Resistant Starch from High-Amylose Maize Increases Insulin Sensitivity in Overweight and Obese Men\(^1\)\(^2\)\(^3\)

Kevin C. Maki,\(^4\)* Christine L. Pelkman,\(^5\) E. Terry Finocchiaro,\(^6\) Kathleen M. Kelley,\(^4\) Andrea L. Lawless,\(^4\) Arianne L. Schild,\(^4\) and Tia M. Rains\(^4\)

\(^4\)Provident Clinical Research and Consulting, Inc., Glen Ellyn, IL; and \(^5\)National Starch, LLC, Bridgewater, NJ

Abstract

This study evaluated the effects of 2 levels of intake of high-amylose maize type 2 resistant starch (HAM-RS2) on insulin sensitivity (SI) in participants with waist circumference \(\geq\) 89 (women) or \(\geq\) 102 cm (men). Participants received 0 (control starch), 15, or 30 g/d (double-blind) of HAM-RS2 in random order for 4-wk periods separated by 3-wk washouts. Minimal model SI was assessed at the end of each period using the insulin-modified i.v. glucose tolerance test. The efficacy of the treatments (overall least squares ln-transformed mean \(\pm\) SEM) age 49.5 \(\pm\) 1.6 y, with a BMI of 30.6 \(\pm\) 0.5 kg/m\(^2\) and waist circumference 105.3 \(\pm\) 1.3 cm. A treatment main effect \((P = 0.018)\) and a treatment \(\times\) sex interaction \((P = 0.033)\) were present. In men, least squares geometric mean analysis for SI did not differ after intake of 15 g/d HAM-RS2 (6.90 \(\times\) \(10^{-5}\) pmol\(^2\) \(\times\) min\(^{-1}\) \(\times\) L\(^{-1}\)) and 30 g/d HAM-RS2 (7.13 \(\times\) \(10^{-5}\) pmol\(^2\) \(\times\) min\(^{-1}\) \(\times\) L\(^{-1}\)), but both were higher than after the control treatment (4.66 \(\times\) \(10^{-5}\) pmol\(^2\) \(\times\) min\(^{-1}\) \(\times\) L\(^{-1}\) \(\times\) min\(^{-1}\)) \((P < 0.05)\). In women, there was no difference among the treatments (overall least squares ln-transformed mean \(\pm\) pooled SEM = 1.80 \(\pm\) 0.08; geometric mean = 6.05 \(\times\) \(10^{-5}\) pmol\(^2\) \(\times\) min\(^{-1}\) \(\times\) L\(^{-1}\)) \((P < 0.05)\). These results suggest that consumption of 15–30 g/d of HAM-RS2 improves SI in men. Additional research is needed to understand the mechanisms that might account for the treatment \(\times\) sex interaction observed. J. Nutr. 142: 717–723, 2012.

Introduction

RS\(^5\) is defined as the fraction of starch resistant to pancreatic \(\alpha\)-amylase hydrolysis in the small intestine that therefore passes undigested to the large bowel, where it can act as a substrate for microbial fermentation (1,2). The digestibility of starch is influenced by processing, how it is cooked and stored, as well as its inherent physiochemical properties, such as variations in granular structure and the ratio of starch types present (amylose and amylopectin). Uncooked high-amylose starches are more resistant to enzymatic hydrolysis than high-amylopectin starches; however, cooking can increase the digestibility of amylose (3,4).

The main sources of RS in the diet include breads, cereals, pastas, and vegetables (5). Recent estimates indicate Americans consume \~4.9 g/d of RS (5), whereas estimated intakes in 10 European countries ranged from 3.2 to 5.7 g/d (6). However, such levels are far below intakes previously demonstrated to confer health benefits (\~20 g/d), including improved bowel health, increased nutrient absorption, and improved glycemic and insulminic responses (7,8). The metabolic effects of commercially available sources of RS have been studied in animals and also investigated in humans at intakes of 10–60 g RS/d (9). Results from studies with a granular, type 2 RS from HAM-RS2 made from corn with an amylose content >50% suggest beneficial effects of consumption on outcomes related to large bowel health, such as changes in colonic cellular events and fecal variables such as reduced pH, bulking, and microbial flora shifts as well as systemic metabolic effects on glycemia and insulinemia (10–13).

More recent work has demonstrated improved SI with consumption of HAM-RS2 (14–16). For example, Robertson et al. (16) showed that insulin sensitivity assessed by mathematical modeling of data from a meal tolerance test improved by 33% relative to control following consumption of 30 g/d HAM-RS2 for 4 wk in healthy men and women. Similar results have been shown in insulin-resistant men and women following 40 g/d HAM-RS2 consumption over a 12-wk period (14). These results have important implications for human health, because insulin...
resistance (i.e., impaired Sg) is a central pathophysiologic feature of metabolic syndrome, a cluster of risk factors for the development of atherosclerotic cardiovascular disease and diabetes mellitus.

The mechanisms underlying the effects of HAM-RS2 on Sg are not well understood. One hypothesis is that fermentation end products, particularly SCFA, are involved in a cascade of events that may lead to improved Sg (15–17). SCFA (acetate, propionate, and butyrate) are absorbed from the colon and appear to suppress the activity of hormone-sensitive lipase, reducing release of FFA and glycerol from adipose depots, although the exact cellular processes through which this occurs have not been fully described (18). Metabolic studies have shown that raising the circulating FFA level for several hours will reduce Sg and that lowering the FFA concentration will have the opposite effect, providing a possible mechanistic link between consumption of HAM-RS2 that undergoes fermentation in the colon and improved Sg (17,19,20).

In the present study, the effects of two doses of HAM-RS2 on Sg were evaluated in overweight and obese participants with increased waist circumference [as defined by the U.S. National Cholesterol Education Program Adult Treatment Panel III in its definition of metabolic syndrome (21)], a group that would be expected to contain a high proportion of insulin-resistant individuals (22).

Materials and Methods

Study design. This was a double-blind, randomized crossover study with three 4-wk treatment periods separated by 3-wk washout periods. The study was conducted at a clinical research center (Provident Clinical Research in Addison, IL) according to Good Clinical Practice Guidelines, the Declaration of Helsinki (2000) and the United States 21 Code of Federal Regulations. An institutional review board (Quorum Review IRB) approved the protocol before the study began and informed consent was obtained from all participants prior to the initiation of any study-related procedures.

Participants. Generally, healthy men and women 18–69 y of age, each with waist circumference 89.0 cm for females or 102.0 cm for males (23), were eligible for enrollment. Participants were excluded if they had a BMI ≥35.0 kg/m²; clinically important abnormal laboratory test results at screening; a history of cardiac, renal, hepatic, endocrine, pulmonary, biliary, pancreatic, gastrointestinal, or neurologic disorders; recent history of cancer; known sensitivity to any of the ingredients in the study foods; or active infections. The use of systemic corticosteroids, antibiotics, medications (other than hormonal contraceptives or postmenopausal sex hormones) or dietary supplements known to influence carbohydrate metabolism were not permitted during the study. Women planning to become pregnant during the study period were eligible for enrollment if they were using a medically acceptable contraceptive. All women of childbearing potential were not pregnant or lactating and not planning to become pregnant during the study period were eligible for enrollment if they were using a medically acceptable contraceptive. All participants agreed to maintain a stable body weight during the trial and follow their usual dietary, smoking, dietary supplement, and physical activity habits, except for consumption of the study products. Participants were queried at each visit to confirm compliance with these instructions.

Test products and study procedures. After screening (wk –1), eligible participants were randomly assigned to 1 of 6 treatment sequences. Participants ingested 1 of 3 study products during each 4-wk intervention period. This duration was based on previous studies that demonstrated changes in Sg after RS feeding at higher levels of intake for periods ranging from 24 h to 12 wk. The study product was high-amylase corn starch (Hi-maize 260) containing ~60% RS or a control starch (Amioca) containing no RS, both supplied by National Starch. Two intake levels of the high-amylase starch were tested, providing 15 or 30 g/d of HAM-RS2 (as measured by AOAC total dietary fiber method 991.43). The control was designed to match the content of digestible starch provided in 15 g/d HAM-RS2 (~11.6 g/d). Using the Atwater factor of 16.8 kJ/g for the digestible portion of starch, the approximate energy value of the control and low-dose products was matched (194 kJ/d), whereas the energy content in the high-dose condition was 388 kJ/d (24). The study product was provided in individually packaged, ready-to-use sachets that could be mixed into cold or room-temperature beverages or foods. Participants were instructed to consume 2 servings daily of their assigned study product at separate eating occasions during the day. During the middle of each treatment period, staff contacted participants via telephone or e-mail to encourage compliance with study product consumption. Participants were asked to consume the last dose of their assigned study product during the evening prior to test visits and to avoid vigorous physical activity the day prior to the test visit. Compliance was assessed by counting unopened sachets at the end of each treatment period in conjunction with a query regarding whether any servings were missed. At baseline and at the end of each treatment phase, participants completed a GI symptom survey that included a series of questions regarding the presence and severity on a 6-point scale from 0 (none) to 5 (much more than usual) of bloating, flatulence, diarrhea/loose stools, constipation, abdominal cramping, and nausea over the previous 7 d (25). Adverse events were assessed at each visit using a nonleading question to assess changes in health status since the previous query.

i.v. glucose tolerance tests. After an overnight fast (9–15 h, only water allowed), the insulin-modified i.v. glucose tolerance test was performed to assess Sg and secretion on the last day of each treatment period. Briefly, an i.v. catheter was placed in the antecubital space of each arm, one for collecting blood samples and the other for injecting glucose and insulin. At t = 0 min, a 300-mg/kg body weight i.v. glucose (50% dextrose solution) injection was administered over ~1.5 min. At t = 20 min, an i.v. injection of regular human insulin (0.03 U/kg, diluted to 1 mL with normal saline) was administered over ~1 min. Blood samples were collected at the following pre- and postglucose administration time points: t = 0, 5, 3, 7, 10, 12, 14, 16, 19, 22, 25, 30, 40, 50, 60, 75, 90, 120, 150, and 180 min.

Plasma glucose and insulin concentrations were measured and the values were entered into the MINMOD MILLENNIUM computer program (version 6.02; RN Bergman, USC) for determination of Sg and Sb (15–18,26). Valid fits were obtained for all tests with the model converging in all cases. AIRC was calculated as previously described (15,19). HOMA%S and HOMA%B were determined from fasting glucose and insulin values using the HOMA calculator (27).

Laboratory measurements. Clinical laboratory measurements were conducted by Medpace Laboratories. Plasma glucose was measured by photometry using a hexokinase reaction (28) and plasma insulin was determined via an electrochemiluminescence immunoassay (29). Serum hsCRP was measured by particle-enhanced immunonephelometry (CarDiaphase hsCRP; Dade Behring) on a BN* Systems Nephelometer (Dade Behring). Serum FFA were assessed by an enzymatic colorimetric assay (HR Series NEFA-HR, Wako) according to the manufacturer's instructions and fructosamine was measured by an end point colorimetric assay (30). Plasma adiponectin was measured by ELISA kit (Quantikine, R&D Systems) according to the manufacturer's instructions. SCFA were measured by GC in the laboratory of Dr. Papasani Subbaiah at the University of Illinois, Chicago, IL (31).

Fasting lipid profiles were drawn at screening and at the end of each treatment period. TC and TG in serum were measured by photometry on a Beckman Coulter AU2700/AU5400 Analyzer using Beckman Coulter reagents OSR 6216 and D8787–5G, respectively. HDL-C was isolated by a 2-step precipitation method with Mg-dextran sulfate (Sigma–Aldrich reagents) and measured by an enzymatic colorimetric assay (HR Series NEFA-HR, Wako) according to the manufacturer’s instructions and fructosamine was measured by an end point colorimetric assay (30). Plasma adiponectin was measured by ELISA kit (Quantikine, R&D Systems) according to the manufacturer’s instructions. SCFA were measured by GC in the laboratory of Dr. Papasani Subbaiah at the University of Illinois, Chicago, IL (31).

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circumstances. Non-HDL-C was calculated as the difference between TC and HDL-C.

Statistical analyses. Statistical analyses were conducted using SAS version 9.2 (SAS Institute). An evaluable sample of 27 participants was required to provide 80% power to detect an effect of 0.67 SD between treatment conditions with a 2-sided α = 0.05 after adjustment for 2 comparisons to the control condition. The assumption of normality of residuals from the final model for each outcome variable was investigated using the Shapiro-Wilk test. If it was determined that the distribution could not be approximated by a normal curve (P ≤ 0.01), then the analysis was completed after applying a natural logarithm transformation to improve kurtosis and/or skew.

The analysis of the primary and secondary outcome variables was completed on an efficacy evaluable and a per protocol sample. The efficacy evaluable sample included all participants who were randomized and controlled the and at least one active test condition. The per protocol sample was a subset of the efficacy evaluable sample that excluded participants who had protocol violations that could have influenced responses (e.g., poor compliance, not completing all test conditions, violations of inclusion/exclusion criteria, illness, use of an excluded medication during the treatment period). All decisions regarding exclusion of participants from the per protocol sample were finalized and documented prior to locking the study database and breaking the treatment code. The safety sample included all participants who were randomized and consumed at least one sachet of study product. Because there were no material differences apparent between the efficacy evaluable and per protocol samples, only data from the efficacy evaluable sample are presented.

Possible differences between treatment conditions for adverse events and other nominal variables were evaluated using Cochran’s chi-square test. Differences between conditions in responses for continuous variables were assessed using SAS PROC MIXED repeated-measures ANOVA, including subject as a random variable and terms for treatment condition, sex, sequence, period, and treatment condition by sex interaction. Models for glucose homeostasis variables derived from the i.v. glucose tolerance test also included the HOMA%S value from the control condition as a covariate based on the a priori expectation that response would be related to pretreatment S₃. Models were reduced in a stepwise manner until only treatment condition and any significant (P < 0.05) terms remained.

Sensitivity analyses were completed to assess the influence of age and menopausal status and to evaluate possible treatment × sequence and treatment × period interactions. Some significant period × sequence interactions were observed, but further investigation indicated there was not a clinically significant pattern, nor were there a greater number than would be expected given the number of tests being run, thus pooling of the data across treatment sequences was judged to be appropriate. A significant treatment × sex interaction was observed for the primary outcome variable, S₃, so results for all variables were analyzed and presented separately for men and women. Pairwise comparisons between treatment conditions were conducted and analyzed using Tukey’s procedure to adjust P values for multiple comparisons for each dependent variable. Values presented are least squares means ± SEM (between-subjects) unless otherwise noted. For variables where the analysis was based on log-transformed values, the geometric least squares mean is also presented.

Results

Of the 50 participants screened, 41 were randomized. One withdrew due to an adverse event (constipation) during the first treatment period (30 g/d HAM-RS2). Seven additional participants withdrew consent without completing at least the control and one other test condition; therefore, 33 participants were included in the efficacy evaluable population (Table 1).

Compliance based on interview and measurement of the unused study product was 98.3 ± 0.6% of expected servings of study product for the control condition, 96.7 ± 1.1% for the 15 g/d HAM-RS2 condition, and 96.4 ± 0.9% for the 30-g/d HAM-RS2 condition. There were no significant or clinically meaningful differences in body weight, waist circumference, or blood lipids at the end of each treatment condition (data not shown).

Glucose homeostasis. For S₃, the primary outcome variable, there were effects for HOMA%S (P = 0.0008), treatment condition (P = 0.018), and a treatment × sex interaction (P = 0.033). Accordingly, values for men and women are presented separately (Fig. 1; Table 2).

In men, values were higher during both the 15-g/d (P = 0.031) and 30-g/d HAM-RS2 (P = 0.019) conditions compared with the control condition (Fig. 1). When expressed as percent differences from control, the increases were 56.5% for the 15-g/d treatment condition (P = 0.018), and a treatment × sex interaction (P = 0.033). Accordingly, values for men and women are presented separately (Table 2).

In women, there were no significant or clinically meaningful differences in body weight, waist circumference, or blood lipids at the end of each treatment condition (data not shown).
Other metabolic variables. There were no significant differences between conditions in fasting concentrations of hsCRP, adiponectin, or fructosamine in men or women assessed at the end of each treatment condition (Table 3). In women, the plasma acetate concentration was greater in the 30-g/d HAM-RS2 condition than in the control ($P = 0.047$) (Table 2). A pooled analysis for acetate showed a main effect for treatment condition ($P = 0.0007$), but no treatment $\times$ sex interaction ($P = 0.93$).

![FIGURE 1](https://academic.oup.com/jn/article-abstract/142/4/717/4630912)

**TABLE 2** Glucose homeostasis and SCFA variables in men and women following 4-wk feeding periods for control (0 g/d HAM-RS2), 15 g/d HAM-RS2, and 30 g/d HAM-RS2

| Variable | Men | Control | 15 g/d HAM-RS2 | 30 g/d HAM-RS2 | $P$ |
|----------|-----|---------|----------------|----------------|-----|
| $n$      |     | 11      | 11             | 11             |     |
| $\ln S_0,$ $100 \times \text{min}^{-1}$ | 0.85 $\pm$ 0.14 (2.35) | 0.79 $\pm$ 0.14 (2.19) | 0.84 $\pm$ 0.14 (2.31) | 0.88 |
| $\ln \text{AIRG},$ pmol $\times$ L$^{-1} \times \text{min}$ | 7.98 $\pm$ 0.28 (2918) | 7.52 $\pm$ 0.28 (1844) | 7.88 $\pm$ 0.28 (2637) | 0.06 |
| Total FFA, mmol/L | 0.46 $\pm$ 0.05 | 0.50 $\pm$ 0.05 | 0.47 $\pm$ 0.05 | 0.81 |
| $\ln \text{Acetate},$ $\mu$mol/L | 4.3 $\pm$ 0.2 (75.2) | 4.5 $\pm$ 0.2 (90.5) | 4.6 $\pm$ 0.2 (96.2) | 0.61 |
| $\ln \text{Butyrate},$ $\mu$mol/L | $-0.2 \pm 0.4 (0.8)$ | $0.5 \pm 0.4 (1.6)$ | $0.9 \pm 0.4 (2.4)$ | 0.21 |
| $\ln \text{Propionate},$ $\mu$mol/L | 2.0 $\pm$ 0.2 (7.1) | 1.9 $\pm$ 0.2 (6.5) | 2.0 $\pm$ 0.2 (7.4) | 0.80 |
| $n$ | 22 | 21 | 22 |
| $\ln S_0,$ $100 \times \text{min}^{-1}$ | 2.54 $\pm$ 0.17 | 2.33 $\pm$ 0.18 | 2.34 $\pm$ 0.18 | 0.41 |
| $\ln \text{AIRG},$ pmol $\times$ L$^{-1} \times \text{min}$ | 2540 $\pm$ 340 | 2120 $\pm$ 344 | 2720 $\pm$ 349 | 0.14 |
| Total FFA, mmol/L | 0.56 $\pm$ 0.04 | 0.67 $\pm$ 0.05 | 0.59 $\pm$ 0.04 | 0.07 |
| $\ln \text{Acetate},$ $\mu$mol/L | 4.2 $\pm$ 0.1$^a$ (68.9) | 4.2 $\pm$ 0.1$^b$ (69.5) | 4.4 $\pm$ 0.1$^a$ (84.5) | 0.03 |
| $\ln \text{Butyrate},$ $\mu$mol/L | $-0.4 \pm 0.3 (0.7)$ | $-0.1 \pm 0.3 (0.9)$ | $-0.1 \pm 0.3 (0.9)$ | 0.73 |
| $\ln \text{Propionate},$ $\mu$mol/L | 1.8 $\pm$ 0.1 (6.0) | 1.7 $\pm$ 0.1 (5.4) | 1.8 $\pm$ 0.1 (6.1) | 0.59 |

1 Data are least squares mean $\pm$ SEM (geometric least squares mean of the transformed data). Means in a row with superscripts without a common letter differ, $P < 0.05$. AIRG, acute insulin response to i.v. glucose; HAM-RS2, high-amylose maize type 2 resistant starch; $S_0$, glucose effectiveness.

2 Glucose homeostasis variables and SCFA concentrations are from measurements in plasma; FFA concentrations were measured in serum.

There were no differences in circulating FFA concentrations in men or women across treatment conditions (Table 2).

**Tolerability and adverse events.** There were no differences between conditions in the frequencies of reported adverse events. Most adverse events were mild and not related to consumption of the study product. There were no differences in mean scores between conditions for the individual symptom components of the GI tolerability questionnaire (data not shown). Scores $\geq 4.0$ indicating that the frequency of each symptom occurred “more than usual” or “much more than usual” for flatulence was 9.1% for the control, 9.1% for the 15-g/d HAM-RS2 condition, and 33.3% for the 30-g/d HAM-RS2 treatment ($P = 0.014$ vs. control). There were no differences between conditions in scores $\geq 4.0$ for gas/bloating, nausea, loose stools, constipation, or GI cramping.

**Discussion**

The results of this study indicate that consumption of 15–30 g/d of HAM-RS2 improved $S_I$ in overweight and obese men. The improvement in $S_I$ relative to control is consistent with data from other studies of HAM-RS2 conducted in men and women in short-term and longer-term feeding trials (14–16). However, the present study is the first to our knowledge to show such improvements in $S_I$ at a level of intake as low as 15 g/d HAM-RS2. A previous study did not show an effect following intakes of 12 g/d HAM-RS2 for 6 wk; however, HOMA%S was used as an indicator of $S_I$, which is less sensitive compared to the method used in the present study (33). The magnitude of the increase in $S_I$ in men is similar to that observed with weight loss of $\sim$10% of body weight in obese individuals (34–36).

It is unclear why $S_I$ increased in men but not women in the present trial. One of the potential mechanisms for the insulin-
overnight periods may be important determinants of SI and suggested that FFA concentrations in the late evening and morning hours may raise levels more in participants with those that prevail overnight, because sympathetic activation in concentrations were obtained in the morning and may not reflect women across treatment conditions. However, fasting FFA more readily detectable in men than in women. In the present large bowel (44). Studies in which transit time is accelerated by a which may influence substrate availability for fermentation in the colon and capacity for colonic fermentation may influence the timing and quantity of SCFA absorption differently in men and women. Although there is considerable individual variability, men generally have accelerated transit times compared with women, which may influence substrate availability for fermentation in the large bowel (44). Studies in which transit time is accelerated by a sensitizing effects of fermentable fiber is that absorption of SCFA generated in the colon due to fermentation may trigger a reduction in release of FFA and glycerol from adipose depots, presumably through direct or indirect inhibition of hormone sensitive lipase (18). Numerous studies have demonstrated that maintenance of a lower FFA level for several hours enhances $S_I$ and elevation for several hours has the opposite effect (37–40). Hoeg et al. (41) recently showed that increasing FFA concentrations via intralipid infusion resulted in a decrease in whole-body $S_I$ by 38% in men but only 26% in matched women (42). There is evidence that SI varies across phases of the menstrual cycle, with observed values higher in the follicular phase and lower in the luteal phase (49–51). In the present study, there was a greater tendency to show improvement among women for whom tests were conducted during the same phase of the menstrual cycle than for women whose tests were not phase concordant. The sample of premenopausal women was too small to provide a meaningful statistical analysis of this effect. There is evidence that $S_I$ varies across phases of the menstrual cycle, with observed values higher in the follicular phase and lower in the luteal phase (49–51). In the present study, there was a greater tendency to show improvement among women for whom tests were conducted during the same phase of the menstrual cycle than for women whose tests were not phase concordant. The sample of premenopausal women was too small to provide a meaningful statistical analysis of this effect. However, postmenopausal women also had a lower response than men, suggesting that confounding due to menstrual cycle phase cannot entirely explain the difference in $S_I$ responses between men and women. Exclusion of women using contraceptive or postmenopausal sex hormones from the analysis did not alter the results.

There is evidence that $S_I$ varies across phases of the menstrual cycle, with observed values higher in the follicular phase and lower in the luteal phase (49–51). In the present study, there was some qualitative evidence that menstrual cycle may have confounded the results in premenopausal women, because there was a greater tendency to show improvement among women for whom tests were conducted during the same phase of the menstrual cycle than for women whose tests were not phase concordant. The sample of premenopausal women was too small to provide a meaningful statistical analysis of this effect. However, postmenopausal women also had a lower response than men, suggesting that confounding due to menstrual cycle phase cannot entirely explain the difference in $S_I$ responses between men and women. Exclusion of women using contraceptive or postmenopausal sex hormones from the analysis did not alter the results.

TABLE 3 Selected laboratory values in men and women following 4-wk feeding periods for control (0 g/d HAM-RS2), 15 g/d HAM-RS2, and 30 g/d HAM-RS2.

| Variable$^a$ | Control | 15 g/d HAM-RS2 | 30 g/d HAM-RS2 | P |
|-------------|---------|----------------|----------------|---|
| Men | | | | |
| $n$ | 11 | 11 | 11 | |
| In hsCRP, mg/L | 0.4 ± 0.2 (1.4) | 0.2 ± 0.2 (1.2) | 0.4 ± 0.2 (1.4) | 0.33 |
| Adiponectin, mg/L | 5.9 ± 0.6 | 5.8 ± 0.6 | 5.6 ± 0.6 | 0.70 |
| Fructosamine, μmol/L | 198 ± 6 | 198 ± 6 | 197 ± 6 | 0.98 |
| In HOMA%B | 4.4 ± 0.1 (78.1) | 4.1 ± 0.1 (61.5) | 4.3 ± 0.1 (70.3) | 0.18 |
| In HOMA%S | 4.6 ± 0.1 (97.7) | 4.7 ± 0.1 (115) | 4.6 ± 0.1 (86.4) | 0.38 |
| Fasting insulin, pmol/L | 62.5 ± 4.7 | 50.1 ± 4.7 | 58.5 ± 4.7 | 0.15 |
| In Fasting glucose, mmol/L | 1.7 ± 0.1 (5.4) | 1.8 ± 0.8 (5.8) | 1.8 ± 0.2 (5.7) | 0.40 |
| Women | | | | |
| $n$ | 22 | 21 | 22 | |
| In hsCRP, mg/L | 0.8 ± 0.2 (2.1) | 0.5 ± 0.2 (1.6) | 0.7 ± 0.2 (2.1) | 0.32 |
| In Adiponectin, mg/L | 2.3 ± 0.1 (10.4) | 2.4 ± 0.1 (10.9) | 2.4 ± 0.1 (10.6) | 0.30 |
| Fructosamine, μmol/L | 207 ± 4 | 205 ± 4 | 206 ± 4 | 0.70 |
| HOMA%B | 89.3 ± 6.1 | 84.2 ± 6.3 | 80.7 ± 6.1 | 0.38 |
| In HOMA%S | 4.5 ± 0.1 (91.1) | 4.6 ± 0.1 (97.6) | 4.7 ± 0.1 (113) | 0.10 |
| Fasting insulin, pmol/L | 56.2 ± 4.9 | 51.6 ± 5.0 | 47.5 ± 4.9 | 0.25 |
| Fasting glucose, mmol/L | 5.5 ± 0.1 | 5.5 ± 0.1 | 5.4 ± 0.1 | 0.29 |

$^a$ Data presented as least squares means ± SEM (geometric least squares means). Means in a row with superscripts without a common letter differ, P < 0.05. AIRG, acute insulin response to i.v. glucose; HAM-RS2, high-amylose maize type 2 resistant starch; HOMA%B, homeostasis model assessment of $β$-cell function; HOMA%S, homeostasis model assessment of insulin sensitivity; hsCRP, high-sensitivity CRP; SCFA, short-chain fatty acids; SG, glucose effectiveness; $S_I$, insulin sensitivity; $S_I$, homeostasis model assessment of insulin sensitivity.

$^b$ All outcomes were measured in plasma, except for hsCRP which was measured in serum.
Another possible explanation may relate to differences between men and women in baseline $S_I$. During the control condition, $S_I$ was ~26% higher for women than for men. It is possible that RS-induced improvements in $S_I$ are more likely in individuals with lower baseline levels. However, a post hoc analysis of responses in participants higher and lower than the median $S_I$ value within each sex did not provide clear evidence to support this possibility. Future research to better understand sex differences in $S_I$ and relationships to fermentation capacity, SCFA, FFA, and circulating hormones is warranted.

The present study has several limitations. Dietary intake, including dietary fiber, was not assessed; therefore, we cannot rule out that changes in dietary composition influenced the study results or a treatment × fiber intake interaction. However, each participant acted as his or her own control and maintained his or her usual dietary habits except for consumption of the study product, reducing the likelihood of such effects. Neither breath hydrogen nor fecal SCFA were measured, and levels of FFA, SCFA, adiponectin, hsCRP, and other blood analytes were measured only once at the end of each treatment condition and in the fasting state. Nevertheless, the improvement in $S_I$ observed in men at an intake as low as 15 g/d extends the results reported in previous studies after feeding 30–60 g/d of HAM-RS2.

In conclusion, the present results showed that consumption of 15 and 30 g/d of HAM-RS2 improved $S_I$ in overweight and obese men. No significant change in $S_I$ was observed in women for reasons that remain to be determined. Additional investigation will be required to further delineate the mechanisms responsible for improved $S_I$ during HAM-RS2 consumption.

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K.C.M., C.L.P., E.T.F., and T.M.R. designed the research; K.C.M., M.K.K., and A.L.L. conducted the research; K.C.M. and A.L.S. analyzed the data; K.C.M., C.L.P., E.T.F., A.L.S., and T.M.R. wrote the paper; and K.C.M. had primary responsibility for the final content. All authors read and approved the final manuscript.

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