staining) than rats fed cellulose (P < .05; Table 2). On a scale of 0 (pathology absent) to 5 (severe), rats fed a PGX-containing diet had significantly lower average scores. Hepatocellular injury was reduced by PGX, although significance was not obtained (P < .07 for macrovesiclar vacuolation and P < .11 for microvesicular vacuolation) (Table 2).

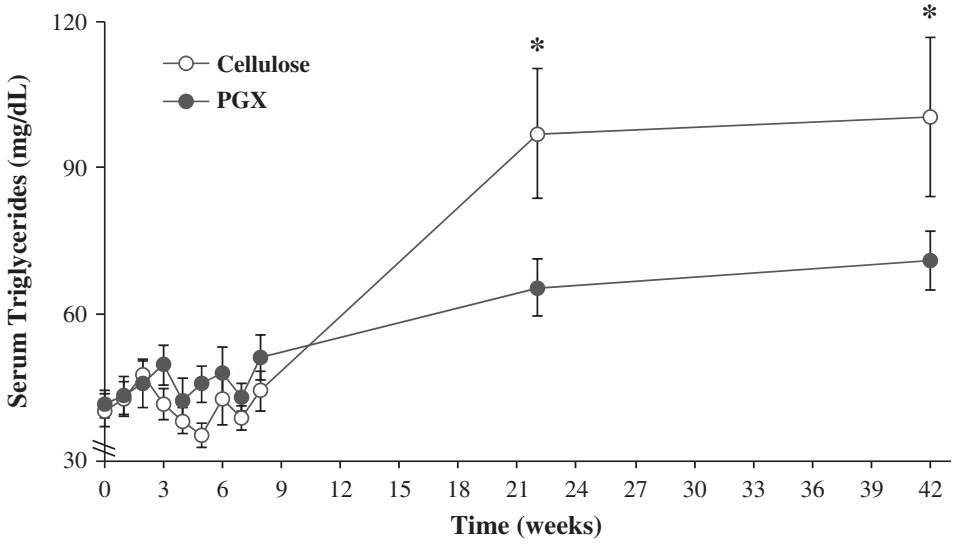

Fig. 2. Terminal serum TGs in rats fed the PGX- or cellulose-containing high-sucrose diet. Data are expressed as mean ± SE; n = 10. The * represents a significant difference between PGX and cellulose (ANOVA, P <.05).

4. Discussion

Unique chemical and physical properties of dietary fibers allow them to elicit distinct physiologic responses [9]. We used the high-sucrose-fed rat model to induce elevated serum TGs and then evaluated the potential for the novel functional fiber PGX to mitigate the hypertriglyceridemic effects of the sucrose diet. We accept our hypothesis that consumption of PGX is associated with attenuated sucrose-induced hypertriglyceridemia and reduced hepatic steatosis compared with cellulose in rats fed a high-sucrose background diet.

Epidemiological studies support the relationship between increased dietary fiber intake and protection against obesity [4]. In rats, the soluble but relatively noviscous fibers, inulin and oligofructose, have been shown to reduce body weight and fat mass in normal and diet-induced obese models [23-25]. Increases in gut satiety hormones and delays in gastric emptying are thought to contribute to the weight-reducing effects of these and other fibers [4,24]. PolyGlycopleX has a level of viscosity that is higher than any currently known polysaccharide, a characteristic that likely contributes to changes in gastric emptying and sensations of fullness. Rats fed the PGX-containing diet in this study had significantly lower food intake in the first 10 weeks of the study. Although the differences in food intake after that time were no longer significantly different, it is possible that the initial lower food intake contributed to sustained lower body weight; and the combined effect of these changes influenced lipid metabolism thereafter. This differs from the increase in body weight that we observed with PGX consumption in the Zucker diabetic rat (ZDF/Crl-Lepr$^{fa/fa}$) [22]. Although PGX was associated with reduced food intake in Zucker rats, there was no associated decrease in body weight; the reasons for which remain unexplained. Similar findings of reduced energy intake in the absence of weight loss have been noted in another monogenic model of leptin receptor defect, the JCR:LA cp rat, which may indicate a compromised ability of these animals to respond in a typical manner to reductions in energy intake induced by the fiber.

Although the hypocholesterolemic effects of soluble viscous dietary fibers are well established, the hypotriglyceridemic effects are less consistent. Soluble fibers reduce dietary fat and cholesterol uptake in the intestine in part by thickening the unstirred water layer that cholesterol diffuses, though [26,27]. Furthermore, they interfere with the enterohepatic circulation of bile acids, thereby increasing the fecal loss of bile acids [28]. The TG-lowering effects of soluble fibers appear less consistent and, in some cases, less robust. For example, barley-derived soluble fiber was found to reduce TGs in 8 trials involving 391 healthy and hypercholesterolemic patients [7]; and insulin-enriched pasta significantly reduced TGs in young healthy subjects [8]. For other soluble fibers including psyllium, oat bran, and guar gum, reductions in cholesterol occur without significant changes in serum TGs [29]. However, reductions in hepatic TG can occur independently of marked reductions in serum TGs [30] and, thereby, still provide some metabolic advantage.

Daubioul et al [30] demonstrated that the soluble and highly fermentable fiber, Synergy 1 (BENEO-Orafti, Tienen, Belgium), a blend of inulin and oligofructose, lowered body weight and reduced TG accumulation in the liver as measured by nuclear magnetic resonance spectroscopy. There were no changes in serum TGs between Synergy 1 and the cellulose-treated group, but hepatocytes isolated from the rats fed the prebiotic fiber synthesized less TG. This finding was largely associated with propionate production, one of the chief short chain fatty acids (SCFAs), that results from the fermentation of dietary fiber. In our rats fed PGX, there was a significant reduction in hepatic steatosis that could be related to the production of SCFAs, although this was not specifically measured. In humans, we have recently shown significantly higher fecal SCFA concentrations in subjects consuming PGX vs placebo for 3 weeks, suggesting that fermentation of PGX may contribute to its ability to reduce hepatic and serum TGs (unpublished data). Many of the metabolic effects of fermentable dietary fibers are mediated via SCFA production, and the future examination of the impact of PGX® on this pathway is warranted.

In the genetically obese JCR:LA cp rat, we have previously demonstrated a 42% decrease in liver TGs in rats fed a blend of the prebiotic fibers, inulin, and oligofructose [31]. This decrease in liver TGs occurred in the absence of any reductions in fatty acid synthase messenger RNA levels, a key enzyme in fatty acid synthesis in the liver. A possible explanation for these seemingly disparate findings is that the prebiotics caused a significant bulking effect in the cecum that likely contributed to greater TG excretion from the intestine [31]. Given the highly viscous nature of PGX, it is plausible that increased TG excretion could contribute to its TG-lowering effects, although this remains to be tested.

Certain limitations of the study exist. Because of constraints on tissue use for histologic examinations, we were unable to perform real-time polymerase chain reaction to examine the messenger RNA levels of genes involved in hepatic fatty acid and cholesterol metabolism. Future studies would also benefit from the analysis of cecal and fecal matter to determine whether differences in fermentation and production of SCFA account for some of the observed differences in lipid metabolism in this model. Determination of fecal TG content would further help in elucidating the intestinal luminal properties of PGX and the potential for greater TG excretion.

Nonalcoholic fatty liver disease is the most common chronic liver disorder in the United States and is rapidly becoming a major risk factor associated with obesity [32]. The hallmark feature of NAFLD is the accumulation of TGs in the liver. Our data suggest that PGX, a highly viscous and soluble fiber, is one polysaccharide that warrants further investigation for its potential to reduce not only serum TGs but also attenuate the accumulation of TGs in the liver.

In conclusion, this study demonstrates that PGX is associated with a reduction in serum TGs and hepatic steatosis in a high-sucrose-fed rat model. Given the growing prevalence of metabolic disease in many Western countries, the findings of this study are promising and need to be further explored in other rodent models of metabolic disease and ultimately in human clinical studies. The mechanisms responsible for these TG-lowering effects are not currently known but may be related to the high viscosity of the product attributed to its ternary complex or, perhaps, the fermentation of the fiber and subsequent production of SCFAs.

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GJG and LK received funding from InovoBiologic, Inc, to perform this study and have no financial interest in PGX. RJG is the owner of the Factors Group of Companies, which retains an interest in PGX. MRL receives consulting fees from the Factors Group of Companies, and SW and RAR receive consulting fees from InovoBiologic, Inc. PolyGlycopleX, PGX, and EnviroSimplex are all trademarks of InovoBiologic Inc.

References

[1] Eaton SB, Eaton III SB. Paleolithic vs. modern diets—selected pathophysiological implications. Eur J Nutr 2000;39:67-70.
[2] Gilbert PA, Khokhar S. Changing dietary habits of ethnic groups in Europe and implications for health. Nutr Rev 2008;66:203-15.
[3] Vuksan V, Rogovik AL, Jovanovski E, Jenkins AL. Fiber facts: benefits and recommendations for individuals with type 2 diabetes. Curr Diabetes Rep 2009;9:405-11.
[4] Anderson JW, Baird P, Davis RH, Ferreri S, Knudston M, Koraym A, et al. Health benefits of dietary fiber. Nutr Rev 2009;67:188-205.
[5] Nakamura Y, Kanazawa M, Liyanage R, Ilijima S, Han KH, Shimada K, Sekikawa M, Yamauchi A, Hashimoto N, et al. Effect of white wheat bread containing sugar beet fiber on serum lipids and hepatic mRNA in rats fed on a cholesterol-free diet. Biosci Biotechnol Biochem 2009;73:1280-5.
[6] Roy S, Vega-Lopez S, Fernandez ML. Gender and hormonal status affect the hypolipidemic mechanisms of dietary soluble fiber in guinea pigs. J Nutr 2000;130:600-7.
[7] Talati R, Baker WL, Pabilonia MS, White CM, Coleman CI. The effects of barley-derived soluble fibers on serum lipids. Ann Fam Med 2009;7:157-63.
[8] Russo F, Riezzo G, Chiloiro M, De Michele G, Chimienti G, Marconi E, et al. Metabolic effects of a diet with inulin-enriched pasta in healthy young volunteers. Curr Pharm Des 2010;16:825-31.
[9] Dikeman CL, Fahey GC. Viscosity as related to dietary fiber: a review. Crit Rev Food Sci Nutr 2006;46:649-63.
[10] Abdelhameed AS, Ang A, Morris GA, Smith I, Lawson C, Gahler R, et al. An analytical ultracentrifuge study on ternary mixtures of konjac glucomannan supplemented with sodium alginate and xanthan gum. Carbohydr Polym 2010;81:145-8.
[11] Harding SE, Smith IH, Lawson CJ, Gahler RJ, Wood S. Studies on macromolecular interactions in ternary mixtures of konjac glucomannan, xanthan gum and sodium alginate. Carbohydr Polym 2011;83:329-38.
[12] Matulka RA, Lyon MR, Wood S, Marone PA, Merkel DJ, Burdock GA. The safety of PolyGlycopleX (PGX) as shown in a 90-day rodent feeding study. Nutr J 2009;8:1-11.
[13] Carabin IG, Lyon MR, Wood S, Pelletier X, Donazzolo Y, Burdock GA. Supplementation of the diet with the functional fiber PolyGlycopleX is well tolerated by healthy subjects in a clinical trial. Nutr J 2009;8:1-11.
[14] Preiss D, Sattar N. Non-alcoholic fatty liver disease: an overview of prevalence, diagnosis, pathogenesis and treatment considerations. Clin Sci (Lond) 2008;115:141-50.
[15] Reaven GM, Ho H. Sugar-induced hypertension in Sprague-Dawley rats. Am J Hypertens 1991;4(7 Pt 1):610-4.
[16] Banos G, Carvajal K, Cardoso G, Zamora J, Franco M. Vascular reactivity and effects on serum in a rat model of hypertension and hypertriglyceridemia. Am J Hypertens 1997;10:379-88.
[17] Lomba A, Milagro FI, Garcia-Diaz DF, Campion J, Marzo F, Martinez JA. A high-sucrose isocaloric pair-fed model induces obesity and impairs NDUFB6 gene function in rat adipose tissue. J Nutrigenet Nutrigenomics 2009;2:267-72.
[18] Roberfroid M. Caloric value of inulin and oligofructose. J Nutr 1999;129:1436S-7S.
[19] Reeves PG, Nielsen FH, Fahey Jr GC. AIN-93 purified diets for laboratory rodents: final report of the American Institute of Nutrition ad hoc writing committee on the reformulation of the AIN-76A rodent diet. J Nutr 1993;123:1939-51.
[20] McAllister TA, Bae HD, Jones GA, Cheng KJ. Microbial attachment and feed digestion in the rumen. J Anim Sci 1994;72:3004-18.
[21] Reimer RA, Russell JC. Glucose tolerance, lipids and GLP-1 secretion in JCR:LA-cp rats fed a high protein fiber diet. Obesity 2008;16:40-6.
[22] Grover GJ, Koetzner L, Wicks J, Gahler RJ, Lyon MR, Reimer RA, et al. Effects of the soluble fiber complex PolyGlycopleX (PGX) on glycemic control, insulin secretion, and GLP-1 levels in Zucker diabetic rats. Life Sci 2011;88:392-9.
[23] Maurer AD, Eller LK, Hallam MC, Taylor K, Reimer RA. Consumption of diets high in prebiotic fiber or protein during growth influences the response to a high fat and sucrose diet in adulthood in rats. Nutr Metab 2011;7:77.
[24] Cani PD, Knauf C, Iglesias MA, Drucker DJ, Delzenne NM, Burcelin R. Improvement of glucose tolerance and hepatic insulin sensitivity by oligofructose requires a functional glucagon-like peptide-1 receptor. Diabetes 2006;55:1484-90.
[25] Delmee E, Cani PD, Gual G, Knauf C, Burcelin R, Maton N, et al. Relation between colonic proglucagon expression and metabolic response to oligofructose in high fat diet-fed mice. Life Sci 2006;79:1007-13.
[26] Schneeman BO. Fiber, inulin and oligofructose: similarities and differences. J Nutr 1999;129:1424S-7S.
[27] Edwards CA, Johnson IT, Read NW. Do viscous polysaccharides slow absorption by inhibiting diffusion or convection? Eur J Nutr 1988;42:307-12.
[28] Rideout TC, Harding SV, Jones PJH, Fan MZ. Guar gum and similar soluble fibers in the regulation of cholesterol metabolism: current understandings and future research priorities. Vasc Health Risk Manag 2008;4:1023-33.
[29] Slavin JL, Savarino V, Paredes-Diaz A, Fotopoulos G. A review of the role of soluble fiber in health with specific reference to wheat dextrin. J Int Med Res 2009;37:1-7.
[30] Daubioul C, Rousseau N, Demeure R, Gallez B, Taper HS, Declerck B, et al. Dietary fructans, but not cellulose, decrease triglyceride accumulation in the liver of obese Zucker fa/fa rats. J Nutr 2002;132:967-73.
[31] Parnell JA, Reimer RA. Effect of prebiotic fiber supplementation on hepatic gene expression and serum lipids: a dose-response study in JCR: LA-cp rats. Br J Nutr 2009;103:1577-84.
[32] Targher G, Bertolini L, Padovani R, Rodella S, Zoppini G, Pichiri I, et al. Prevalence of non-alcoholic fatty liver disease and its association with cardiovascular disease in patients with type 1 diabetes. J Hepatol 2010;53:713-8.