

Inverse association between the effect of carbohydrates on blood glucose and subsequent short-term food intake in young men¹⁻³

G Harvey Anderson, Nicole LA Catherine, Dianne M Woodend, and Thomas MS Wolever

ABSTRACT

Background: A primary mechanism by which carbohydrates are thought to regulate satiety and food intake is through their effect on blood glucose.

Objectives: The objectives were to describe the effect of defined carbohydrate preloads on food intake and blood glucose and to determine the association between food intake and blood glucose.

Design: Three experiments were conducted in which selected carbohydrates as 1255-kJ isovolumetric beverages were administered to young men after an overnight fast. Measurements of blood glucose and appetite were made at specified times during the next 60 min. Food intake was measured at 60 min.

Results: Glucose resulted in the highest glycemic response, which was followed, in order, by the responses to polycose, sucrose, amylopectin, a fructose-glucose mixture, and amylose. The high-glycemic-index preloads (glucose, polycose, and sucrose) resulted in lower mealtime energy intake during a test meal at 1 h, but the low-glycemic-index preloads (amylose, amylopectin, and a fructose-glucose mixture) did not. An inverse relation was observed between the blood glucose concentrations in the area under the curve and the subjective appetite ($r = -0.23$, $P < 0.05$) and food intake at 60 min ($r = -0.24$, $P < 0.05$).

Conclusions: Food intake and subjective appetite are inversely associated with blood glucose response in the 60 min after consumption of carbohydrates. Carbohydrates with a high glycemic index (glucose, polycose, and sucrose) suppress subjective appetite and food intake in the short term, but those with a low glycemic index (amylose and amylopectin) do not. *Am J Clin Nutr* 2002;76:1023-30.

KEY WORDS Glucose, sucrose, fructose, sugars, carbohydrates, amylose, amylopectin, glycemic response, hunger, satiety, appetite, energy intake, preloads, young men

INTRODUCTION

Carbohydrates are the main source of energy in our diets (1), and, in addition, their ingestion affects many aspects of brain function, including the regulation of food intake (2). The concept that glucose regulates satiety and food intake is the basis for the glucostatic theory of food intake regulation (3), which proposes that blood glucose concentrations be closely monitored and that food be ingested when the utilization of glucose by various organs is insufficient (4). Conversely, satiety and the termination of eating will occur after an increase in blood glucose.

In recent years, the concept has emerged that foods with a low glycemic index are associated with greater satiety than are foods with a high glycemic index. An inverse relation between the glycemic response to mixed meals and satiety within 2-6 h has been reported (5). However, the temporal associations among satiety, the ingestion of high- and low-glycemic-index foods, and blood glucose concentrations have not been delineated. Thus, the rapid increase in blood glucose after the ingestion of rapidly digestible, high-glycemic-index carbohydrates may increase satiety in the short term, whereas the consumption of slowly digestible, low-glycemic-index carbohydrates, which results in slow, prolonged glucose disposal, may be more effective in sustaining satiety in the long term.

Although blood glucose has not been monitored concurrently, several studies have shown an inverse relation between the consumption of high-glycemic-index carbohydrates and food intake within the next hour. Compared with a water control, 25-, 50-, and 75-g sucrose preloads in the form of a beverage decreased the amount of energy consumed at a test meal 1 h later (6). Similarly, many studies have reported that the ingestion of beverages containing 50 g glucose suppresses food intake within 1 h (7-10). The threshold dose required for the detection of glucose energy has not been determined (10). However, its glycemic effect suggests that the dose might be lower than that observed for sucrose. Glucose has a glycemic index that is $\approx 40\%$ higher than that of sucrose (11).

Thus, the purpose of this study was to test the hypothesis that the short-term response of appetite and food intake to the consumption of carbohydrates is inversely related to the effects of carbohydrates on blood glucose. Pure carbohydrate preloads with a range of glycemic responses were selected, and their effects on satiety and energy intake in young men within 1 h were examined.

¹ From the Department of Nutritional Sciences, Faculty of Medicine, University of Toronto, Canada.

² Supported by a grant from the International Life Science Institute (ILSI) of Japan. NLAC was the recipient of a University of Toronto Open Fellowship and an International Student Recruitment Award.

³ Address reprint requests to GH Anderson, Department of Nutritional Sciences, Faculty of Medicine, University of Toronto, Fitzgerald Building, 150 College Street, Toronto, Ontario, Canada M5S 3E2. E-mail: harvey.anderson@utoronto.ca.

Received September 19, 2001.

Accepted for publication January 17, 2002.

SUBJECTS AND METHODS

Subjects

Healthy, nonsmoking men aged 18–35 y with a body mass index (BMI; in kg/m²) of 20–25 (12) were recruited to participate in 3 experiments through advertisements posted across the University of Toronto campus. Those with diabetes, those who did not eat breakfast, and those who were on a diet or taking medicine were excluded from all studies. Those who scored ≥ 11 on a questionnaire on eating habits were identified as restrained eaters (13) and were excluded.

Eight subjects were recruited for experiment 1, and all 8 completed the study. Eighteen subjects were recruited for experiments 2 and 3, and 14 subjects in each experiment provided complete data for all sessions. The treatments were randomly assigned to subjects in each experiment. The study procedures were approved by the Human Subjects Review Committee, Ethics Review Office, of the University of Toronto.

Study design

The objective of experiment 1 was to define the glycemic response to the test carbohydrates. Four treatment substances were tested in a counterbalanced order, including polyose (Abbott Laboratories, North Chicago, IL), amylopectin (Amioca; National Starch and Chemical Company, Bridgewater, NJ), high-amylose cornstarch (Hylon VII; National Starch and Chemical Company), and sucrose (Redpath sugar; Tate and Lyle North American Sugars, Toronto, Canada). All substances were provided as 200-mL beverages containing 75 g carbohydrate. An additional 100 mL water was given in a separate glass in an effort to minimize the aftertaste.

The objective of experiment 2 was to determine the effect of the 4 carbohydrate sources on subjective measures of satiety and short-term food intake. Five substances were tested: polyose, sucrose, amylose, amylopectin, and sucralose. Sucralose functioned as a sweet control. Each treatment contained 75 g carbohydrate and was dissolved in 200 mL cold spring water. An additional 200 mL spring water was consumed in a separate glass to minimize the aftertaste; this brought the total volume consumed to 400 mL. Substances were matched for sweetness by the addition of sucralose, a nonenergetic sweetener (McNeil Specialty Products Company, New Brunswick, NJ). Sucralose was chosen because it does not affect carbohydrate metabolism, blood glucose, blood fructose, or insulin secretion (14). All test beverages were prepared 1 h before consumption, stored in a refrigerator, and served chilled. Besides sucralose, lemon from concentrate was added in an attempt to match for palatability.

The objective of experiment 3 was to directly examine the relation between the glycemic response to the selected carbohydrates and the effect on satiety and food intake. Five test beverages—polyose, sucrose, glucose, a fructose-glucose mixture, and the sucralose control—were administered in a counterbalanced order. The fructose-glucose mixture contained 80% fructose and 20% glucose. Glucose was added to decrease the extent of malabsorption observed with the consumption of high doses (> 50 g) of fructose (15). Each test beverage contained 75 g carbohydrate dissolved in 200 mL spring water. An additional 200 mL spring water was consumed in a separate glass, which brought the total volume consumed to 400 mL. Sucralose and lemon concentrate were added in an attempt to match for sweetness and palatability.

Protocol

Subjects chose a time between 0700 and 1000 at which to participate in each experiment, and they were asked to arrive at the

same time for each subsequent session. Subjects arrived for each session after an overnight (10–12 h) fast. Water was allowed up to 1 h before the start of each session. On arrival, those participants whose answers on a questionnaire on sleep habits and stress factors indicated feelings of illness, atypical fatigue, or stress were asked to reschedule.

In experiment 1, a baseline blood sample was taken and the participants were then asked to proceed to a taste panel room where they were given 1 of the 5 test beverages in an opaque cup and a separate glass containing water. All beverages were consumed in < 5 min. The subjects then returned to a study room and filled out a questionnaire assessing the palatability and sweetness of the test beverages. At precisely 15, 30, 45, and 60 min after consumption of the test beverage, finger-prick blood samples were obtained with the use of a Monojector Lancet Device (Sherwood Medical, St Louis). One drop of blood was placed on a One Touch, *FastTake* test strip for immediate readings of glucose concentration with the *FastTake* monitor (LifeScan Canada Ltd, Burnaby, Canada). Subjects remained seated throughout the experimental session.

On arrival for experiment 2, subjects filled out a questionnaire on sleep habits and stress factors and completed baseline visual analogue scale (VAS) questionnaires measuring their motivation to eat and physical comfort. The motivation-to-eat VAS questions were also administered at 15, 30, 45, and 60 min. The physical-comfort VAS questionnaires were administered at baseline and at 60 min, immediately before the test meal. Each page of the questionnaire was folded out of view after each rating. The subjects remained seated throughout the study period.

The experimental procedure in experiment 3 was similar to that in experiment 2, with the exception of the frequency and timing of the physical-comfort VAS questionnaire and the addition of blood glucose measures. Blood glucose was measured at baseline and at 20, 37, and 65 min after consumption of the test beverage. The physical-comfort questionnaire was completed at 15, 30, 45, and 60 min.

At 60 min after treatment during experiments 2 and 3, the subjects returned to the taste panel room and were served a pizza lunch and 1.5 L bottled spring water (Crystal Springs; Aquaterre Corp, St-Laurent, Canada). Four varieties of small, round (5-inch diameter) pizzas (Deluxe, Pepperoni, 3 Cheese, and Deli Lovers; McCain Foods Ltd, Florenceville, Canada) purchased from local retailers were available. The cooked pizzas were weighed before serving, and the amount left after the meal was subtracted from the initial weight to provide a measure of food intake. An advantage of using these pizzas was the lack of an outer crust, which results in a pizza with a more uniform energy content and eliminates the possibility that the subject will eat the energy-denser filling and leave the outside crust of the pizza.

The subjects ranked the pizza according to their preference before the sessions. The participants were served 2 pizzas of their first choice and 1 each of their second and third choices per tray. The subjects were told that a second identical hot tray would be presented in 6 min and were specifically instructed to eat until they were “comfortably full.”

Each variety of pizza was weighed separately and the energy consumed (in kJ) was calculated by converting the net weight consumed to kJ consumed by use of information provided by the manufacturer (McCain). The bottled water was also weighed before and after the test meal to calculate the net amount ingested during the meal. On termination of the test meal, the subjects



TABLE 1Effects of time and treatments on changes from baseline blood glucose concentrations in experiment 1¹

Time (min)	Treatment			
	Amylopectin	Amylose	Polycose	Sucrose
	<i>mmol/L</i>			
15	1.11 ± 0.5 ^a	0.39 ± 0.3 ^b	3.19 ± 0.9 ^c	2.6 ± 0.4 ^d
30	1.73 ± 0.6 ^a	0.26 ± 0.4 ^b	3.58 ± 1.7 ^c	3.16 ± 1.6 ^c
45	1.79 ± 0.9 ^{a,b}	0.35 ± 0.5 ^c	2.93 ± 1.8 ^b	1.70 ± 1.4 ^a
60	1.28 ± 0.8 ^a	0.10 ± 0.4 ^b	1.48 ± 0.9 ^a	0.93 ± 1.1 ^a

¹ $\bar{x} \pm \text{SEM}$; $n = 8$. Means in the same row with different superscript letters are significantly different, $P < 0.05$. Overall ANOVA: Treatment effect, $P < 0.001$; time effect, $P < 0.001$; time-by-treatment interaction, $P < 0.001$. Mean baseline blood glucose did not differ significantly between treatments. The overall mean baseline blood glucose concentration was 5.05 ± 0.5 mmol/L.

rated the palatability of the test meal and completed the postmeal motivation-to-eat questionnaire.

The motivation-to-eat VAS questionnaire, used to assess appetite, was composed of 4 questions or scales: 1) How strong is your desire to eat? (“very weak” to “very strong”), 2) How hungry do you feel? (“not hungry at all” to “as hungry as I’ve ever felt”), 3) How full do you feel? (“not full at all” to “very full”), and 4) How much food do you think you could eat? (“nothing at all” to “a large amount”). Each VAS consisted of a 100-mm line anchored at the beginning and end by opposing statements (6, 16). The subjects marked an “X” on the line to indicate their feelings at that given moment. Scores were determined by measuring the distance (in mm) from the left starting point of the line to the intersection of the “X.”

The palatability and sweetness of the test solutions were measured with the VAS. To measure palatability, the question “How pleasant have you found the drinks?” could be answered anywhere on a line anchored at the beginning and end by the statements “not at all pleasant” and “very pleasant.” To measure sweetness, the question “How sweet have you found the drinks?” could be answered anywhere on a line anchored at the beginning and end by the statements “not at all” and “very sweet.” Similarly, physical comfort was assessed by answers to the question “How well do you feel?” that could range from “not well at all” to “very well.”

Statistical analysis

All statistical analyses were conducted with SAS software, version 7.1 (SAS Institute, Inc, Cary, NC). One-way repeated-measures analysis of variance (ANOVA) was performed to test for the effect of the test beverage (treatment) on outcome variables, including the area under the curve (AUC) for blood glucose, energy intake, water intake, palatability, sweetness, and physical comfort.

An average appetite score was calculated at each time of measurement for each test beverage by the formula

$$\text{Appetite score} = [\text{desire to eat} + \text{hunger} + (100 - \text{fullness}) + \text{prospective consumption}] / 4 \quad (1)$$

which reflected the 4 questions on the motivation-to-eat questionnaire. Average appetite was therefore used as a summary measure of subjective appetite for statistical analyses, and a two-way repeated-measures ANOVA was used to test for treatment and time.

A two-way repeated-measures ANOVA was also used to test for the effect of treatment (test beverage) and time on mean blood glucose

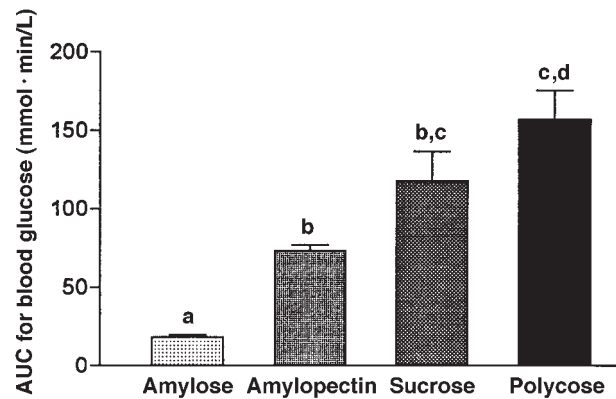


FIGURE 1. Mean (\pm SEM) area under the curve (AUC) for blood glucose concentrations to 60 min after the consumption of 4 carbohydrate-containing drinks in experiment 1. $n = 8$. Bars with different letters are significantly different, $P < 0.05$.

concentrations in experiment 1 and on the absolute scores and change from baseline scores for average appetite and the motivation-to-eat questionnaire questions in experiments 2 and 3. To test for the effect of time and treatment on the multiple ratings of physical comfort in experiment 3, a two-way repeated-measures ANOVA was used.

Correlation analysis in experiment 3 was conducted with the use of Pearson’s partial correlation coefficients, controlling for subject. Tukey’s post hoc tests were performed when treatment effects were statistically significant. The general linear models procedure was used for ANOVAs. All values are presented as means \pm SEMs. A P value of < 0.05 was considered to indicate statistical significance.

RESULTS

Blood glucose

In experiment 1, blood glucose concentrations, expressed as the difference from baseline, were affected by treatment ($P < 0.001$) and time ($P < 0.001$), and there was a time-by-treatment interaction ($P < 0.001$) (Table 1). As anticipated, polycose and sucrose produced greater increases in blood glucose than did amylose: after consumption of polycose and sucrose, blood glucose peaked at 30 min and returned to baseline by 60 min. Amylopectin produced a gradual and intermediate increase in blood glucose by 30 min, which became similar to the blood glucose concentrations at 45 and 60 min after polycose and sucrose consumption. At 60 min, the blood glucose concentration was significantly above baseline only after amylopectin consumption.

The effect of time was a general pattern whereby blood glucose concentrations increased from baseline to 15 min, were sustained from 15 to 30 min, and then decreased between 45 and 60 min after ingestion of the carbohydrate test beverages. The AUC for blood glucose differed among treatments ($P < 0.05$), which explains the time-by-treatment interaction (Figure 1). The AUC for polycose (156.6 ± 18.4 mmol · min/L), although not significantly different from that for sucrose (117.7 ± 19.1 mmol · min/L), was significantly greater than that for amylopectin (73.35 ± 10.0 mmol · min/L). The AUC for all treatments was higher than that for amylose (18.19 ± 18.4 mmol · min/L) at 1 h.

In experiment 3, mean blood glucose concentrations, expressed as the difference from baseline, were affected by treatment ($P < 0.0001$) and time ($P < 0.0001$), and a time-by-treatment interaction ($P < 0.001$)

TABLE 2Effects of time and treatments on changes from baseline blood glucose concentrations in experiment 3¹

Time (min)	Treatment				
	Sucralose	Fructose-glucose	Sucrose	Glucose	Polycose
	<i>mmol/L</i>				
20	0.01 ± 0.1 ^a	1.89 ± 0.2 ^b	3.09 ± 0.3 ^c	3.3 ± 0.3 ^c	3.5 ± 0.3 ^c
37	0.05 ± 0.09 ^a	1.75 ± 0.2 ^b	2.59 ± 0.5 ^c	3.91 ± 0.5 ^d	3.85 ± 0.5 ^d
65	1.02 ± 0.9 ^a	0.34 ± 0.2 ^a	1.23 ± 0.3 ^b	2.59 ± 0.4 ^c	2.55 ± 0.3 ^c

¹ $\bar{x} \pm \text{SEM}$; $n = 14$. Means in the same row with different superscript letters are significantly different, $P < 0.05$. Overall ANOVA: treatment effect, $P < 0.0001$; time effect, $P < 0.0001$; time-by-treatment interaction, $P < 0.001$. Mean baseline blood glucose did not differ significantly between treatments. The overall mean baseline blood glucose concentration was 5.17 ± 0.1 mmol/L.

was observed (**Table 2**). Polycose, glucose, and sucrose caused a greater increase in blood glucose at 20 min than did the fructose-glucose mixture. Blood glucose after these 3 treatment beverages remained elevated above baseline at 65 min. The combined fructose-glucose beverage elicited a smaller increase in blood glucose than did all other carbohydrate beverages, and blood glucose returned to baseline by 65 min. Sucralose did not significantly affect blood glucose over time.

The mean blood glucose AUC was affected by treatment beverage ($P < 0.05$) (**Figure 2**). The AUCs were significantly different among treatments, except those for polycose and glucose, which differed significantly from those of the other treatments but not from each other. Glucose (190.5 ± 19.1 mmol · min/L) and polycose (177.5 ± 19.4 mmol · min/L) resulted in the greatest AUCs, followed by sucrose (131.6 ± 16.9 mmol · min/L), the fructose-glucose mixture (71.5 ± 8.3 mmol · min/L), and sucralose (7.97 ± 2.2 mmol · min/L).

Physical comfort

No significant effect of treatment (data not shown) was observed on ratings of well-being at baseline ($P = 0.98$) or at 60 min ($P = 0.49$) or on the difference between scores at 60 min and baseline ($P = 0.66$) in experiment 2. In experiment 3, neither a significant effect of treatment ($P = 0.45$) or time ($P = 0.53$) nor a time-by-treatment interaction ($P = 0.25$) was observed for

ratings of well-being (data not shown) taken during the hour after the consumption of each test beverage.

Palatability

No significant differences in subjective ratings of palatability for the pizza test meal were found in experiment 2 ($P = 0.6$) or experiment 3 ($P = 0.12$) (data not shown). However, the subjective ratings of palatability differed significantly among treatments. In experiment 2, sucralose (61 ± 8), sucrose (58 ± 9), and polycose (55 ± 8) were rated as significantly more palatable than were amylopectin (20 ± 6) and amylose (28 ± 8) ($P < 0.05$). In experiment 3, the palatability ratings for the fructose-glucose mixture (55 ± 6), glucose (52 ± 6), and sucrose (51 ± 6) were not significantly different from those for the sucralose control (38.8 ± 6), but they were significantly greater than those for polycose (29 ± 5) ($P < 0.05$).

Perceived sweetness

In experiment 2, the perceived-sweetness ratings for sucrose (88 ± 3), polycose (80 ± 3), and the sucralose control (80 ± 3) did not differ significantly from those for amylose (72 ± 5), but they were significantly higher than those for amylopectin (61 ± 6) ($P < 0.05$) (data not shown). In experiment 3, the perceived-sweetness ratings for glucose (80 ± 3), the fructose-glucose mixture (78 ± 3), and sucrose (78 ± 4) did not differ significantly from those for polycose (72 ± 4), but they were significantly higher than those for the sucralose control (64 ± 4) ($P < 0.05$) (data not shown).

Average appetite

In experiment 2, treatment did not significantly affect the overall absolute appetite scores ($P = 0.52$) (data not shown). Average appetite increased with time ($P = 0.0004$), and a time-by-treatment interaction occurred because of an initial decrease and then a rapid recovery with time after the amylose and amylopectin treatments ($P = 0.001$). The one-way ANOVA indicated that there was a treatment effect at 15 min and that the consumption of the amylose test beverage resulted in the largest decrease ($P < 0.05$). When the data were analyzed as the difference from baseline, significant treatment ($P = 0.049$) and time ($P = 0.0001$) effects and a time-by-treatment interaction ($P = 0.045$) were observed (**Table 3**). The interaction occurred because the decrease with time in average appetite and the recovery were greatest for amylopectin and amylose, followed by polycose, sucrose, and then sucralose. At 30 min, a significant treatment difference was detected by the one-way ANOVA ($P < 0.05$): polycose suppressed average appetite to a significantly greater extent than did the sucralose control.

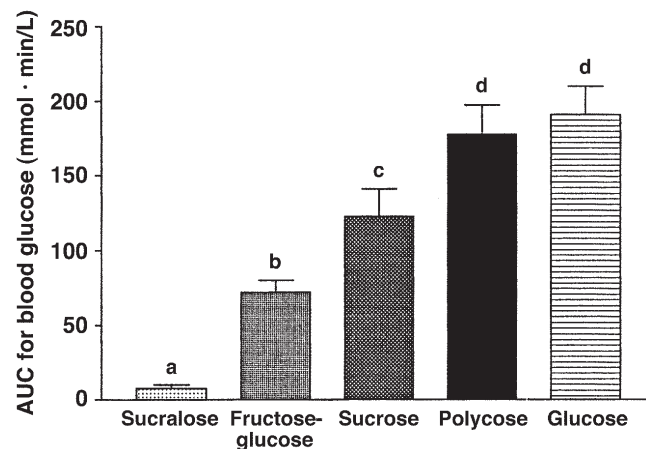


FIGURE 2. Mean (\pm SEM) area under the curve (AUC) for blood glucose concentrations to 60 min after the consumption of the control drink and 4 carbohydrate-containing drinks in experiment 3. $n = 14$. Bars with different letters are significantly different, $P < 0.05$.

TABLE 3Effects of time and treatments on changes from baseline average appetite scores in experiment 2¹

Time (min)	Treatment				
	Polycose	Sucrose	Amylopectin	Amylose	Sucralose
	<i>mm</i>				
15	-12.4 ± 5.0	-5.7 ± 2.6	-16.2 ± 6.9	-13.3 ± 4.7	-2.7 ± 4.3
30	-14.9 ± 5.8 ^a	-7.8 ± 2.9 ^{a,b}	-13.9 ± 6.0 ^{a,b}	-3.8 ± 4.3 ^{a,b}	0.07 ± 4.3 ^b
45	-11.0 ± 4.9	-4.6 ± 1.8	-7.9 ± 5.3	-1.7 ± 5.0	3.1 ± 4.0
60	-8.8 ± 4.3	-2.1 ± 1.7	-2.3 ± 4.1	2.3 ± 5.6	3.9 ± 4.4

¹ $\bar{x} \pm \text{SEM}$; $n = 14$. Means in the same row with different superscript letters are significantly different, $P < 0.05$. Overall ANOVA: treatment effect, $P = 0.049$; time effect, $P = 0.0001$; time-by-treatment interaction, $P = 0.045$.

In experiment 3, neither a significant effect of time ($P = 0.09$) or treatment ($P = 0.36$) nor a time-by-treatment interaction ($P = 0.367$) was observed for absolute average appetite at 1 h after the consumption of the test beverages (data not shown). When the data were expressed as the difference from baseline, there was an effect of time ($P = 0.02$) but not of treatment ($P = 0.65$) and no time-by-treatment interaction ($P = 0.14$) (Table 4). After all treatments, average appetite was lowest at 15 min and then increased to 60 min.

Food intake

One hour after the preloads were consumed in experiment 2, there was a significant effect of treatment on the amount of energy consumed at the test meal ($P = 0.006$) (Table 5). According to Tukey's comparison, with significance set at $P < 0.05$, treatments with polycose resulted in significantly less food intake than did treatments with sucralose control and amylopectin. Energy intake after consumption of the sucrose and amylose beverages was intermediate in relation to all treatments. Energy intake after sucrose consumption tended to be significantly less than that after sucralose consumption ($P < 0.06$).

There was a significant treatment effect on the percentage of compensation for the energy consumed ($P < 0.05$). Compensation for the polycose (65%) and sucrose (44%) preloads was not significantly different from that for amylose (23%), but it was significantly greater than that observed for amylopectin (0%). The amount of water consumed with the test meal was not significantly affected by treatment ($P = 0.19$).

In experiment 3, a significant effect of treatment was observed on mealtime energy intake ($P = 0.049$) (Table 6). On the basis of Tukey's comparison, the glucose resulted in a significantly lower food intake than did the sucralose control, but food intake after the sucrose, fructose-glucose mixture, and polycose treatments was not significantly different from that after all other treatments ($P < 0.05$). However, food intake after sucrose consumption

tended to be less than after consumption of the sucralose control ($P < 0.06$).

There was no significant effect of treatment on the compensation (in %) at mealtime for the energy consumed in the 1255-kJ preload ($P = 0.22$). However, an average of 40% compensation was observed for all treatments except for the fructose-glucose mixture, which resulted in < 12% compensation. The amount of water consumed with the test meal was not significantly affected by treatment ($P = 0.86$).

Relations among dependent measures

A positive correlation was found between average appetite scores at 60 min and the mealtime food intake in the pooled data from all treatments in both experiment 2 (Figure 3) ($r = 0.39$, $P < 0.001$) and experiment 3 (Figure 4) ($r = 0.45$, $P < 0.0001$). In experiment 3, average appetite ($r = -0.23$, $P = 0.045$) (data not shown) and food intake ($r = -0.24$, $P = 0.05$) (Figure 5) were negatively associated with AUC blood glucose concentrations.

No significant relation was found between preload palatability ($r = 0.006$, $P = 0.96$; $r = 0.15$, $P = 0.21$) or sweetness ($r = -0.003$, $P = 0.79$; $r = -0.79$, $P = 0.14$) and food intake in experiment 2 and experiment 3, respectively (data not shown).

DISCUSSION

The hypothesis that there is an inverse association between the effect of carbohydrates on blood glucose and subsequent short-term food intake is supported by these data. Specifically, the greater the glycemic response, as measured by AUC after carbohydrate consumption, the greater the reduction in food intake at 60 min.

The correlations between the blood glucose response, as measured by AUC, and appetite or food intake, although significant ($P < 0.04$), were not strong, averaging $r = -0.24$. Thus, the glycemic response may serve to depict only the absorption

TABLE 4Effects of time and treatments on changes from baseline average appetite scores in experiment 3¹

Time (min)	Treatment				
	Polycose	Sucrose	Fructose-glucose	Glucose	Sucralose
	<i>mm</i>				
15	-5.6 ± 2.4	-6.3 ± 2.7	-4.4 ± 3.2	-4.7 ± 3.5	-3.7 ± 2.7
30	-3.6 ± 3.1	-0.7 ± 2.7	-0.4 ± 4.2	-4.4 ± 3.8	-0.3 ± 2.7
45	-4.4 ± 3.1	-3.1 ± 3.4	-3.0 ± 4.8	-4.4 ± 4.6	1.7 ± 3.4
60	0.1 ± 3.1	-3.8 ± 4.1	1.3 ± 4.0	-1.2 ± 4.5	5.4 ± 3.9

¹ $\bar{x} \pm \text{SEM}$; $n = 14$. Overall ANOVA: treatment effect, $P = 0.65$; time effect, $P < 0.02$; time-by-treatment interaction, $P = 0.14$.

TABLE 5
Food and water intake after treatments in experiment 2¹

Treatment	Energy intake ²	Compensation ³	Water intake
	<i>kJ</i>	%	<i>g</i>
Sucralose	4255 ± 292 ^a	NA	348 ± 52
Amylose	3958 ± 238 ^{a,b}	23.7 ± 15.6 ^{a,b}	338 ± 50
Amylopectin	4259 ± 387 ^a	-0.2 ± 21.7 ^b	327 ± 34
Polycose	3443 ± 364 ^b	64.9 ± 19.4 ^a	303 ± 40
Sucrose	3699 ± 351 ^{a,b,4}	44.4 ± 13.1 ^a	387 ± 54
<i>P</i> ⁵	0.006	0.03	0.19

¹ $\bar{x} \pm \text{SEM}$; $n = 14$. Means in the same column with different superscript letters are significantly different, $P < 0.05$ (Tukey's t test).

²Energy consumed (kJ) in a test meal 60 min after preload.

³Energy consumed after control – energy consumed after treatment/energy in preload $\times 100$.

⁴Sucrose < sucralose and amylopectin, $P < 0.06$.

⁵Overall ANOVA of treatment effect.

characteristics of the carbohydrates and not the specific mechanism by which they provide satiety signals. Carbohydrates stimulate the release of insulin and many gut peptides, eg, glucagon-like peptide 1, which are known to suppress food intake (17, 18). Nevertheless it is clear that the high-glycemic-index carbohydrates suppressed food intake, but the low-glycemic-index carbohydrates did not.

The results are consistent with the glucostatic hypothesis of food intake regulation, which states that a rise in blood glucose concentrations signals satiety and the termination of feeding (3). However, these results appear to be in conflict with the hypothesis that high-glycemic-index foods promote excessive energy intake and that low-glycemic-index foods suppress appetite, thereby preventing obesity (5, 19). This hypothesis is based in part on the notion that a sharp initial rise in blood glucose is followed by a postprandial dip in blood glucose, which initiates eating. Indeed, a drop in blood glucose predicts the initiation of feeding in both animals and humans (20, 21). Possibly this effect of the high-glycemic-index beverages would be detected if satiety measurements were extended and food intake was measured at 2 h.

Because the measurements in these studies were limited to a 60-min span, the results are not in conflict with those from other studies that suggest a reduction in hunger or increased satiety at

TABLE 6
Food and water intake after treatments in experiment 3¹

Treatment	Energy intake ²	Compensation ³	Water intake
	<i>kJ</i>	%	<i>g</i>
Sucralose	4176 ± 292 ^a	NA	451 ± 70
Fructose-glucose	4033 ± 323 ^{a,b}	11.5 ± 15.7	441 ± 47
Sucrose	3644 ± 330 ^{a,b,4}	42.3 ± 14.3	416 ± 55
Polycose	3719 ± 303 ^{a,b}	36.4 ± 16.05	416 ± 53
Glucose	3573 ± 341 ^b	48.1 ± 25.5	438 ± 50
<i>P</i> ⁵	0.049	0.22	0.87

¹ $\bar{x} \pm \text{SEM}$; $n = 14$. Means in the same column with different superscript letters are significantly different, $P < 0.05$ (Tukey's t test).

²Energy consumed (kJ) in a test meal 60 min after preload.

³Energy consumed after control – energy consumed after treatment/energy in preload $\times 100$.

⁴Sucrose < sucralose, $P < 0.06$.

⁵Overall ANOVA of treatment effect.

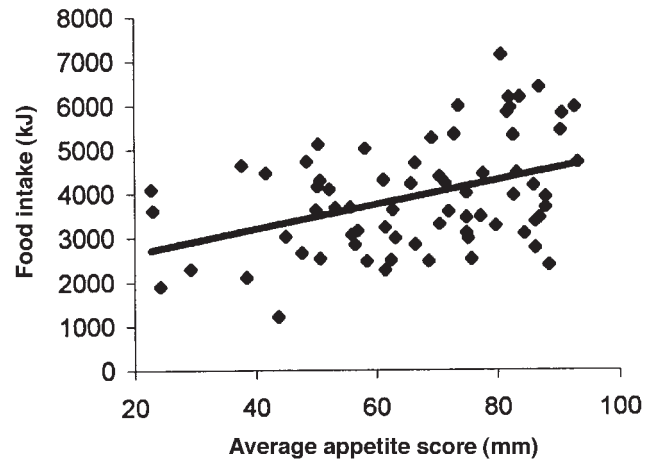


FIGURE 3. Relation between 60-min average appetite scores and food intake (kJ) after the consumption of drinks containing sucralose, amylose, amylopectin, polycose, and sucrose in experiment 2 ($r = 0.40$, $P < 0.01$).

later times after the consumption of low-glycemic-index foods than after the consumption of high-glycemic-index foods (5, 19). Most studies showing increased satiety after the consumption of low- but not high-glycemic-index foods observed this effect of the preload at 2–6 h (22–26), but those studies did not measure food intake. In contrast, high-glycemic-index carbohydrates such as glucose and sucrose (≥ 50 g) suppress short-term food intake 1–1.5 h after the consumption of the preload (6–8, 10). Because a cascade of satiety signals is produced upon the ingestion of food (10), it is likely that the signals are time dependent, varying with the composition of the food ingested and its digestion process. Therefore, whereas our measurement of food intake at 1 h was appropriate for detecting the effects on satiety of the high-glycemic-index treatments, such as those with polycose and glucose, it is possible that an effect on energy intake of the low-glycemic-index treatments amylose and amylopectin would be detected at a later time. Supporting this prediction are the results

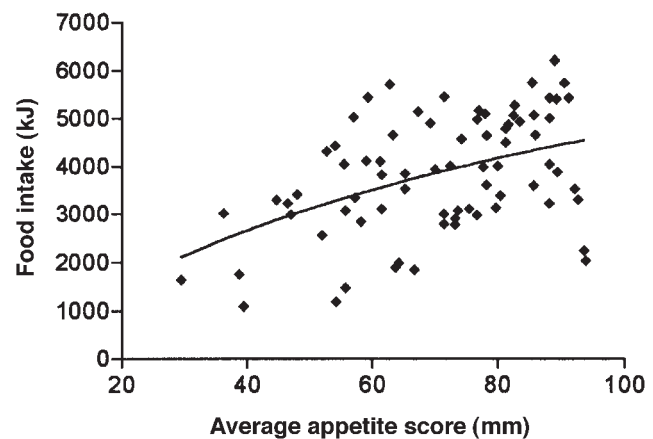


FIGURE 4. Relation between 60-min average appetite scores and food intake (kJ) after the consumption of drinks containing sucralose, fructose-glucose mixture, sucrose, polycose, and glucose in experiment 3 ($r = 0.45$, $P < 0.01$).

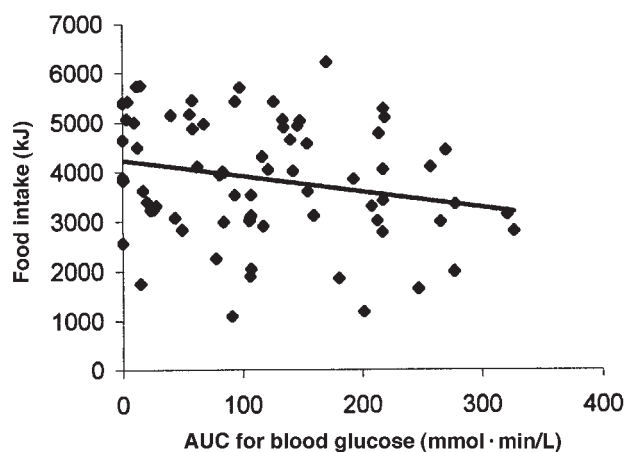


FIGURE 5. Relation between food intake at 60 min and the area under the curve (AUC) for blood glucose concentrations after the consumption of drinks containing sucralose, fructose-glucose mixture, sucrose, polyose, and glucose in experiment 3 ($r = -0.24$, $P < 0.05$).

of mixed-meal studies showing that the addition of high-amylose starch leads to greater satiety 2–6 h after a meal than is seen with low-amylose meals (24, 27).

Similarly, a time > 1 h may be required to observe the satiating capacity of fructose. Most studies have detected the suppression of food intake after fructose consumption when the time between the preload and the test meal was 1.5–2.25 h (9, 28–31). The later expression of the effect of fructose on energy intake in comparison with that of other carbohydrates is consistent with the slower effect of fructose on thermogenesis and oxidation (32, 33).

A mixture of fructose and glucose, rather than fructose alone, was given as a treatment in experiment 3 because $< 50\%$ of the population has a limited absorptive capacity for fructose and presents with symptoms of nausea and diarrhea after consuming as little as 25 g fructose (15, 33). To increase fructose absorption (33), 20% glucose was added to the fructose preload in our study. For the purpose of examining the relation between blood glucose and food intake, this was an appropriate treatment because the fructose-glucose mixture gave the lowest blood glucose response, except for the control, and the subjects reported no symptoms of nausea or discomfort.

No relation was observed between the perceived sweetness or palatability of the treatments and the energy intake at the test meal, even though the final solutions were not found to be equal in palatability or sweetness. This lack of correlation was not surprising because previous studies showed no relation between the palatability of treatments and food intake if the interval from the preload to the meal is ≥ 1 h (34).


In the present study, sucrose suppressed subsequent food intake somewhat less than did the carbohydrates with the highest glycemic indexes, glucose and polyose, but more than did the polysaccharide amylopectin (Tables 5 and 6). However, a strong effect of sucrose, but not of safflower oil, on food intake was previously shown in a dose-response study in which the consumption of beverage preloads of 418, 837, and 1255 kJ resulted in a reduction in food intake among young men (6). For all sucrose treatments (25, 50, and 75 g), compensation in the next meal averaged 92% of that with a water control and 70% of that with a sweet control. It is difficult to explain the weaker effect of sucrose

observed in the present study compared with the former, but if glycemic response is a factor (Figures 1 and 2), it is not surprising to find that it has a lesser effect than does glucose or polyose. The glycemic index of sucrose is 59, and that of glucose is 100 (11). Although the glycemic index of polyose has not been specifically tested, given its composition and glycemic response, polyose would be expected to have a glycemic index similar to that of glucose.

Children also reduce food intakes after sugar consumption. Sucrose (380 kJ) consumed in water by children aged 2–5 y suppressed food intake by an equivalent amount in a test meal both 30 and 90 min after the preload (35). Children 9–10 y of age compensated for 65% of the energy in 45 and 90 g of sucrose at a test meal 30 min later (36). In accord with these observations, the present experiments showed that $< 43\%$ of the energy intake in the sucrose preload was compensated for at a test meal 1 h later.

Thus, it is clear that, under laboratory conditions, sugars suppress food intake. These data challenge the suggestion that sugars, especially in beverages, lead to obesity by bypassing regulatory systems (37, 38). However, the conclusions arising from these studies are specific to the carbohydrates used, the form of their administration, and the interval between the preload and the test meal.

It is possible that the effects of these carbohydrates on food intake will change when they are ingested with other nutrients in mixed meals. However, the relation with blood glucose is clear. In the short term, meals producing a greater elevation in blood glucose would be expected to induce satiety more effectively than would meals with a lower glycemic response.

In summary, the present study shows an inverse association between the blood glucose response and food intake and subjective appetite in the 60 min after carbohydrate consumption. High-glycemic-index carbohydrates (glucose, polyose, and sucrose) suppress subjective appetite and food intake in the short term, but low-glycemic-index carbohydrates (amylose and amylopectin) do not. There is a need, however, for further consideration of the temporal relations between the glycemic response to food and satiety and food intake to determine whether the glycemic index of a food predicts food intake. 

REFERENCES

1. Asp N. Nutritional classification and analysis of food carbohydrates. *Am J Clin Nutr* 1994;59(suppl):679S–81S.
2. Anderson GH. Regulation of food intake. In: Shils ME, Olson JA, Shike M, eds. *Modern nutrition in health and disease*. Philadelphia: Lea & Febiger, 1994:524–36.
3. Mayer J. Glucostatic mechanism of the regulation of food intake. *N Engl J Med* 1953;249:13–6.
4. Westerterp-Plantega M, Fredix E, Steffens AB. *Food intake and energy expenditure*. Boca Raton, FL: CRC Press, 1994:141–54.
5. Ludwig D. Dietary glycemic index and obesity. *J Nutr* 2000;130:280S–3S.
6. Woodend DM, Anderson GH. Effect of sucrose and safflower oil preloads on short term appetite and food intake in young men. *Appetite* 2001;37:185–95.
7. Rogers PJ, Blundell JE. Separating the actions of sweetness and calories: the effects of saccharin and carbohydrate on hunger and food intake in humans. *Physiol Behav* 1989;45:1093–9.
9. Rogers PJ, Carlyle J, Hill AJ, Blundell JE. Uncoupling sweet taste and calories: comparison of the effect of glucose and three intense

- sweeteners on hunger and food intake. *Physiol Behav* 1989;43:145–53.
9. Blundell JE, Green S, Burley V. Carbohydrates and human appetite. *Am J Clin Nutr* 1994;59(suppl):728S–34S.
 10. Anderson GH. Sugars, sweetness and food intake. *Am J Clin Nutr* 1995;62(suppl):195S–202S.
 11. Jenkins DJ, Wolever TMS, Taylor RH, et al. Glycemic index of foods: a physiological basis for carbohydrate exchange. *Am J Clin Nutr* 1981;34:362–6.
 12. World Health Organization. Obesity: preventing and managing the global epidemic. Report of a WHO consultation on obesity. Geneva: WHO, 1997:276.
 13. Herman CP, Polivy J. Restrained eating. In: Stunkard AJ, ed. Obesity. Philadelphia: WB Saunders, 1980:208–25.
 14. Mezitis NH, Maggio CA, Koch P, Quddoos A, Allison DB, Pi-Sunyer FX. Glycemic effect of a single high oral dose of the novel sweetener sucralose in patients with diabetes. *Diabetes Care* 1996;19:1004–5.
 15. Rumessen JJ, Gudmand-Hoyer E. Absorption capacity of fructose in healthy adults. Comparison with sucrose and its constituent monosaccharides. *Gut* 1986;27:1161–8.
 16. Stewart SL, Black R, Wolever T, Anderson GH. The relationship between the glycaemic response to breakfast cereals and subjective appetite and food intake. *Nutr Res* 1997;17:1249–60.
 17. Chapman IM, Goble EA, Wittert GA, Morley JE, Horowitz M. Effect of intravenous glucose and euglycemic insulin infusions on short term appetite and food intake. *Am J Physiol* 1998;274:R596–603.
 18. Lavin JH, Wittert GA, Andrews J, et al. Interaction of insulin, glucagon-like peptide-1, gastric inhibitory polypeptide and appetite in response to intraduodenal carbohydrate. *Am J Clin Nutr* 1998;68:591–8.
 19. Roberts SB. High glycemic index foods, hunger and obesity: is there a connection? *Nutr Rev* 2000;58:163–9.
 20. Campfield LA, Smith FJ. Transient declines in blood glucose signal meal initiation. *Int J Obes* 1990;14(suppl):15–33.
 21. Campfield LA, Smith FJ, Rosenbaum M, Hirsch J. Human eating: evidence for a physiological basis using a modified paradigm. *Neurosci Biobehav Rev* 1996;20:133–7.
 22. Leathwood P, Pollet P. Effects of slow release carbohydrates in the form of bean flakes on the evolution of hunger and satiety in man. *Appetite* 1988;10:1–11.
 23. Holt S, Brand J, Soveny C, Hansky J. Relationship of satiety to postprandial glycaemic, insulin and cholecystokinin responses. *Appetite* 1992;18:129–41.
 24. Van Amelsvoort JMM, Weststrate JA. Amylose-amylopectin ratio in a meal affects postprandial variables in male volunteers. *Am J Clin Nutr* 1992;55:712–8.
 25. Holt S, Brand-Miller J. Increased insulin responses to ingested foods are associated with lessened satiety. *Appetite* 1995;24:43–54.
 26. Raben A, Christensen NJ, Madsen J, Holst JJ, Astrup A. Decreased postprandial thermogenesis and fat oxidation but increased fullness after a high-fiber meal compared with a low-fiber meal. *Am J Clin Nutr* 1994;59:1386–94.
 27. Granfeldt Y, Liljeberg H, Drews A, Newman R, Bjork I. Glucose and insulin responses to barley products: influence of foods structure and amylose-amylopectin ratio. *Am J Clin Nutr* 1994;59:1075–82.
 28. Rayner CK, Park HS, Wishart JM, Kong M, Doran SM, Horowitz M. Effects of intraduodenal glucose and fructose on antipyloric motility and appetite in healthy humans. *Am J Physiol* 2000;278:R360–6.
 29. Spitzer L, Rodin J. Effects of fructose and glucose preloads on subsequent food intake. *Appetite* 1987;8:135–45.
 30. Rodin J, Reed D, Jamner L. Metabolic effects of fructose and glucose: implications for food intake. *Am J Clin Nutr* 1988;47:683–9.
 31. Rodin J. Effects of pure sugar versus mixed starch fructose loads on food intake. *Appetite* 1991;17:683–9.
 32. Schwarz JM, Schultz Y, Piolino V, Schneider H, Felber JP, Jequier E. Thermogenesis in men and women induced by fructose versus glucose added to a meal. *Am J Clin Nutr* 1989;49:667–74.
 33. Henry R, Crapo P. Current issues in fructose metabolism. *Annu Rev Nutr* 1991;11:21–39.
 34. De Graaf C, De Jong LS, Lanbers AC. Palatability affects satiation and satiety. *Physiol Behav* 1999;66:681–8.
 35. Birch LL, McPhee L, Sullivan S. Children's food intake following drinks sweetened with sucrose or aspartame: time course effects. *Physiol Behav* 1989;45:387–95.
 36. Black RM, Anderson GH. Sweeteners, food intake and selection. In: Fernstrom JD, Miller GD, eds. Appetite and body weight regulation: sugar, fat, and macronutrient substitutes. Boca Raton, FL: CRC Press, 1994:125–36.
 37. Ludwig DS, Majzoub JA, Al-Zaharani A, Dallal GE, Blanco I, Roberts SB. High glycemic index foods, overeating and obesity. *Pediatrics* 1999;103:1–6.
 38. Ludwig DS, Peterson KE, Gortmaker SL. Relation between consumption of sugar-sweetened drinks and childhood obesity: a prospective, observational analysis. *Lancet* 2001;357:505–8.

