NUTRIOSE dietary fiber supplementation improves insulin resistance and determinants of metabolic syndrome in overweight men: a double-blind, randomized, placebo-controlled study

Shuguang Li, Laetitia Guerin-Deremaux, Marine Pochat, Daniel Wils, Cheryl Reifer, and Larry E. Miller

Abstract: The influence of dietary fiber on determinants of metabolic syndrome is controversial. The objective of this study was to determine the effects of NUTRIOSE supplementation on insulin resistance and the determinants of metabolic syndrome in overweight men. In this double-blind, randomized, placebo-controlled study, we supplemented the diets of overweight Chinese men with 250 mL of fruit juice that contained NUTRIOSE (Test group: n = 60, age = 30.4 ± 4.3 years, body mass index (BMI) = 24.5 ± 0.2 kg·m⁻²) or a maltodextrin placebo (Control group: n = 60, age = 31.6 ± 4.1 years, BMI = 24.5 ± 0.3 kg·m⁻²) at a dosage of 17 g twice daily for 12 weeks. Daily caloric intake, body composition, blood chemistry, and blood pressure were evaluated every 4 weeks during the trial. Test subjects consumed fewer calories per day and had greater reductions in body weight, BMI, body fat percentage, and waist circumference than Control subjects. All markers of glucose metabolism improved in the Test group, with increases in adiponectin and reductions in glucose, insulin, homeostasis model assessment-estimated insulin resistance, glycated hemoglobin, and glycated albumin (all p < 0.01). Similarly, all lipid measures improved with increases in high-density lipoprotein cholesterol and reductions in total cholesterol, low-density lipoprotein cholesterol, very low-density lipoprotein cholesterol, and triglycerides (all p < 0.01). No changes were observed in systolic blood pressure between groups. Most components of glucose metabolism and the lipid profile were significantly better in the Test than in the Control subjects. No adverse events or gastrointestinal complaints were reported in either group. Supplementation with NUTRIOSE for 12 weeks is well tolerated, lowers insulin resistance, and improves determinants of metabolic syndrome in overweight men.

Key words: cholesterol, dietary supplement, fiber, glucose, insulin resistance, metabolic syndrome, men, randomized.

Résumé: On ne s’entend pas sur l’influence des fibres alimentaires sur les déterminants du syndrome métabolique. Cette étude se propose d’analyser les effets de la supplémentation en NUTRIOSE sur l’insulinorésistance et sur les variables du syndrome métabolique chez des hommes présentant un surpoids. Dans cette étude à double insu avec répartition aléatoire et la présence de groupes de contrôle, on a ajouté au régime de Chinois présentant un surpoids 250 mL de jus de fruit contenant 17 g de NUTRIOSE (Test : n = 60, âge = 30.4 ± 4.3 ans, IMC = 24.5 ± 0.2 kg·m⁻²) ou 17 g de maltodextrine (Contrôle : n = 60, âge = 31.6 ± 4.1 ans, IMC = 24.5 ± 0.3 kg·m⁻²), et ce, deux fois par jour durant 12 semaines. Toutes les quatre semaines de cet essai, on évalue l’énergie à jour, la composition corporelle, la chimie du sang et la pression sanguine. Comparativement aux sujets du groupe de contrôle, les sujets du groupe Test consomment moins de calories chaque jour, présentent une plus grande perte de poids et une plus grande diminution de l’IMC, du pourcentage de gras et du tour de taille. Chez les sujets du groupe Test, on observe une amélioration de la concentration des marqueurs du métabolisme du glucose: une augmentation d’adiponectine et une réduction de glucose, d’insuline, de résistance à l’insuline selon l’indice HOMA, d’hémoglobine glycosylée et d’albumine glyquée (p < 0.01 pour toutes). Aussi, toutes les variables lipidiques s’améliorent: augmentation du HDL-cholestérol et diminution du cholestérol total, du LDL-cholestérol, du VLDL-cholestérol et des triglycérides (p < 0.01 pour toutes). On n’observe pas de modification de la pression systolique dans les groupes. Quand on compare les résultats du groupe Test à ceux du groupe de contrôle, on observe une amélioration significative de la plupart des variables du métabolisme du glucose et du profil lipidique. Dans tous les groupes, on ne rapporte aucune plainte de troubles gastro-intestinaux ou autres. La supplémentation en NUTRIOSE sur une période de 12 semaines est bien tolérée, diminue l’insulinorésistance et améliore les variables du syndrome métabolique chez des hommes présentant un surpoids.

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Introduction

Obesity, hypertension, dyslipidemia, and dysglycemia are associated with a higher risk for many chronic diseases, such as coronary heart disease, peripheral artery disease, cancer, and diabetes (Fujishima et al. 1996; Hanley et al. 2002; Carr and Brunzell 2004; Reaven et al. 2004). Despite ongoing research on the impact of diet, lifestyle, and pharmacological approaches for treating these diseases and their risk factors, the prevalence of these chronic diseases, nonetheless, continues to rise (Levesque and Lamarche 2008). Risk factors for chronic disease are rarely diagnosed alone, but tend to present in clusters because of the complex metabolite relationships. The term metabolic syndrome has been used to describe the presence of at least 3 of the following 5 risk factors: elevated waist circumference, elevated triglyceride levels, reduced high-density lipoprotein cholesterol (HDL-C), elevated blood pressure, and elevated fasting glucose levels (Alberti et al. 2009). Patients with metabolic syndrome have twice the risk of developing cardiovascular disease over the next 10 years and have a 5-fold risk of developing diabetes mellitus (Alberti et al. 2009). Although preventative measures, such as physical activity (O’Gorman and Krook 2008; Kujala 2009; Misogij-Duraković and Duraković 2009) and dietary modification (Babio et al. 2009; Hill et al. 2009; Jew et al. 2009), are somewhat effective in the prevention of metabolic syndrome, compliance with these lifestyle factors is generally low (Newell et al. 2000; Shephard 2001; Kirk and De Feo 2007; Marzolini et al. 2009). There is an obvious need for alternative approaches that effectively lower disease risk, yet are easily implemented by the general public.

Dietary fiber, especially soluble fiber, has been reported to have distinct lipid-lowering effects. Every 3 g of fiber consumed per day is associated with a 0.13 mmol-L⁻¹ decrease in total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) levels (Brown et al. 1999). Furthermore, every 10 g of fiber included in the diet each day lowers the risk of coronary events by 14% and lowers the risk for coronary death by 27% (Pereira et al. 2004). However, several randomized studies have reported no effect of fiber on lipid levels (Abbasi et al. 2000; Lovegrove et al. 2000). Furthermore, there is generally no effect of fiber on triglycerides (Brown et al. 1999), and HDL-C levels often remain the same or slightly decreased (Hunninghake et al. 1994; Brown et al. 1999). Equivocal findings of fiber’s effects on fasting glucose levels (Davy et al. 2002; Ylönén et al. 2003) and insulin sensitivity (Ludwig et al. 1999; Ylönén et al. 2003; McKeown et al. 2004) have also been reported. The effects of fiber on blood pressure (Davy and Melby 2003) and waist circumference (Wood et al. 2007) are largely nonexistent.

The question of fiber’s effectiveness is further complicated by the different fiber types, dosages, and length of supplementation that has been used across clinical studies. Although most people do not consume adequate amounts of fiber (Park et al. 2005), the addition of fiber supplements to the diet, which are combined with typical foods, may yield better compliance rates while still offering similar health benefits (Anderson et al. 2009).

Wheat dextrin is a type of soluble fiber with distinct health benefits, including regulation of the digestive system, improved micronutrient absorption, and prevention of gastrointestinal disorders (Slavin et al. 2009). Dextrins are starch polymers derived through solid-state heating from partially hydrolyzed starch. The process of dextrinification yields a soluble polysaccharide that is resistant to digestion and has a low viscosity, which helps with incorporation into liquids and soft foods (Truhaut et al. 1962). Although soluble fibers, such as wheat dextrin, are effective in lowering fasting glucose levels in type 2 diabetics (Anderson et al. 2004) and TC levels in subjects with hyperlipidemia (Brown et al. 1999), the effects on people without major underlying health problems are debatable. In fact, a meta-analysis by Brown and colleagues (1999) suggested that increasing soluble fiber intake has little impact on TC levels. We, therefore, designed this study to overcome the limitations of many previous trials of fiber supplementation by using a double-blind, randomized, placebo-controlled design and a 12-week supplementation period, and by measuring a comprehensive set of glucose and lipid metabolism markers.

The purpose of this study was to determine the effects of a soluble dextrin dietary fiber supplement (NUTROISE, Roquette Frères, Lestrem, France) on insulin resistance and the determinants of metabolic syndrome in overweight men. We hypothesized that supplementation with NUTROISE over 12 weeks would lower insulin resistance and, secondarily, would reduce the prevalence of metabolic syndrome.

Materials and methods

Subjects

This double-blind, randomized, placebo-controlled study was approved by Tongji University Medical College Ethics Committee (Shanghai, China), and all participants provided written informed consent. This clinical trial is registered at clinicaltrials.gov (NCT01044680).

Males were included in the study if they were 20 to 35 years of age, had a body mass index of 24 to 28 kg·m⁻² (Zhou 2002), and were employed by and lived at 1 of 3 manufacturing plants with a controlled setting and with similar regimented working conditions 7 days a week. Exclusion criteria were current or recent dietary fiber supplementation, use of lipid-lowering and (or) hypertension medication, current insulin injection use, contraindication to fiber supplements (e.g., Crohn’s disease), allergy to wheat products, and recent or current antibiotic use.

Product description

NUTROISE is a glucose polysaccharide produced from
maize, wheat, or other edible starch heated at high temperatures. The final product, NUTRIOSE, is a mixture of glucose polymers with a fairly narrow range of molecular weight (number average molecular weight = 2600 g·mol⁻¹; weight average molecular weight = 5000 g·mol⁻¹) (Lefranc-Millot 2008). The degree of polymerization is 12 to 25. In comparison, starch may contain up to 1 million glucose units. During the heating step, hydrolysis and repolymerization occur. In addition to the typical starch α-1,4 and α-1,6 glucosidic linkages, the recombination can result in other specific linkages that are not found in starch, including both linear and branched linkages: α-1,6 and (or) β-1,6; α-1,2 and (or) β-1,2; α-1,3 and (or) β-1,3; and β-1,4. This confers to the product a resistance against the action of endogenous glucidolytic enzymes and permits classification of the product among the soluble dietary fibers with a total fiber content of nearly 85%.

Interventions

All research procedures in this study were performed according to a predefined protocol. Test subjects consumed 250 mL of fruit juice, twice daily, containing 17 g NUTRIOSE for 12 weeks. A daily NUTRIOSE dosage of 34 g was selected to ensure subjects met or exceeded recommended daily fiber intakes while maintaining a daily NUTRIOSE dose at levels that resulted in no gastrointestinal symptoms (up to 45 g) (van den Heuvel et al. 2004). Control subjects consumed 250 mL fruit juice, twice daily, containing 17 g maltodextrin (GLUCIDEX, Roquette Frères), over the same period. The supplements were consumed each day at 1000 and 1600 hours in the presence of research staff, who verified and recorded product consumption. Subjects ate their usual meals in the canteen at the same time (breakfast at 0700 hours, lunch at 1200 hours, and dinner at 1830 hours) every day throughout the 12-week study period. Subjects worked from 0700 to 1830 hours each day, and had no access to additional food during this period. Subjects were allowed to eat ad libitum between 1830 and 0700 hours, but were instructed to maintain typical food intake. Subject compliance with study product consumption, defined as the number of product doses divided by the number of possible doses, was 100% in each group.

Outcomes

Study personnel at each site received training in the protocol, and study procedures at each site were identical. Daily caloric intake and body composition outcomes with NUTRIOSE are the focus of future study. Briefly, daily energy intake was assessed using a 24-h dietary recall every 3 days during the trial. Interviewers used standard, open-ended questions to obtain descriptions and portion sizes of consumed food and drink. Once answers were obtained, interviewers cross-checked subject responses with a predefined list of foods and food categories to minimize potential underreporting. Height, body weight, and body mass index were measured using standard anthropometric techniques. Waist circumference was measured with a steel tape measure while the subject was standing, and the measure was made around the smallest circumference between the lateral costal margin and the iliac crest. Body fat percentage was estimated with bioelectrical impedance (Omron, Model HBF-306, Kyoto, Japan).

Subjects rested in a seated position for 5 to 10 min before each blood pressure measurement. Systolic blood pressure (mm Hg) was measured on the right arm, using a manual sphygmomanometer, with the subject in a seated position. The average of 2 readings taken 5 min apart was reported for each subject.

Blood samples were drawn at the pretreatment visit and at 4, 8, and 12 weeks post-treatment, between 0800 and 1000 hours, following an overnight fast of at least 12 h. The blood samples (10 mL) were collected in tubes and were centrifuged within 30 min at 3000 r/min⁻¹ (1560g) and 4 °C for 10 min to separate and collect the plasma. Samples were stored at −70 °C until the laboratory assays were performed. Plasma glucose, TC, HDL-C, and triglyceride levels were determined using the hexokinase method with an automated analyzer ( Bayer 1650, Tarrytown, N.Y.). Low-density lipoprotein cholesterol was calculated using the Friedewald equation (Friedewald et al. 1972). Plasma insulin and adiponectin were measured with an enzyme-linked immunosorbent assay (ALB-600, Morinaga, Yokohama, Japan). Glycated serum albumin and glycated hemoglobin were measured with an enzyme-linked boronate immunoassay (Asahi Kasei Pharma Co., Tokyo, Japan).

Plasma glucose and insulin concentrations were used to estimate insulin resistance using the homeostasis model assessment of insulin resistance (HOMA-IR), defined as fasting glucose (mmol·L⁻¹) × fasting insulin (μU·mL⁻¹) / 22.5 (Gungorl and Lanes 2006). Metabolic syndrome was defined by the presence of at least 3 of the following 5 conditions: waist circumference ≥ 85 cm (Zhou 2002), triglyceride levels ≥ 1.7 mmol·L⁻¹, HDL-C < 1.0 mmol·L⁻¹, systolic blood pressure ≥ 130 mm Hg, and fasting glucose ≥ 5.5 mmol·L⁻¹ (Alberti et al. 2009).

Sample size

Sample size was estimated (Power and Sample Size, Kaysville, Utah) using an assumed between-group effect size of 0.6 (moderate), a power of 80%, and an α of 0.05, which corresponds to a change in estimated insulin resistance of 1.5 HOMA units. This yielded an estimate of 50 subjects in each group. We enrolled 60 subjects per group to account for possible subject attrition.

Randomization

We randomized 120 subjects to either Test (n = 60) or Control (n = 60) groups, stratified across the 3 manufacturing plants (n = 20 per group per plant), and implemented a permuted block design, with a 1:1 treatment allocation ratio and a block size of 4. The blinded randomization sequence was computer-generated by a biostatistician at Sprim Advanced Life Sciences (San Francisco, Calif.). The study coordinator at the investigative site enrolled and assigned subjects to treatment groups. Study products were labeled with sequential subject identification numbers within each stratum, and were provided to the site by the sponsor. The site was instructed to enroll subjects consecutively within the appropriate plant stratum. Subjects were enrolled in the trial between October 2006 and February 2007.
Blinding
This study was conducted using triple-blinding procedures. Subjects were blinded to the treatment received throughout the trial, and the products were of identical taste, smell, and flavor. Investigators and all involved clinicians were also blinded to the treatment allocation throughout the trial. Finally, all study coordinators, clinical monitors, and biostatisticians were blinded to treatment allocation throughout the trial and until all analyses were completed.

Statistical methods
Data were assessed for normality with the Shapiro-Wilk test. Continuous outcome variables are reported as means ± SD, and categorical outcomes are reported as n (%). Independent t tests were used to evaluate between-group differences in baseline subject characteristics. Repeated-measures analysis of variance was used to evaluate within-subject changes over time for continuous outcomes. Mixed-model analysis of covariance was used to evaluate between-group treatment effects (2 groups) over time (4 time points) while controlling for baseline differences. McNemar's test was used to assess the change in prevalence of subjects with metabolic syndrome. All analyses were conducted according to the intent-to-treat principle (i.e., outcome measures were based on the original denominator of 120 patients and each subject was analyzed according to the original treatment assignment). The significance level for statistical tests was set at 0.05. Statistical analyses were performed using SAS/STAT software version 9.2 (SAS Institute Inc., Cary, N.C.).

Results
A total of 120 subjects (60 per group) participated in the study. Subject attrition was low in the Test (n = 3) and Control (n = 4) groups, and all dropouts were unrelated to the study. Overall, baseline characteristics were generally well matched between the Test and Control groups, although Test subjects tended to have an inferior lipid profile (Table 1).

Energy intake and body composition
Baseline energy intake in all subjects was 3243 ± 395 calories per day (1 calorie = 4.186 J). Across the 12-week study period, Test subjects consumed 736 fewer calories per day than Control subjects (p < 0.001). Test subjects had greater reductions in body weight (72.4 ± 3.3 kg vs. 73.9 ± 3.3 kg; p < 0.001), body mass index (24.0 ± 0.5 kg·m⁻² vs. 24.5 ± 0.3 kg·m⁻²; p < 0.001), and body fat percentage (21.2% ± 1.0% vs. 21.6% ± 0.9%; p < 0.001) than Control subjects at 12 weeks. In the Test group, the reductions in body weight and fat mass, but not waist circumference, exhibited overall weak to moderate correlations with glucose metabolism markers and lipids (Table 2). Physical activity status between groups was similar throughout the study.

Glucose metabolism markers
Adiponectin increased by 14% in Test subjects and decreased by 11% in Control subjects after 12 weeks; this group difference approached statistical significance (p = 0.05) (Fig. 1). Test subjects demonstrated significant reductions in glucose (4%) and insulin (12%), although these changes were not significantly different than the Control subjects (Figs. 2 and 3). HOMA-estimated insulin resistance decreased 18% in the Test group, and to a greater degree than in the Control group (p = 0.04) (Fig. 4). Intermediate and long-term glucose control, measured by glycated albumin and glycosylated hemoglobin, improved over time and in relation to Control subjects (Figs. 5 and 6).

Lipids
In the Test group, TC decreased 2%, LDL-C decreased by 1%, and HDL-C increased by 1%; all of these lipid changes were significantly different than changes in the Control

Table 1. Baseline subject characteristics.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Test group, n = 60</th>
<th>Control group, n = 60</th>
<th>p</th>
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<tbody>
<tr>
<td>Age, y</td>
<td>30.4±4.3</td>
<td>31.6±4.1</td>
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<tr>
<td>Body mass index, kg·m⁻²</td>
<td>24.5±2.0</td>
<td>24.5±0.3</td>
<td>0.49</td>
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<tr>
<td>Waist circumference, cm</td>
<td>91.7±4.5</td>
<td>90.8±4.2</td>
<td>0.25</td>
</tr>
<tr>
<td>Systolic blood pressure, mmHg</td>
<td>117±5</td>
<td>118±6</td>
<td>0.40</td>
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Glucose metabolism markers

<table>
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<tr>
<th>Adiponectin, μg·L⁻¹</th>
<th>Test group, n = 60</th>
<th>Control group, n = 60</th>
<th>p</th>
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<tbody>
<tr>
<td>5.40±0.57</td>
<td>6.89±5.43</td>
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</table>

Glucose, mmol·L⁻¹

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<th>Test group, n = 60</th>
<th>Control group, n = 60</th>
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<tr>
<td>5.6±1.10</td>
<td>5.8±1.22</td>
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Insulin, μU·mL⁻¹

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<th>Test group, n = 60</th>
<th>Control group, n = 60</th>
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<tr>
<td>16.2±0.10</td>
<td>17.2±0.10</td>
<td>0.61</td>
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Insulin resistance, HOMA-IR

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<tr>
<td>4.3±0.37</td>
<td>4.8±0.43</td>
<td>0.55</td>
</tr>
</tbody>
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Glycosylated hemoglobin, %

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<th>Control group, n = 60</th>
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<tr>
<td>5.78±0.84</td>
<td>5.7±0.8</td>
<td>0.94</td>
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Glycated albumin, %

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<th>Control group, n = 60</th>
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<tbody>
<tr>
<td>10.23±3.48</td>
<td>11.2±3.3</td>
<td>0.11</td>
</tr>
</tbody>
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Lipids

<table>
<thead>
<tr>
<th>Total cholesterol, mmol·L⁻¹</th>
<th>Test group, n = 60</th>
<th>Control group, n = 60</th>
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<tr>
<td>4.65±0.82</td>
<td>4.7±1.05</td>
<td>0.63</td>
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HDL-C, mmol·L⁻¹

<table>
<thead>
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<th>Test group, n = 60</th>
<th>Control group, n = 60</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.29±0.28</td>
<td>1.59±0.31</td>
<td>&lt;0.001</td>
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</table>

LDL-C, mmol·L⁻¹

<table>
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<th>Test group, n = 60</th>
<th>Control group, n = 60</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.58±0.63</td>
<td>2.48±0.70</td>
<td>0.43</td>
</tr>
</tbody>
</table>

VLDL-C, mmol·L⁻¹

<table>
<thead>
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<th>Test group, n = 60</th>
<th>Control group, n = 60</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.32±0.21</td>
<td>0.22±0.18</td>
<td>&lt;0.001</td>
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</tbody>
</table>

Triglyceride, mmol·L⁻¹

<table>
<thead>
<tr>
<th>Test group, n = 60</th>
<th>Control group, n = 60</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.99±1.34</td>
<td>1.53±0.88</td>
<td>0.03</td>
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</table>
group (Figs. 7 to 9). Although very low-density lipoprotein cholesterol (VLDL-C) decreased by 10% and triglycerides decreased by 16% in Test subjects, these changes were not different than those in Control subjects (Figs. 10 and 11).

**Systolic blood pressure**

No changes were reported in systolic blood pressure for either group over the 12-week study period.

**Metabolic syndrome**

The prevalence of metabolic syndrome after the 12-week supplementation period decreased in Test subjects and increased in Control subjects (Table 3). In general, Test subjects who presented with metabolic syndrome had greater improvements in glucose metabolism markers than subjects with no disease (Table 4).

**Safety**

No adverse events or gastrointestinal complaints, such as gas, bloating, or diarrhea, were reported in either group during the trial.

**Discussion**

The outcomes of this study demonstrate that 12 weeks of NUTRIOSE supplementation lowered insulin resistance, reduced the prevalence of metabolic syndrome, and improved most glucose metabolism and lipid markers in overweight
Fig. 5. Glycosylated hemoglobin change over 12 weeks in Test and Control groups. Values are expressed as means ± SE.

Fig. 6. Glycated albumin change over 12 weeks in Test and Control groups. Values are expressed as means ± SE.

Fig. 7. Total cholesterol change over 12 weeks in Test and Control groups. Values are expressed as means ± SE.

Fig. 8. High-density lipoprotein cholesterol (HDL-C) change over 12 weeks in Test and Control groups. Values are expressed as means ± SE.

Men. These outcomes agree with several studies that concluded dietary fiber can prevent, and possibly benefit, the pathologies linked to metabolic syndrome (Vuksan et al. 2000; Davy and Melby 2003; Brock et al. 2006; Alexandre and Miguel 2008). However, only 1 previous study has been conducted on the effects of NUTRIOSE on glucose metabolism markers or lipids. Pasman and colleagues (2006) reported that neither 30 g nor 45 g daily doses of NUTRIOSE affected blood lipids or glucose metabolism markers in young men with mild hypercholesterolemia. However, the 5-week supplementation period was likely too short for product benefits to be realized. Our 12-week study was designed to overcome this limitation.

The proposed mechanism of NUTRIOSE on metabolic syndrome is likely multifactorial. A common link among the components of metabolic syndrome may be related to inflammation, since these patients generally present in a prothrombic and proinflammatory state (King 2005; Alberti et al. 2009). In fact, people who consume the most fiber have the lowest concentrations of C-reactive protein, which suggests that fiber may control the inflammatory processes that are characteristic of metabolic syndrome (King et al. 2003). Another proposed mechanism of the effects of NUTRIOSE may be related to the release of adiponectin. Adiponectin is a cytokine that is secreted by adipose tissue and regulates glucose metabolism, stimulates fatty acid oxidation, lowers plasma triglycerides, and improves insulin sensitivity. It is possible that adiponectin mediated the improvements in glucose metabolism, especially insulin resistance, and in triglyceride levels. In fact, we found a weak to moderate inverse
relationship ($r = -0.24$ to $-0.52$) between adiponectin change and change in glucose, TC, LDL-C, VLDL-C, triglycerides, glycated albumin, and glycosylated hemoglobin. Furthermore, adiponectin change positively correlated with HDL-C change ($r = 0.37$). It is well established that fermentation of dietary fiber helps improve glucose metabolism by releasing gut peptides (Delzenne and Cani 2005). NUTRIOSE fermentation begins 5 h after consumption, and subsequently releases short-chain fatty acids, which stimulate gut peptide release. To date, several randomized controlled trials have demonstrated that insoluble fiber intake improves insulin sensitivity when measured with euglycemic-hyperinsulinemic clamps, the accepted gold standard (Robertson et al. 2005; Weickert et al. 2006). However, the effect of soluble fiber on insulin sensitivity is unknown, since no randomized trials using euglycemic-hyperinsulinemic clamps have been conducted.

Another potential reason for the beneficial effects of NUTRIOSE on glucose metabolism and lipids is the reduction in daily energy intake, which resulted in modest weight loss over 12 weeks. In support of this theory, we showed that the change in weight loss in Test subjects was moderately correlated with changes in these variables. Similar effects of weight loss have been previously shown; a meta-analysis by Dattilo and Kris-Etherton (1992) demonstrated that every 1 kg of weight loss lowered TC by 0.06 mmol-L$^{-1}$ and LDL-C by 0.02 mmol-L$^{-1}$. For reference, our study resulted in similar decreases of 0.05 and 0.03 mmol-L$^{-1}$ for each 1 kg weight loss, respectively, with NUTRIOSE supplementation. Additionally, improvements in glucose metabolism and lipids may have been observed because weight loss lowers free fatty acid flux into the liver, thereby lowering fasting glucose levels, improving insulin resistance, and decreasing VLDL-C production (Björntorp 1990; Després et al. 1990).

The lack of effect on systolic blood pressure was anticipated, given that blood pressure decreases with higher fiber consumption are uncommon (Streppel et al. 2005). It is possible that, because our sample consisted of relatively young and normotensive men, any positive influence of fiber on blood pressure was blunted; the greatest benefits of fiber are generally observed in people who are older and hypertensive (Streppel et al. 2005).

The addition of high-fiber foods and fiber supplements to the diet can cause gastrointestinal symptoms, such as gas, bloating, and diarrhea. The fact that no gastrointestinal complaints were reported during our study is not surprising. In fact, NUTRIOSE dosages as high as 80 to 100 g per day are well tolerated in humans (Coudray et al. 2003; van den Heuvel et al. 2004). Natriose is partly digested and absorbed in the small intestine (15%), 10% is excreted in the feces,
and the remainder (75%) is fermented in the colon (Lefranc-Millot 2008).

A limitation of this study is the fact that daily macronutrient and fiber intake was not calculated. Subjects ate, ad libitum, the same menu at the same facilities 7 days per week, and were asked to continue their typical dietary practices. Nonetheless, the impact of diet cannot be ruled out as a confounding factor. In addition, caution should be exercised in applying these outcomes to women or persons of other ethnicities. Strengths of this study are the strong study design and the stringent data collection and data analysis methods, which included triple blinding, double data entry with verification, independent data monitoring, and an intent-to-treat analysis.

In conclusion, twice-daily supplementation with NUTRIOSE over a 12-week period is well tolerated, lowers insulin resistance, and improves determinants of metabolic syndrome in overweight men.

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