A Snack Formulated with Ingredients to Slow Carbohydrate Digestion and Absorption Reduces the Glycemic Response in Humans: A Randomized Controlled Trial

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ABSTRACT This study compared the effect of a snack with ingredients to slow carbohydrate digestion (Test-snack) on postprandial blood glucose and insulin concentrations and subjective appetite ratings. We hypothesized that Test-snack would lower glucose and insulin responses and reduce appetite compared with a Control-snack. Overweight or obese subjects ($n = 17$) completed a randomized crossover study. Glucose, insulin, and appetite ratings were measured before consuming each snack or white bread (Bread) and over a period of 4 h. Subjects received Test-snack, Control-snack, or Bread in random order at least a week apart. The *a priori* primary outcome was the glucose response, and the secondary outcomes were appetite ratings and insulin responses. Mixed effects statistical models were used to perform analysis of variance in terms of the area under curve (AUC) and at specific time points. The 2-h AUC for glucose was significantly lower with Test-snack compared to Control-snack and Bread (AUC and 95% confidence intervals: Test = 2186.43 [1783.36–2589.51]; Control = 3293.75 [2893.97–3693.54]; Bread = 2800.28 [2405.79–3194.77] mg/dL · min). Four-hour AUC for glucose, and insulin, followed a similar pattern except that Test-snack did not differ from Bread. The glucose concentrations peaked at 45 min under all three conditions, but Test-snack elicited a lower response than Control-snack and Bread ($P < .01$). Test increased fullness and satisfaction and reduced hunger and prospective intake compared to Bread ($P < .02$), but was not significantly different from Control-snack. Ingredients that slow carbohydrate digestion in a snack reduce the postprandial glucose and insulin responses compared to a product without these ingredients.

KEYWORDS: • appetite • functional food • glucose • insulin • starch digestion

INTRODUCTION

DIETARY CARBOHYDRATES are digested and absorbed in the human gastrointestinal tract at different rates and to different extents depending upon the degree of polymerization, the crystalline form in the starch granule, and the processing or cooking.¹ The rate, extent, and location of carbohydrate digestion and absorption are factors that influence metabolic outcomes.² Growing scientific evidence suggests that an exaggerated postprandial glycemic response is a risk factor for several chronic diseases, such as diabetes and cardiovascular diseases.^{3–5} Recommendations to follow a healthy eating pattern to reduce the risk of chronic disease necessitate making the right food choices, including snacks. Thus, the identification of foods which are likely to have a positive impact on health is important.^{6,7}

The terms rapidly available glucose and slowly available glucose reflect the rate at which glucose becomes available for absorption in the human small intestine, and to a large extent this availability is determined by the rate of starch digestibility. Slowly digestible starch produces moderate changes in the postprandial glycemia compared to rapidly digestible starch, which is characterized by a fast increase in blood glucose concentration.⁸ The microstructure, mechanical properties, and degree of gelatinization of starch, the food matrix, and the interactions between the protein, starch, and lipid content influence starch digestibility.^{2,9}

This study investigated the effect of a savory snack (Test-snack) on the glycemic response in humans. Test-snack was formulated using a process in which whole grains, nuts, flour, and soluble fiber are packed into a hemisphere mold. The product is baked using a proprietary, low-moisture low-temperature process to minimize starch gelatinization, which reduces the rate at which it is digested. Since some of the ingredients also influence appetite, the effect on subjective appetite ratings was also evaluated. We hypothesized that Test-snack would reduce the blood glucose and insulin

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TABLE 1. ENERGY AND NUTRIENT AND STARCH DIGESTIBILITY CONTENT OF THE SNACKS

Test meal	Weight (g)	Energy (kcal) ^a	Protein (g)	Fat (g)	Carbohydrate (g)				Digestibility (g)	
					Total	Fiber	Sugar	Available ^b	RAG	SAG
Test-snack	56	224	5	12	34	10	1	24	16.2	6.7
Control-snack	56	250	5	11	35	2	13	33	30.2	2.8
Bread	45	121	3.6	1.2	24	0	2.4	24	22.6	1.4

Data provided by sponsor.

^aEnergy = 4 × protein + 9 × fat + 4 × available carbohydrate.

^bTotal carbohydrate minus dietary fiber (rounded to nearest 0.1 g).

RAG, rapidly available glucose; SAG, slowly available glucose.

responses, subjective ratings of hunger, and the desire to eat while increasing fullness and satisfaction, compared to a Control-snack made from ingredients commonly used in commercially available snacks (oats, peanuts, and corn syrup) and baked using conventional procedures. Test- and Control-snack contained similar amounts of carbohydrate, protein, and fat, but the available carbohydrate (avCHO) in Test-snack was 27% lower than Control-snack. Therefore, the two snacks were also compared with commercially available white bread (Bread) having the same amount of avCHO as Test-snack.

MATERIALS AND METHODS

Subjects

Twenty subjects, 18–60 years of age, were enrolled in a randomized, controlled crossover trial. Subjects having a body mass index between 25 and 30 kg/m² and who had no known history of diseases requiring regular medications were included in the study. Female subjects also completed a menstrual cycle questionnaire so that test days would fall within the luteal phase of the menstrual cycle.¹⁰ Exclusion criteria were as follows: (i) Intake of regular medications other than oral or injectable contraceptives, multivitamins, or aspirin taken in a stable dose for health maintenance, (ii) women who were pregnant or nursing, (iii) self-reported weight gain or loss of ≥5 kg in the last 3 months, (iv) fasting glucose >126 mg/dL, triglycerides >600 mg/dL, liver enzymes >3-fold above upper limits of normal and abnormal hemoglobin/immune status, and (v) allergy to nuts.

The study was approved by the Institutional Review Board of the Pennington Biomedical Research Center (PBRC), Baton Rouge. All procedures were in accordance with PBRC's ethical standards and with the Helsinki Declaration. Participants provided written informed consent. The trial was registered on ClinicaTrials.gov with registration number NCT02688283.

Study design

Subjects were tested on three days separated by at least 1 week. Each subject was randomly assigned to one of six unique orders for receiving the three interventions using computer-generated pseudo random numbers. The randomization was done by the study statistician. Study staff

except the study dietitian who assigned the snacks to subjects were blinded until data analysis. A nutrient analysis of the snacks is provided in Table 1.

At the first test visit, subjects arrived at the Center after a 10-h overnight fast (except water) and having refrained from alcohol and strenuous exercise for 24 h before the visit. An intravenous line was placed, and blood was drawn for baseline serum glucose and insulin measurements. Electronic visual analog scales (VASs)^{11,12} were then administered. Hunger, fullness, prospective intake, and satisfaction were assessed. The subjects were presented with the snack and given 5 min to eat it, following which blood was drawn from the intravenous line at 15, 30, 45, 60, 75, 90, 105, 120, 150, 180, and 240 min. VAS ratings were completed at 30, 60, 90, 120, 180, and 240 min. Subjects were asked about adverse events at each of the times that the VAS ratings were completed. Subjects returned on another day to repeat the test and were presented with a snack that they did not receive on a previous occasion.

Physicochemical properties

The characterization of the physicochemical properties of the Test- and Control-snack is previously described. Briefly, Test-snack had higher moisture content, peak force, porosity, and dietary fiber (soluble, insoluble, and total) than Control-snack.¹³

Statistical analysis

The sample size and power estimates were based on the incremental area under the curve (iAUC) ignoring the area below the fasting level for blood glucose measurements during a 2-h meal tolerance test. The null hypothesis was formulated to test equality in iAUC means after consuming test-snack, control-snack, or white bread. An estimate of variability (standard deviation) was obtained from findings reported in a similar study.¹⁴ The global level of significance for pairwise tests was controlled at the nominal 0.05 level using the Tukey–Kramer method. A sample of at least 18 protocol-completer participants was estimated to provide minimum power of 80% for detecting a difference of 13 mmol/L (10% of expected white bread mean) or more in any of the pairwise comparisons. It was estimated that 17 subjects would provide 76% power for detecting the differences in the main outcomes. To allow for ~20%

attrition, 20 subjects were enrolled. The 2-h value for the power analysis was selected, since it was hypothesized that the greatest difference would be at the 2-h time point. Assessments were made for an additional 2 h to ensure that the time of the maximal difference was not missed.

A mixed model analysis of variance (ANOVA) for a crossover trial was performed to analyze the glucose response, which was the primary outcome of the study. The secondary outcomes were VAS appetite ratings and insulin responses to the snack meals. The iAUC and the total AUC (tAUC, adding a constant to bring all values above fasting) for glucose and insulin were calculated. The tAUC for VAS ratings of hunger, fullness, satisfaction, and prospective food intake was determined. The changes in glucose and insulin concentrations and VAS ratings from baseline to 240 min were analyzed using a mixed model ANOVA for a doubly repeated measures crossover trial where the first repeated measure variable was test day, and the second variable was elapsed time since start of the snack meal. Given the spacing between assessment days, the analysis made the plausible assumption that the effects of intervention did not carry over from one day of assessments to a subsequent day of assessments for any of the outcomes.

The changes from baseline were summarized as least square means plotted for each snack across the assessment times. The model included factors with fixed effects, test day main effects, and treatment main effects, in addition to the random effects of subjects within treatment groups. Thus, differences in treatment effects were compared with respect to AUC and per time point. Furthermore, the model was adjusted for baseline value of glucose and insulin concentrations and VAS scores, as well as gender and age. Since some of the cells were hemolyzed during the blood draw, the effects within various models were adjusted for hemolysis in the analyses of the glucose and insulin concentrations. All analyses were performed using SAS 9.4 (SAS Institute, Cary, NC, USA).

RESULTS

Twenty subjects were enrolled in the study. Three subjects dropped out of the study due to schedule conflicts. There were no adverse events determined to be related to the study products. Differences in insulin concentrations and VAS scores were log transformed; hence, the confidence intervals (CIs) are provided. Descriptive characteristics of the subjects at baseline are summarized in Table 2.

Glucose

The 2-h iAUC for the glucose response was significantly lower with Test-snack compared to Control-snack and Bread ($P \leq .02$). Although the iAUC over the 4-h period showed that the Test-snack reduced the glucose response compared to Control ($P < .001$), it did not differ from Bread. The iAUC and tAUC over 2 and 4 h are presented in Table 3. The least square means of the change from baseline are presented in Figure 1a. The glucose peak concentration was at 45 min under all conditions, but the rise elicited by the

TABLE 2. SUBJECT CHARACTERISTICS AT BASELINE, INCLUDING AGE, BODY MASS INDEX, GENDER, AND RACE

	n = 17 Mean $\pm$ standard deviation
Age	29.2 $\pm$ 6.5
BMI (kg/m ²)	27.0 $\pm$ 1.6
	n (%)
Gender	
Female	9 (53)
Male	8 (47)
Race	
White	8 (47)
Black	9 (53)

BMI, body mass index.

Test-snack was less than that elicited by the Control-snack and Bread ($P < .01$).

Insulin

The 2-h iAUC for the serum insulin response was significantly higher with Control-snack compared to Test-snack and Bread ($P < .01$), but was not significantly different between Test-snack and Bread. The iAUC over the 4-h period showed a similar pattern. The tAUC and iAUC over 2 and 4 h are presented in Table 3. The least square means of the change from baseline are presented in Figure 1b. The change from baseline in serum glucose and insulin responses over four hours are presented in Table 4.

Hunger

The tAUC for the VAS ratings of hunger was significantly lower with Test-snack compared to Bread ($P = .024$), but was not significantly different between Test- and Control-snack or between Control-snack and Bread (tAUC [95% CI]: Test = 52.55 [41.77–61.47], Control = 60.22 [51.30–67.98], Bread = 64.19 [56.17–71.32], mm $\cdot$ min). Mean change in hunger ratings was significantly lower with Test-snack compared to Bread at 90 min ($P = .018$, Fig. 2a).

Fullness

The tAUC for the VAS ratings of fullness was significantly higher with Test- and Control-snack compared to Bread ($P \leq .01$), but was not significantly different between Test-snack and Control (tAUC [95% CI]: Test = 35.13 [25.21–48.95], Control = 31.30 [22.52–43.49], Bread = 19.54 [14.20–26.91], mm $\cdot$ min). Mean change in fullness ratings was significantly higher with Test-snack compared to Bread at 30, 60, 90, 120, and 180 min ($P < .03$). Mean change in fullness ratings was significantly higher with Control-snack compared to Bread at 30, 60, and 120 min ($P < .01$, Fig. 2b).

Prospective intake

The tAUC for the VAS ratings of the prospect of future consumption was significantly lower with Test- and

TABLE 3. TOTAL AND INCREMENTAL AREA UNDER THE CURVE (AUC AND IAUC, RESPECTIVELY) FOR THE SERUM GLUCOSE AND INSULIN RESPONSE OVER TWO AND FOUR HOURS

	AUC 0–2h	iAUC 0–2h	AUC 0–4h	iAUC 0–4h
Glucose (mg/dL · min)				
Test-snack	2186.43 (1783.36–2589.51) ^a	1038.94 (646.37–1431.51) ^a	5622.54 (5146.12–6098.96) ^a	1509.58 (1088.13–1931.04) ^a
Control-snack	3293.75 (2893.97–3693.54) ^b	2113.84 (1724.51–2503.17) ^b	7026.69 (6555.07–7498.31) ^b	2985.07 (2567.86–3402.28) ^b
Bread	2800.28 (2405.79–3194.77) ^b	1626.57 (1242.48–2010.67) ^b	5925.27 (5462.55–6387.98) ^a	1976.20 (1566.85–2385.55) ^a
Insulin (μ U/mL · min)				
Test-snack	1381.50 (987.41–1775.59) ^a	968.11 (576.18–1360.04) ^a	2520.11 (2054.13–2986.09) ^a	1256.58 (800.79–1712.37) ^a
Control-snack	2264.73 (1876.93–2652.52) ^b	1848.87 (1463.19–2234.55) ^b	3809.80 (3351.75–4267.86) ^b	2530.07 (2082.03–2978.12) ^b
Bread	1637.42 (1250.81–2024.03) ^a	1220.70 (836.19–1605.21) ^a	2646.09 (2191.45–3100.74) ^a	1400.63 (955.71–1845.54) ^a

Values are mean (95% confidence intervals).

^{ab}Means within a column with a different superscript are significantly different.

AUC, area under the curve; iAUC, incremental area under the curve.

Control-snack compared to Bread ($P \leq .02$), but was not significantly different between Test- and Control-snack (tAUC [95% CI]: Test = 62.07 [52.65–70.24], Control = 67.37 [58.96–74.85], Bread = 77.06 [69.96–83.55], mm · min). Mean difference in the ratings for prospective intake was significantly lower with Test-snack at 30, 60, 90, 120,

and 180 min compared to Bread and at 30, 60, and 90 min ($P < .03$) with Control-snack compared to Bread (Fig. 2c).

Satisfaction

The tAUC for the VAS ratings of satisfaction was significantly higher with Test- and Control-snack compared to Bread ($P \leq .02$), but was not significantly different between the Test- and Control-snack (tAUC [95% CI]: Test = 34.57 [26.08–45.83], Control = 35.79 [27.24–47.01], Bread = 22.68 [17.28–29.78], mm · min). Mean change in satisfaction ratings was significantly higher with Test-snack compared to Bread at 60 min and with Control-snack compared to Bread at 30, 60, and 120 min ($P \leq .02$, Fig. 2d). The change from baseline in subjective appetite ratings over four hours are presented in Table 5.

DISCUSSION

The results of this study are consistent with our hypothesis that Test-snack formulated with ingredients and processes to slow carbohydrate digestion would lower the glycemic response compared to Control-snack. Over a 2-h period, Test-snack reduced the postprandial glycemic response compared to Control-snack having the same amount of total carbohydrates but lacking some of the components that slow starch digestion and absorption. Although Test-snack and Bread had the same amount of avCHO, the postprandial glycemic response was lower with Test-snack compared to Bread. However, similar to Test-snack, Bread lowered the glycemic response compared to Control-snack. The differences between the Test-snack, Control-snack, and Bread conditions in the insulin response followed a pattern similar to the glucose response except that there was no difference between Test-snack and Bread. The glucose concentrations peaked at 45 min under all three conditions, but Test-snack elicited a significantly lower response than Control-snack and Bread.

Test-snack contained 24 g of avCHO per serving compared to 33 g in Control-snack. This 27% reduction in avCHO would be expected to reduce the glycemic response over a 2-h period in a nonlinear manner.^{15,16} The 2-h iAUC for the glucose response relative to that of 50 g of glucose,

FIG. 1. Changes in glucose and insulin concentrations from time 0 (before consuming the snack) to 4 h assessed through a meal tolerance test. (a) glucose (b) insulin. The least square means and confidence intervals are presented in Table 4.

FIG. 2. VAS appetite ratings from time 0 (before consuming the snack) to 4 h. (a) Hunger, (b) fullness, (c) prospect of future consumption, (d) satisfaction. The least square means and confidence intervals are presented in Table 5. VAS, visual analog scale.

termed the relative glucose response (RGR), can be estimated from the glycemic index (GI) and the grams of avCHO consumed (g) following the equation:

$$\text{RGR} = 1.49 \times \text{GI} \times (1 - e^{-0.222 \text{ g}})^{13,17}$$

From the equation, the RGR for 33 g of glucose is 77.4 (GI=100) and that for 24 g of glucose is 61.5. Thus, the 2-h iAUC for 24 g of glucose would be expected to be 79.5% that of 33 g (20.5% reduction). In our study, the mean 2-h iAUC elicited by Test-snack was 51% that of Control-snack. A reduction of 20.5% is 433.34 mg/dL · min; however, the observed difference between Test- and Control-snack was 1074.9 mg/dL · min. Therefore, 40% of the observed difference in the glycemic response can be attributed to the difference in the avCHO; the additional 60% reduction may be attributed to the slowing of avCHO digestion in Test-snack compared to Control-snack.

Test- and Control-snack were matched for their macro-nutrient content but the avCHO in the Test snack was lower than the Control snack. Therefore, the two snacks were also compared with white bread with the same amount of avCHO as Test-snack. The 2-h iAUC was lower with Test-snack compared to Bread. The fat content of Test-snack was greater

than the fat content of Bread. Adding 0, 5, 10, 20, and 40 g fat to a portion of white bread containing 50 g avCHO has been shown to reduce the glycemic response in a nonlinear manner over 2 h following the equation:

$$\text{iAUC} = (47 \times e^{-0.0522 \times \text{g}}) + 119^{13,18}$$

Test-snack had 25 g of fat per 50 g of avCHO and based on the equation may be expected to elicit a glycemic response that is 132 or 82% of the 2-h iAUC for 2.5 g of fat per 50 g avCHO in Bread. The Test-snack elicited a 2-h iAUC for glucose that was 64% of that after Bread (a 36% reduction). After adjusting for the fat content (64% divided by 0.82) results were in a value of 78% (22% reduction), which represent the glycemic response of Test-snack compared to Bread adjusted for fat, and may be attributed to the slowing of carbohydrate digestion by Test-snack.

The reduction in the serum glucose and insulin responses following consumption of Test-snack compared to the Control-snack is consistent with other studies,^{19–22} including a study by Peronnet *et al.* which showed that slowly digested starch reduces the postprandial plasma glucose and insulin concentrations in lean healthy adults. In that study,¹⁹ 16 female subjects consumed a breakfast meal (biscuits)

TABLE 4. CHANGES IN GLUCOSE (MG/DL) AND INSULIN (μ U/ML) CONCENTRATIONS FROM BASELINE (TIME 0) ASSESSED OVER FOUR HOURS THROUGH A MEAL TOLERANCE TEST

Time (min)	Glucose			Insulin		
	Control snack	Test snack	Bread	Control snack	Test snack	Bread
15	5.97 (1.91–10.02)	–0.56 (–4.79 to 3.68)	2.38 (–1.45 to 6.20)	2.32 (0.19–5.19)	–0.23 (–1.76 to 1.86)	0.14 (–1.35 to 2.09)
30	23.36 (18.69–28.02)	9.83 (5.03–14.63)	12.05 (7.64–16.46)	9.52 (5.45–15.05)	6.05 (2.78–10.54)	4.85 (2.16–8.43)
45	26.48 (21.10–31.87)	12.90 (7.38–18.42)	21.88 (16.75–27.00)	12.60 (8.23–18.31)	8.04 (4.59–12.61)	9.48 (6.09–13.83)
60	21.59 (16.34–26.83)	10.63 (5.23–16.03)	21.75 (16.72–26.78)	11.74 (7.92–16.62)	6.94 (3.99–10.76)	10.14 (6.91–14.18)
75	17.80 (12.81–22.78)	7.31 (2.12–12.49)	18.36 (13.58–23.13)	9.89 (6.43–14.32)	5.21 (2.62–8.58)	8.42 (5.49–12.08)
90	16.14 (10.86–21.42)	4.52 (–0.80 to 9.85)	13.06 (7.96–18.17)	10.92 (7.32–15.49)	3.56 (1.43–6.31)	5.56 (3.27–8.41)
105	10.77 (6.03–15.51)	2.05 (–2.78 to 6.87)	7.29 (2.78–11.79)	7.89 (5.07–11.42)	1.56 (–0.06 to 3.63)	2.90 (1.24–4.94)
120	9.69 (5.11–14.27)	3.79 (–0.95 to 8.53)	4.89 (0.57–9.22)	5.80 (3.21–9.12)	1.07 (–0.56 to 3.21)	1.96 (0.34–3.99)
150	4.93 (–0.13 to 10.00)	3.25 (–1.88 to 8.39)	0.33 (–4.42 to 5.07)	2.85 (0.65–5.78)	0.87 (–0.90 to 3.25)	0.06 (–1.35 to 1.90)
180	3.88 (–1.03 to 8.80)	–0.25 (–5.38 to 4.88)	–1.21 (–5.88 to 3.46)	1.05 (–1.22 to 4.39)	–0.38 (–2.23 to 2.38)	–1.27 (–2.73 to 0.83)
240	–3.06 (–7.91 to 1.79)	–4.39 (–9.40 to 0.63)	–3.65 (–8.36 to 1.06)	–1.30 (–2.51 to 0.33)	–1.99 (–3.06 to –0.53)	–1.62 (–2.70 to –0.20)

Values are least square means (95% confidence intervals).

TABLE 5. CHANGES IN SUBJECTIVE APPETITE RATINGS FROM BASELINE (TIME 0) ASSESSED OVER FOUR HOURS THROUGH VISUAL ANALOG SCALES

Time (min)	Hunger			Fullness		
	Control snack	Test snack	Bread	Control snack	Test snack	Bread
30	–13.90 (–27.59 to –1.67)	–24.19 (–39.59 to –10.49)	–13.14 (–26.33 to –1.32)	38.15 (25.64–51.89)	39.49 (26.64–53.64)	17.01 (6.68–28.33)
60	–12.86 (–27.43 to 0.06)	–12.19 (–27.14 to 1.02)	–9.98 (–23.76 to 2.28)	32.42 (22.05–43.67)	39.65 (28.56–51.67)	17.10 (8.15–26.79)
90	–5.33 (–15.39 to 3.86)	–19.41 (–31.17 to –8.70)	–2.99 (–12.53 to 5.75)	26.59 (16.47–37.59)	33.93 (23.07–45.74)	15.70 (6.68–25.48)
120	0.39 (–10.52 to 10.24)	–10.39 (–22.87 to 0.83)	5.68 (–4.24 to 14.66)	26.07 (16.31–36.65)	30.62 (20.38–41.72)	10.12 (1.89–19.01)
180	2.44 (–10.12 to 13.57)	–2.22 (–15.61 to 9.63)	11.95 (1.10–21.63)	12.87 (3.75–22.78)	15.25 (5.93–25.39)	3.58 (–4.48 to 12.30)
240	20.55 (6.97–32.17)	7.23 (–8.80 to 20.92)	26.82 (14.68–37.25)	6.07 (–3.51 to 16.61)	7.67 (–2.24 to 18.59)	–1.08 (–9.79 to 8.45)
Time (min)	Prospective intake			Satisfaction		
	Control snack	Test snack	Bread	Control snack	Test snack	Bread
30	–24.03 (–35.00 to –13.94)	–21.38 (–32.40 to –11.28)	–6.56 (–15.78 to 1.94)	33.77 (20.98–47.91)	20.34 (8.38–33.61)	7.95 (–2.27 to 19.23)
60	–16.65 (–27.43 to –6.78)	–19.16 (–30.45 to –8.84)	–2.28 (–11.52 to 6.20)	29.41 (19.01–40.70)	28.66 (17.87–40.43)	11.48 (2.56–21.16)
90	–15.98 (–26.47 to –6.36)	–19.20 (–30.26 to –9.08)	–0.16 (–9.01 to 7.99)	23.63 (12.88–35.39)	16.04 (5.53–27.59)	8.69 (–0.69 to 18.94)
120	–8.76 (–19.12 to 0.71)	–18.62 (–30.23 to –8.05)	1.94 (–7.09 to 10.21)	19.86 (9.56–31.13)	16.03 (5.62–27.45)	2.07 (–6.58 to 11.52)
180	–1.60 (–11.29 to 7.25)	–7.98 (–18.42 to 1.55)	6.24 (–2.40 to 14.14)	10.81 (1.99–20.39)	7.04 (–1.80 to 16.66)	–1.34 (–9.10 to 7.08)
240	5.17 (–5.67 to 14.90)	4.32 (–6.92 to 14.39)	13.70 (4.10–22.35)	3.48 (–6.24 to 14.20)	0.17 (–9.51 to 10.87)	–8.03 (–16.58 to 1.38)

Values are least square means (95% confidence intervals) in mm.

containing a high content of slowly digested starch or a meal with low content of slowly digested starch, and plasma glucose kinetics was evaluated by AUC analysis. Over a 3-h period, the mean plasma glucose concentration was significantly lower by ~38–44% following consumption of biscuits high in slowly digested starch. The slowly digested starch ranged from 15.3 to 17 g in the high content groups compared with 0.1 g in the low content group. In our study, Test-snack had 2.4 times (Table 1) the slowly available glucose in Control-snack and produced a 51% reduction. However, the glycemic response depends upon physicochemical properties of the dietary carbohydrates. Compared to Control-snack, Test-snack had lower porosity, which may have reduced the surface area available for amylase activity and greater viscosity, which may have lowered starch gelatinization.^{2,9} These qualities may also be responsible for the lower peak glucose concentration and more sustained elevation in the glycemic response curve elicited by Test-snack compared to Control-snack and Bread.

The improvement in the glycemic response may occur as a result of a reduction in the blood glucose response with insulin being unchanged or a reduction in the insulin response with glucose remaining unchanged or a reduction in glucose and insulin responses. We observed a reduction in the glucose and insulin responses to the Test-snack compared to Control-snack. However, in other studies, slowly and rapidly digested starch elicited similar glycemic responses,^{23,24} but the insulin response, as well as the rate of exogenous glucose appearance and the rate of endogenous glucose production, reduced when the digestibility of starch was slowed. Furthermore, the glucose clearance rate also reduced, which may account for the lack of a difference in the glycemic response as glucose remains in circulation for a longer period of time following consumption of foods containing slowly digested starch.²⁴

Interestingly, over 4 h, both Test- and Control-snack significantly increased subjective ratings of fullness and satisfaction and reduced the prospect of future consumption compared to Bread. Test-snack also reduced hunger compared to Bread. These effects were observed even though there was no difference in the glycemic response between Test-snack and Bread over 4 h, and the glycemic response was lower after consumption of Bread compared to Control-snack. There were no significant differences in the appetite ratings over 4 h between Test- and Control-snack, despite the difference in the glycemic response following their consumption. However, Test- and Control-snack were similar in their energy content, whereas Bread had lower energy content. Nevertheless, studies that have evaluated the effect of the glycemic response on satiety by comparing foods with low or high glycemic indices have produced inconsistent results.^{25–28}

The study is limited in that techniques to enable calculation of glucose kinetics were not used in this study, which would have provided a better understanding of the differences in the serum glucose excursions. Furthermore, only subjective ratings of appetite were assessed. Quantifying caloric intake through a food intake test would have corroborated the results.

In conclusion, including ingredients and processes to slow carbohydrate digestion and absorption in a snack reduces the glycemic and insulinemic responses compared to a product without these components. Slowing of starch digestion influences subjective appetite ratings independent of the glycemic response. Foods designed to slow starch digestion can help consumers meet their need to moderate the postprandial glycemic response.

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AUTHORS' CONTRIBUTIONS

C.J.R. helped design the study, drafted the article, and had final authority to determine its content. F.L.G. supervised in the designing of the study and the conduct of the study. Y.P., J.J., and Y.C. conceived of the study and assisted in designing the study. M.N. developed and produced the test- and control clusters. W.D.J., S.L., and D.Z. performed the statistical analyses. All coauthors reviewed and approved the final version of the article.

AUTHOR DISCLOSURE STATEMENT

Y.P., M.N., J.J., and Y.C. are employees of PepsiCo Inc. The Pennington Biomedical Research Center received the grant to conduct the study. C.J.R., W.D.J., S.L., D.Z., and F.L.G. have no conflicts of interest to report.

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REFERENCES

1. Cummings JH, Roberfroid MB, Andersson H, *et al.*: A new look at dietary carbohydrate: Chemistry, physiology and health. Paris Carbohydrate Group. *Eur J Clin Nutr* 1997;51:417–423.
2. Parada J, Santos JL: Interactions among starch, lipids, and proteins in foods: microstructure control for glycemic response modulation. *Crit Rev Food Sci Nutr* 2015;56:2362–2369.
3. Bhupathiraju SN, Tobias DK, Malik VS, *et al.*: Glycemic index, glycemic load, and risk of type 2 diabetes: Results from 3 large US cohorts and an updated meta-analysis. *Am J Clin Nutr* 2014; 100:218–232.
4. Larsen TM, Dalskov SM, van Baak M, *et al.*: Diets with high or low protein content and glycemic index for weight-loss maintenance. *N Engl J Med* 2010;363:2102–2113.

5. Jakobsen MU, Dethlefsen C, Joensen AM, *et al.*: Intake of carbohydrates compared with intake of saturated fatty acids and risk of myocardial infarction: Importance of the glycemic index. *Am J Clin Nutr* 2010;91:1764–1768.
6. USDA, HHS: Dietary Guidelines for Americans 2015–2020. https://health.gov/dietaryguidelines/2015/resources/2015–2020_Dietary_Guidelines.pdf
7. US National Library of Medicine: Snacks for Adults. 2017; <https://medlineplus.gov/ency/patientinstructions/000338.htm>
8. Englyst HN, Kingman SM, Cummings JH: Classification and measurement of nutritionally important starch fractions. *Eur J Clin Nutr* 1992;46 Suppl 2:S33–S50.
9. Singh J, Kaur L, Singh H: Food microstructure and starch digestion. *Adv Food Nutr Res* 2013;70:137–179.
10. Dye L, Blundell JE: Menstrual cycle and appetite control: Implications for weight regulation. *Hum Reprod* 1997;12:1142–1151.
11. Flint A, Raben A, Blundell JE, Astrup A: Reproducibility, power and validity of visual analogue scales in assessment of appetite sensations in single test meal studies. *Int J Obes Relat Metab Disord* 2000;24:38–48.
12. Blundell J, de Graaf C, Hulshof T, *et al.*: Appetite control: Methodological aspects of the evaluation of foods. *Obes Rev* 2010;11:251–270.
13. Wolever TMS, Jenkins AL, Yang J, *et al.*: An optimized, slowly digested savory cluster reduced postprandial glucose and insulin responses in healthy human subjects. *Curr Dev Nutr* 2019;3:nzz006.
14. Panahi S, Ezatagha A, Jovanovski E, *et al.*: Glycemic effect of oat and barley beta-glucan when incorporated into a snack bar: A dose escalation study. *J Am Coll Nutr* 2014;33:442–449.
15. Lee BM, Wolever TM: Effect of glucose, sucrose and fructose on plasma glucose and insulin responses in normal humans: Comparison with white bread. *Eur J Clin Nutr* 1998;52:924–928.
16. Wolever TM, Bolognesi C: Source and amount of carbohydrate affect postprandial glucose and insulin in normal subjects. *J Nutr* 1996;126:2798–2806.
17. Jenkins DJ, Wolever TM, Taylor RH, *et al.*: Glycemic index of foods: A physiological basis for carbohydrate exchange. *Am J Clin Nutr* 1981;34:362–366.
18. Owen B, Wolever TMS: Effect of fat on glycaemic responses in normal subjects: A dose-response study. *Nutr Res* 2003;23:1341–1347.
19. Peronnet F, Meynier A, Sauvinet V, *et al.*: Plasma glucose kinetics and response of insulin and GIP following a cereal breakfast in female subjects: Effect of starch digestibility. *Eur J Clin Nutr* 2015;69:740–745.
20. Vinoy S, Normand S, Meynier A, *et al.*: Cereal processing influences postprandial glucose metabolism as well as the GI effect. *J Am Coll Nutr* 2013;32:79–91.
21. Nazare JA, de Rougemont A, Normand S, *et al.*: Effect of postprandial modulation of glucose availability: Short- and long-term analysis. *Br J Nutr* 2010;103:1461–1470.
22. Eells LJ, Seal CJ, Kettlitz B, Bal W, Mathers JC: Postprandial glycaemic, lipaemic and haemostatic responses to ingestion of rapidly and slowly digested starches in healthy young women. *Br J Nutr* 2005;94:948–955.
23. Eelderink C, Moerdijk-Poortvliet TC, Wang H, *et al.*: The glycemic response does not reflect the in vivo starch digestibility of fiber-rich wheat products in healthy men. *J Nutr* 2012;142:258–263.
24. Eelderink C, Schepers M, Preston T, Vonk RJ, Oudhuis L, Priebe MG: Slowly and rapidly digestible starchy foods can elicit a similar glycemic response because of differential tissue glucose uptake in healthy men. *Am J Clin Nutr* 2012;96:1017–1024.
25. Holt SH, Miller JC, Petocz P, Farmakalidis E: A satiety index of common foods. *Eur J Clin Nutr* 1995;49:675–690.
26. Anderson GH, Catherine NL, Woodend DM, Wolever TM: Inverse association between the effect of carbohydrates on blood glucose and subsequent short-term food intake in young men. *Am J Clin Nutr* 2002;76:1023–1030.
27. Anderson GH, Woodend D: Effect of glycemic carbohydrates on short-term satiety and food intake. *Nutr Rev* 2003;61(5 Pt 2): S17–S26.
28. Liu AG, Most MM, Brashear MM, Johnson WD, Cefalu WT, Greenway FL: Reducing the glycemic index or carbohydrate content of mixed meals reduces postprandial glycemia and insulinemia over the entire day but does not affect satiety. *Diabetes Care* 2012;35:1633–1637.