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Highly Methoxylated Pectin Improves Insulin Resistance and Other Cardiometabolic Risk Factors in Zucker Fatty Rats

D. SÁNCHEZ,[†] B. MUGUERZA,[‡] L. MOULAY,[‡] R. HERNÁNDEZ,[§] M. MIGUEL,[†] AND A. ALEIXANDRE*,[†]

Departamento Farmacología, Facultad Medicina, Universidad Complutense, Avenida Complutense s/n, 28040 Madrid, Spain, Natraceutical Group, Autovía A-3, Salida 343, Camino de Torrent s/n, Quart de Poblet, 46930 Valencia, Spain, and Hospital Central de la Defensa (CDEAS), C/Arturo Soria, 82, 28027, Madrid, Spain

In this study, we evaluated the effect of a highly methoxylated apple pectin (HMAP) on cardiometabolic risk factors in Zucker fatty rats. β-Glucan, a fiber known for its hypocholesterolemic properties, also was used. The rats fed both fiber-enriched diets exhibited a reduction in body weight and in total cholesterol and triglycerides when compared to the Zucker fatty rats fed the standard diet. The effect on the lipid profile was more remarkable in the HMAP group. A decrease in blood glucose was only noticed in this group. Moreover, a decrease in plasma insulin, HOMA-IR, and HOMA-β was noticed in the fiber groups, and in particular in the HMAP group, these variables being similar to the lean rats. Blood pressure and endothelial function were similar in all the Zucker fatty rats. These results warrant evaluation in humans to determine if HMAP could be used as a functional ingredient to reduce lipid profile, insulin resistance, and other cardiometabolic risk factors.

KEYWORDS: Apple pectin; β-glucan; fiber; metabolic syndrome; Zucker rats

INTRODUCTION

Metabolic syndrome is associated with abdominal obesity and a clustering of abnormalities that together lead to a significantly increased risk of cardiovascular disease (*1, 2*). The prevalence of metabolic syndrome has increased dramatically in recent years (*3–5*), but being a multifactorial condition, no single treatment for the clustering of its cardiometabolic risk factors exists. However, it is known that lifestyle modifications, for example, changes in diet and an increase in physical activity, form the underlying strategy for both prevention and treatment. Dietary fiber plays, in particular, a role in managing the risk of this chronic disease. Many studies have, in fact, shown the beneficial effects of soluble fibers on body weight management (*6*), plasma cholesterol and lipoprotein levels (*7–10*), and diabetes (*11–13*). Pectin is a soluble fiber found in the cell walls of many plants. Some studies describe the healthy properties of this fiber. Apple pectin has demonstrated a better cholesterol-lowering effect than other pectins including orange pectin (*14*), but only a few studies have investigated the effects of apple pectin (*14–17*). Moreover, in this context, it is important to note that the health effects of this type of fiber are related not only to the pectin source but also to its physicochemical properties. Gel forming properties in apple pectin are related to the degree of methoxylation (*18*), and it has been demonstrated that high-methoxyl pectins had a greater inhibitory effect in glucose uptake than low-methoxyl pectins (*19, 20*).

Zucker fatty rats are considered the best-known and most widely used experimental model of genetic obesity. These animals present also dyslipidemia, mild glucose intolerance, and hyperinsulinemia, alterations similar to those that appear in human metabolic syndrome. These animals can, in fact, also be considered to be a model of resistance to insulin. By contrast, lean Zucker rats are insulin-sensitive, normoinsulinemic, and have a normal tolerance of glucose (*21–24*). The link between obesity and hypertension has been recognized for some time, and it is also true that the systolic arterial blood pressure values in the aged Zucker fatty rats are higher than in their lean counterparts (*25*).

The aim of this study was to evaluate the effects of a highly methoxylated apple pectin (HMAP) on the main cardiometabolic risk factors that characterize the human metabolic syndrome (obesity, impaired glucose tolerance, dyslipidemia, hypertension, and endothelial dysfunction), by feeding Zucker fatty rats a HMAP-enriched diet. Lean Zucker rats were used in the study for result comparison, and β-glucan, a fiber with cholesterol-lowering properties and well-recognized positive health benefits in cardiovascular disease (*26–28*), also was included as the positive control fiber.

* Author to whom correspondence should be addressed. Tel.: 34-91-3941475; fax: 34-91-3941463; e-mail: amaya@med.ucm.es.
[†] Universidad Complutense.
[‡] Natraceutical Group.
[§] Hospital Central de la Defensa.

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MATERIALS AND METHODS

General Protocol. Thirty female 8 week old Zucker fatty rats weighing 260–275 g and 10 female 8 week old lean Zucker rats weighing 150–175 g, purchased from Charles River Laboratories (Charles River Laboratories), were used in this study. The Zucker fatty rats were randomly divided into three groups of 10 animals that were fed the following diets until the 15th week of life: standard diet, 10% HMAP-enriched diet and 10% β-glucan-enriched diet. The 10 lean Zucker rats were in turn fed the standard diet until the 15th week of life. During the experimental period, the animals were maintained at a temperature of 23 °C, with 12 h light/dark cycles, and were fed ad libitum with free access to water. Total cholesterol, cholesterol transported by HDL, triglyceride and glucose were determined in the plasma on a weekly basis. To carry out these determinations, blood extractions from the jugular vein were performed weekly in the rats after an overnight fasting. Since the biochemical procedures to determine cholesterol transported by LDL cholesterol in this animal model are not reliable, we calculated the value of non-HDL cholesterol in the rats by obtaining the corresponding difference between total cholesterol and HDL cholesterol. Food intake, water intake, and body weight gain also were recorded on a weekly basis. Moreover, SBP and DBP were measured weekly in the rats during the experimental period, by the tail cuff method (*29*). The original technique for measuring arterial blood pressure using the tail cuff method provides only SBP values, but the equipment used in this study, LE 5001 (Letica, Hospitalet), has a high-sensitivity pulse transducer coupled with an accurate microprocessor program and allowed us to distinguish between SBP and DBP. Before the measurements, the rats were kept at 38 °C for 10–15 min to make the pulsations of the tail artery detectable. Arterial blood pressure measurements were performed at the same time of day (between 9 a.m. and 1 p.m.) to avoid the influence of the circadian cycle, and the values of SBP and DBP were obtained by estimating the average reading of five measurements.

At the end of the experimental period, the rats were sacrificed by decapitation after an overnight fasting. Their thoraxes were opened, and the aorta was extracted quickly to evaluate the endothelial function of the animals in accordance with the studies published by Furchgott (*30, 31*). The in vitro experiments in aorta rings are mentioned next. Blood was obtained from the sacrificed rats to carry out the same biochemical determinations that we had performed weekly, and the correspondent values of non-HDL cholesterol also were calculated. In addition, the plasma insulin was determined. Moreover, fasting plasma concentrations of both glucose and insulin were used to calculate the indices of insulin resistance [homeostasis model assessment (HOMA)-IR] and insulin secretion (HOMA-β) with the following formulas (*32*): HOMA-IR = fasting insulin (μU/mL) × fasting glucose (mM)/22.5 and HOMA-β = 20 × fasting insulin (μU/mL)/(fasting glucose (mM) − 3.5). The QUICKI also was calculated (*33*). QUICKI = 1/log fasting insulin (μU/mL) + log fasting glucose (mg/dL). In this study, all the experiments were performed as authorized for scientific research (European Directive 86/609/CEE and Royal Decree 223/1988 of the Spanish Ministry of Agriculture, Fisheries, and Food).

Diets. Three synthetic diets were used in this study (**Table 1**). They were prepared by Harlan Interfauna Ibérica (Barcelona, Spain). The first one (AIN-93 M purified Rodent Diet) was a standard diet that provides the nutrients required by adult rats according to the National Research Council guidelines (*71*). The other two diets contained either 10% HMAP (apple pectin with 73% methylation degree, provided by Obipektin) or 10% β-glucan (oat bran concentrate provided by Glambia Nutritionals). The three diets were prepared and formulated to provide the same amount of protein (14%), fat (4%), and carbohydrates (72%) and, therefore, the same energy value. In particular, the β-glucan-enriched diet was formulated, taking into account the amount of protein, fat, and carbohydrates provided by oat bran.

Analytical Procedures. Blood samples were collected in tubes containing lithium heparin as the anticoagulant. These samples were centrifuged at 2500*g* for 20 min at 4 °C to obtain the plasma that was divided into aliquots and kept frozen at −80 °C until analysis.

Plasma glucose was assayed by using the glucoseoxidase enzymatic test with commercial kits (Roche Diagnostics S.L.), and the lipid profile (triglycerides, total, and HDL cholesterol) were assayed by using enzymatic and colorimetric methods with commercial kits (Roche Diagnostics S.L.). The different concentrations were determined spectrophotometrically using a Hitachi 911 autoanalyzer (wavelength of 700 nm). The plasma insulin concentration was spectrophotometrically quantified by using an ultrasensitive rat insulin enzyme immunoassay kit (Mercodia AB) with a Molecular DevicesThermo max (microplate reader). The absorbance was measured at 450 nm.

Table 1. Composition of Diets (g/100 g of Dry Weight)[a]

	standard diet	10% apple pectin	10% β-glucan
protein	14	14	14
casein	14	14	10.5
fat	4	4	4
soybean oil	4	4	3.63
carbohydrate	72	72	72
sucrose	10	8.27	7.97
dextrin	15.5	12.81	12.35
corn starch	46.56	38.48	37.11
powdered cellulose	5	5	5
Brown Ribbon pure apple pectin[b]	0	12.5	0
oat bran concentrate[c]	0	0	18.52
TBHQ[d]	0.0008	0.0008	0.0008
AIN 93 mineral mixture	3.5	3.5	3.5
AIN 93 vitamin mixture	1	1	1
L-cysteine	0.18	0.18	0.18
choline bitartrate	0.25	0.25	0.25
energy (kJ/100 g)[e]	1589	1589	1589

[a] Carbohydrate substitution in both experimental diets was formulated at the expense of sucrose, dextrin, and starch proportionally. [b] Brown Ribbon pure apple pectin contains 80% dietary fiber, 8–10% sugar, 8.7% water, and 2–5% salts (viscosity = 188 mPas in 2% solution and density = 0.6–0.9 g/cm^3). The fiber is a HMAP with a 73% methylation degree and a polygalacturonic acid content of 65%. [c] Oat bran concentrate contains protein (19%), fat (<2%), and carbohydrate (>77%); the amount of oat β-glucan is 54%. [d] *t*-Butylhydroquinone. [e] Energy value was determined by calculation in the order Atwater system.

Experiments in Aorta Rings. Excess fat and connective tissue were removed from the aorta, and the tissue was cut into rings (approximately 4 mm in length). The aortic rings were mounted between two steel hooks in isolated tissue chambers containing Krebs−Henseleit solution with the following composition (mmol/L): NaCl, 118.2; KCl, 4.7; $CaCl_2$, 2.5; KH_2PO_4, 1.2; $MgSO_4$, 1.2; $NaHCO_3$, 25; and glucose, 10.0. The medium was maintained at 37 °C and continuously bubbled with a 95% O_2/5% CO_2 mixture, which gave a pH of 7.4. An optimal resting tension of 2 g was applied to all aortic segments. This tension was adjusted every 15 min during a 60–90 min equilibration period before adding drugs. Isometric tension was recorded by using an isometric force displacement transducer connected to an acquisition system (Protos 5, Panlab). After the equilibration period, the rings were first contracted by 80 mmol/L KCl to assess the arterial functionality, and when the contraction had reached a steady state (about 15 min after administration), the preparations were washed until the basal tension was recovered. Then, the rings were exposed to 10^{-6} mol/L metoxamine, and dose–response curves to acetylcholine (10^{-9} to 10^{-5} mol/L) were acquired in the methoxamine precontracted rings. Relaxant responses to ACh were expressed as a percentage of precontraction induced by metoxamine.

Statistical Analysis. The results are expressed as mean values ± SEM for a minimum of eight rats. The data that were obtained weekly were analyzed by a two-way analysis of variance (ANOVA), and the data obtained only at the end of the experimental period were analyzed by a one-way ANOVA. In both cases, GraphPad Prism 4 software was used. Differences between the groups were assessed by the Bonferroni test. Differences between the means were considered to be significant when $p < 0.05$.

RESULTS

Food and Water Intake and Body Weight. The diets were well-tolerated by both strains of rats, but food intake throughout the study was significantly higher in the Zucker fatty rats than

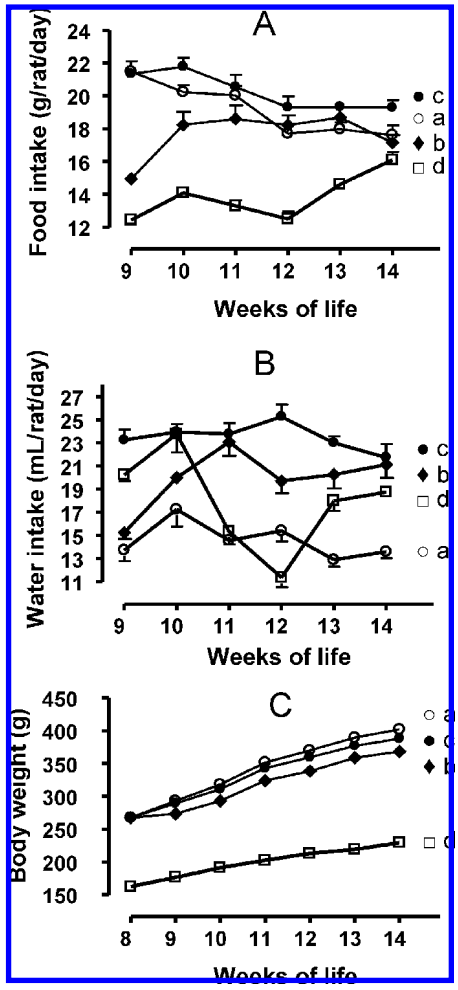

Figure 1. Food intake (**A**), water intake (**B**), and body weight (**C**) of the different groups of rats: Zucker fatty rats fed the standard diet (○), Zucker fatty rats fed the 10% β-glucan-enriched diet (●), Zucker fatty rats fed the 10% highly methoxylated apple pectin-enriched diet (♦), and lean Zucker rats fed the standard diet (□). The results are expressed as mean values ± SEM for a minimum of eight rats. Different letters represent statistical differences ($p < 0.05$).

in the lean Zucker rats. When the three groups of Zucker fatty rats were compared, it could be established that food intake was significantly higher in the β-glucan group than in the groups fed the standard or the HMAP diet. During the first and second weeks of the study, the food intake was especially low in the group fed the HMAP-enriched diet. Water intake was significantly higher in the groups fed the fiber-enriched diets than in the Zucker fatty rats and the lean Zucker rats fed the standard diet. This was particularly high in the group fed the β-glucan-enriched diet. However, during the first and second weeks of the study, water intake was quite similar in the group of Zucker fatty rats fed the HMAP-enriched diet and in the group of Zucker fatty rats fed the standard diet (**Figure 1A**,**B**).

All the groups progressively gained weight during the experimental period. Nevertheless, the lean Zucker rats exhibited a significantly reduced weight as compared to the Zucker fatty rats. However, the weight gain was slower in the groups fed the fiber-enriched diets and particularly in the group fed the HMAP-enriched diet, where the values of the body weight were significantly lower than those of the Zucker fatty rats fed the standard or the β-glucan-enriched diets (**Figure 1C**).

Plasma Biochemistry. Fasting blood glucose was higher in the three groups of Zucker fatty rats than in the lean Zucker rats. The consumption of the HMAP-enriched diet resulted in a significant decrease of fasting blood glucose, and therefore, this variable was lower in the HMAP group than in the Zucker fatty rats fed the standard or the β-glucan diet. No difference was found between the fasting blood glucose levels of the Zucker fatty rats fed the standard diet and the rats fed the β-glucan-enriched diet. The decrease in blood glucose levels in the Zucker fatty rats fed the HMAP-enriched diet can be clearly observed from the third week of study, and at the end of the experimental period, no significant differences in blood glucose were observed in these animals and in the lean Zucker rats (**Figure 2A**).

Plasma triglycerides and cholesterol levels were significantly higher in the three groups of Zucker fatty rats than in the lean Zucker rats. The groups fed the fiber-enriched diets revealed a significant decrease in plasma triglycerides and cholesterol levels when compared to the Zucker fatty rats fed the standard diet. In addition, the decrease in plasma triglycerides was more significant in the HMAP group than in the β-glucan group (**Figure 2B**,**C**). At the end of the experimental period, the Zucker fatty rats fed the standard diet had lower values of HDL cholesterol and the highest values of non-HDL cholesterol, and the HMAP group showed the highest values of HDL cholesterol. Both groups fed the fiber-enriched diets had significantly lower levels of non-HDL cholesterol than the Zucker fatty rats fed the standard diet (**Figure 2D**,**E**).

The consumption of fiber-enriched diets by the Zucker fatty rats resulted in a significant reduction in plasma insulin concentrations. The decrease was more remarkable in the rats fed the HMAP-enriched diet than in the rats fed the β-glucan-enriched diet, to the extent that the rats fed the HMAP-enriched diet showed insulin plasma levels similar to those of the lean Zucker rats (**Figure 3A**). At the end of the experimental period, the values of HOMA-IR and HOMA-β also were similar in the Zucker fatty rats fed the HMAP-enriched diet and in the lean Zucker rats. These groups showed lower values of HOMA-IR than the remaining Zucker fatty rats. However, the HOMA- β values in the rats fed the β-glucan-enriched diet were similar to those of the rats fed the HMAP-enriched diet. The Zucker fatty rats fed the standard diet exhibited the highest values of HOMA-IR and HOMA- β (**Figure 3B**,**C**). The Zucker fatty rats fed the HMAP-enriched diet showed a significant increase in the QUICKI, but the lean rats showed the highest value of this index (**Figure 3D**).

Blood Pressure and Experiments in Aorta Rings. SBP and DBP throughout the study were significantly higher in the lean Zucker rats than in the Zucker fatty rats, but these variables were similar in the animals of the three established groups of Zucker fatty rats. No significant differences were therefore observed between SBP and DBP of the groups fed the fiber-enriched diets and those fed the standard diet (data not shown). No differences were found in the endothelium-dependent vasodilator responses to acetylcholine of the arteries in the different groups of Zucker fatty rats, but the responses to acetylcholine were more accentuated in the lean Zucker rats than in the Zucker fatty rats (data not shown).

DISCUSSION

In this study, Zucker fatty rats were used to assess the potential health effects of HMAP. These rats are a model of obesity accompanied by hyperlipidemia and hyperglycemia. They undergo obesity between the third and fifth week of life, and when the animals are 14 weeks old, about 40% of their body weight is fat. The results obtained in the present study

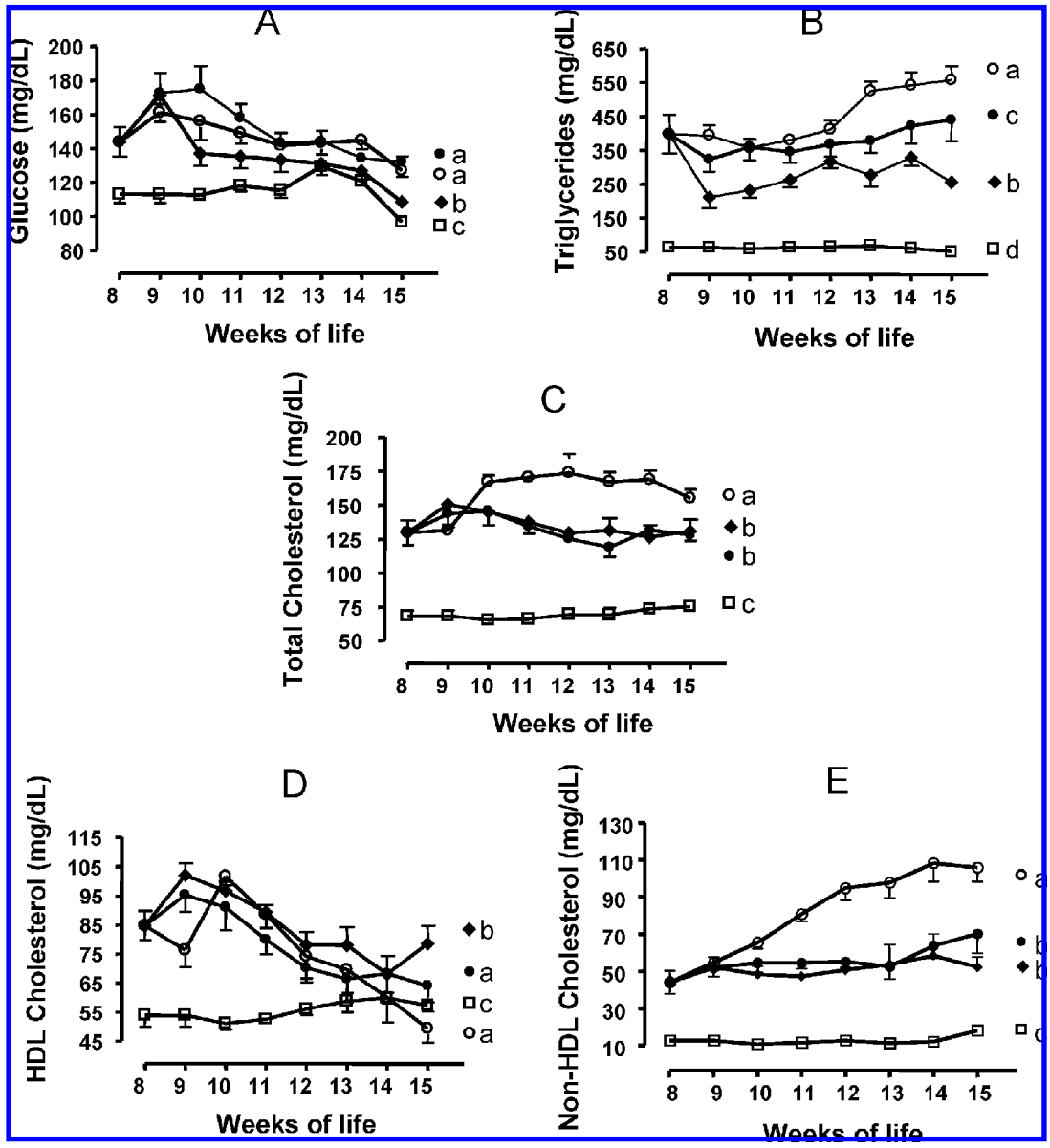

Figure 2. Plasma glucose (**A**), plasma triglycerides (**B**), plasma total cholesterol (**C**), plasma HDL cholesterol (**D**), and plasma non-HDL cholesterol (**E**) of the different groups of rats: Zucker fatty fed the standard diet (○), Zucker fatty rats fed the 10% β-glucan-enriched diet (●), Zucker fatty rats fed the 10% highly methoxylated apple pectin-enriched diet (♦), and lean Zucker rats fed the standard diet (□). The results are expressed as mean values ± SEM for a minimum of eight rats. Different letters represent statistical differences ($p < 0.05$).

relate to the intake of a HMAP-enriched diet with the prevention of some abnormalities clustered in the metabolic syndrome, including obesity, dyslipidemia, and glycemic profile. In fact, a decrease in body weight was noticed, as well as a reduction in glycemia, insulinemia, and plasma lipids in the group fed the HMAP-enriched diet.

Epidemiological or cross-sectional observational studies claim that fiber consumption is inversely correlated to body weight (*34*). However, in the intervention studies, the association between soluble fiber consumption and body weight loss is not evident, and it depends on the source of fiber used (*35*). In the present study, the intake of both soluble fiber-enriched diets resulted in a reduction of body weight in this animal model of obesity. Similar effects were observed in other studies when a pectin-supplemented diet was fed to Zucker fatty rats for 7 weeks (*36*). A reduction in body weight gain was reported in spite of an equivalent caloric intake. In our study, the decrease in body weight observed in the group fed the HMAP-enriched diet was higher than in the β-glucan group. In this context, it previously was reported that fruit fiber was more efficient in reducing body weight than cereal fiber (*34, 37*). According to Adams et al., the reduction in body weight observed in animals fed highly methoxylated pectins suggests that these fibers can be used as aids in weight management, helping to control obesity, which is considered to be a major risk factor for type 2 diabetes (*38*).

Recent experimental data suggest that the modification of gut peptides—involved in appetite and glucose homeostasis—could constitute a metabolic relay, allowing specific (fermentable) dietary fiber to act upon appetite suppression (*34, 39*). However, the reduction in body weight observed in this study did not seem to be associated with a satiety effect. In fact, food intake in the β-glucan group was even higher than in the group fed the standard diet. The low food intake noticed in the group fed the HMAP-enriched diet was probably due to the adaptation period to this diet rather than to a possible satiety effect. The increase in liquid consumption of the groups fed the soluble fiber-enriched diets could be a consequence of the gel forming

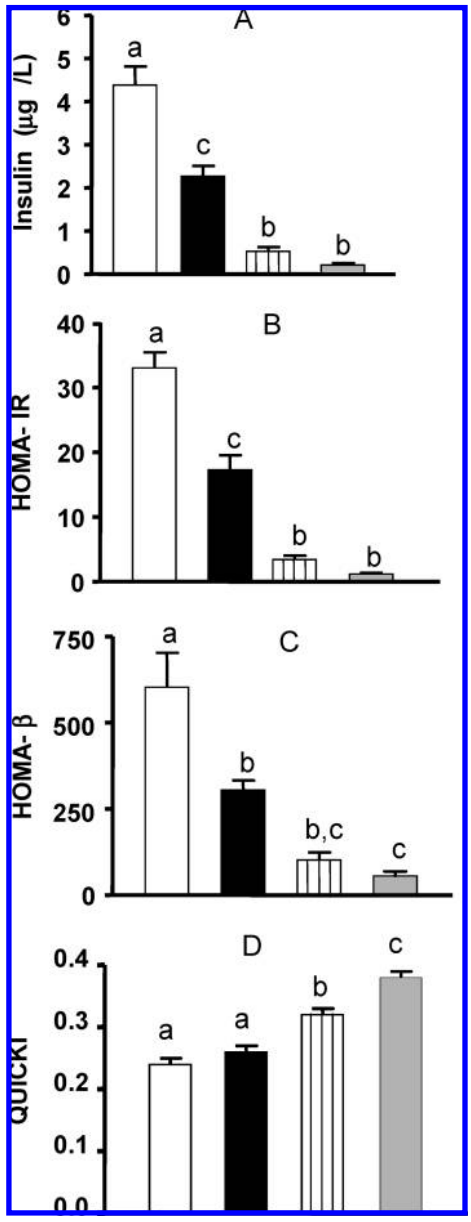

Figure 3. Plasma insulin (**A**), homeostasis model assessment of insulin resistance (HOMA-IR) values (**B**), homeostasis model assessment of insulin secretion (HOMA-β) values (**C**), and quantitative insulin sensitivity check index (QUICKI) values (**D**) of the different groups of rats at the end of the experimental period: Zucker fatty fed the standard diet (white bars), Zucker fatty rats fed the 10% β-glucan-enriched diet (black bars), Zucker fatty rats fed the 10% apple pectin-enriched diet (striped bars), and lean Zucker rats fed the standard diet (gray bars). The results are expressed as mean values $\pm$ SEM for a minimum of eight rats. Different letters represent statistical differences ($p < 0.05$).

properties of pectin and β-glucan. The slight increase in water intake in the β-glucan group as compared to the HMAP group could be explained as a consequence of the food intake and the higher viscosity in the gut.

Blood glucose level in the HMAP group was significantly lower than in the Zucker fatty rats fed the standard diet. Moreover, the HMAP group reached the glucose values of the lean Zucker rats. However, β-glucan failed to induce a blood-lowering glucose effect. These results are in agreement with reports of other studies that described decreases in fasting glucose levels due to the intake of pectin (*40, 19*). The decrease in the glucose levels seems to be related to the gel forming property of the pectin (*19*). The delay in gastric emptying and unstirred layer thickness formed in the intestine due to pectin viscosity are the causes of a decreased intestinal absorption of glucose (*41–43*). In this study, we used a HMAP, and it is important to emphasize that the gel forming properties of pectin are related to its high degree of methoxylation (*18*) and that the high-methoxyl pectins had a greater inhibitory effect in glucose uptake than the low-methoxyl pectins (*19, 20*).

The reduction in insulin concentrations observed in this study when the animals were fed the fiber-enriched diets is in accordance with a decrease previously described by other authors (*44–46*). In fact, the fiber consumption remained significantly associated with fasting insulin (*47*). The lower insulin concentrations obtained in the group fed the HMAP-enriched diet as compared to the β-glucan group could be due to the reduction in the rate of glucose absorption produced by viscous fibers as was previously reported by Jenkins et al. (*12*). A link of low insulin concentrations and reduction in body weight gain previously was described (*47–49*). This connection could explain the decrease in body weight observed in the rats fed the fiber-enriched diets, in particular, in those fed the HMAP-enriched diet.

According to the low fasting glucose and insulin obtained values, HOMA-IR was consequently reduced in the groups fed the fiber-enriched diets, especially in the HMAP group. These results are in agreement with other authors, who reported that the intake of dietary fiber was inversely associated with HOMA-IR (*50, 51*). A direct effect of soluble fiber on the insulin resistance previously was described via the reduction of TNF-α and an increase of adiponectin (*52*). The improvement of glucose homeostasis noticed in our study could be associated with the low glucose uptake induced by HMAP. As a consequence of the low blood glucose levels, the pancreatic secretor capacity could be reduced, producing smaller amounts of insulin, confirmed by the assessed low HOMA-β and insulin values obtained in the HMAP group. Moreover, the elevated QUICKI value observed in the HMAP group indicated that these animals also develop a compensatory mechanism to increase the sensitivity to this hormone. Therefore, HMAP exhibited a beneficial effect on glucose homeostasis when it was consumed by Zucker fatty rats, likely due to blood glucose reduction.

As expected, the cholesterol levels of the Zucker fatty rats fed the standard diet increased during the study. However, hypercholesterolemia was notably reduced when 10% of soluble fiber was added to the diet. This drop in total cholesterol was not produced at the expense of HDL cholesterol because there was no difference in the HDL cholesterol levels between the three groups of Zucker fatty rats. Fiber has been shown to be a potential tool in the prevention and dietary treatment of hypercholesterolemia, especially soluble dietary fiber (*7, 8, 40, 53, 54*). The obtained results indicate that HMAP has the same potential as β-glucan to decrease the plasma cholesterol levels. This finding is important because β-glucan is a fiber with well-known hypocholesterolemic effects (*26–28*), to the extent that the U.S. Food and Drug Administration allows cardiovascular risk reduction claims for oat β-glucan (*10*). The lipid-lowering capacity of pectin has been reported previously in rats (*14, 16, 18, 36, 55*) and in humans (*15*). Similar effects were observed when apple-supplemented diets were used (*17, 56, 57*). However, other studies did not observe the pectin cholesterol-lowering effects (*58–60*). This apparent controversy could be due to the physicochemical properties of the used pectin in these studies. As was described for glucose uptake, it has been

proposed that characteristics such as the degree of methoxylation and viscosity could be important factors in determining the lipid-lowering potency of pectin (*61, 62*). The pectin used in the present study is highly methoxylated, and this could be considered to be a key factor in explaining our results on the lipid profile. In fact, many beneficial health effects of soluble fiber, including hypocholesterolemic effects, are related to the degree of viscosity (*54*). It also was suggested that the possible mechanisms responsible for the hypocholesterolemic action of pectin are related to the interruption of the enterohepatic circulation of bile acids or the inhibition of cholesterol absorption, leading to an increased excretion of sterols in faeces (*59, 63*).

Hypertriglyceridemia has been described in Zucker fatty rats (*64, 65*). In this study, the addition of 10% of soluble fiber to the diet resulted in a significant decrease in triglycerides in these animals. This effect is in agreement with other studies carried out in Zucker fatty rats (*52, 66*) and in humans (*53*). The decrease was higher in the rats fed HMAP than in the rats fed β-glucan. It is noteworthy that this triglyceride-lowering effect is consistent with a possible effect of the diffusion of micelles in the intestinal lumen produced by soluble fiber (*67*).

Although significant changes in SBP and DBP have been reported with fiber supplementation in hypertensive and older humans (*68*), we did not observe a decrease in these variables in the rats fed the fiber-enriched diets. Nevertheless, we have to bear in mind that most studies agree that obese Zucker rats are not a true model of hypertension (*25, 69*). In our study, the lean Zucker rats showed higher SBP and DBP values than the Zucker fatty rats, but it is also true that it has been reported that the SBP in Zucker fatty rats is lower than that in the lean Zucker rats of between 8 and 12 weeks of life. At 24 weeks, the phenomenon goes into reverse, and at 28 weeks, SBP in Zucker fatty rats is significantly higher than in their lean counterparts. We can also mention that the period of our study was of 6 weeks and that in the study of Whelton et al., 8 weeks of fiber intake was required to obtain the hypotensive effect in humans (*70*). Since the arterial blood pressure of the Zucker fatty rats was not modified by the fiber-enriched diets, it was not surprising to find that these diets did not modify the endothelial function of these animals in our study. The arteries from the lean Zucker rats showed better responses to acetylcholine than the arteries from Zucker fatty rats. The improved endothelial function in the lean Zucker rats also could explain the decreased response to methoxamine observed in the aorta of these animals.

The obtained results point out that HMAP may modulate parameters that appear to be altered in the metabolic syndrome such as body weight, glycemia, insulinemia, and blood lipids. It is worth mentioning that HMAP has demonstrated itself to be more efficient than β-glucan in preventing some of these cardiovascular risk factors related to metabolic syndrome. The difference in the chemical structure of HMAP and β-glucan, responsible for their physical properties, may explain the more remarkable results obtained in this study when HMAP was used. More studies with these fibers are nevertheless desirable, and the use of other experimental models may help to completely elucidate the mechanism(s) involved in HMAP effects.

ABBREVIATIONS USED

DBP, diastolic blood pressure; HDL, high-density lipoproteins; HMAP, highly methoxylated apple pectin; HOMA-IR, insulin resistance homeostasis model assessment; HOMA-β, insulin secretion homeostasis model assessment; QUICKI, quantitative insulin sensitivity check index; LDL, low-density lipoproteins; SBP, systolic blood pressure.

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