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Effect of glucose, sucrose and fructose on plasma glucose and insulin responses in normal humans: comparison with white bread

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Objective: To determine the plasma glucose and insulin responses of various doses of glucose, sucrose, fructose and white bread in normal human subjects.
Design: Plasma glucose and insulin were measured before and at various times after 8 subjects ate 13 different test meals in randomized order on separate days after an overnight fast. Test meals consisted of 500 ml of tea or water to which was added either nothing, 25, 50, or 100 g of glucose or sucrose, 25 or 50 g fructose, 50 g glucose plus 50 g fructose, or a 25, 50 or 100 g carbohydrate portion of white bread. The glycaemic (GI) and insulinaemic index (II) values of the sugars were calculated by expressing the incremental areas under the plasma glucose and insulin curves (AUC) after glucose, sucrose and fructose as a percentage of the respective AUC after white bread containing the same amount of carbohydrate.
Setting: University teaching hospital clinical nutrition centre.
Subjects: Lean, normal subjects (4 male, 4 female) 21–33 y of age.
Results: Plasma insulin responses increased nearly linearly as carbohydrate intake increased from 0 to 100 g, but glycaemic responses increased by only 68% and 38% as carbohydrate intake increased from 25 to 50 g and 50 to 100 g, respectively. The GI and II values of glucose, 149±16 and 147±18, respectively, were significantly greater than those of bread (100; $P<0.05$), while the values for fructose, 16±4 and 22±3 were significantly less than those of bread ($P<0.001$). GI values did not differ significantly from II values.
Conclusions: It is concluded that, in normal subjects, as carbohydrate intake is increased from 0 to 100 g, plasma insulin responses increase at a greater rate than plasma glucose responses. The insulinaemic responses elicited by glucose, sucrose or fructose are similar to those that would be expected from a starchy food with the same glycaemic index.
Descriptors: carbohydrates; diet; glucose; glycaemic index; insulin; sugars

Introduction

The role that sugars play in the diet and their relationship to a range of health concerns is an area of tremendous interest in nutritional sciences (Clydesdale, 1995). An important issue in this respect is the effect of sugars on postprandial glucose and insulin responses. The glycaemic index values of hundreds of foods, including glucose, sucrose and fructose, have been determined (Foster-Powell & Brand Miller, 1995). These data show that many starchy foods produce higher glycaemic responses than sucrose, and that fructose elicits a lower glycaemic response than most other foods (Wolever & Brand Miller, 1995). Recently, the insulin index of some common foods was determined (Holt *et al*, 1997), but glucose, sucrose and fructose were not included.

Few studies have attempted to compare the plasma glucose and insulin responses of glucose with those of sucrose or fructose in normal subjects,. The results of these studies are not easy to interpret because unequal amounts of glucose, sucrose and fructose were fed (Crapo *et al*, 1976, Reiser *et al*, 1987) or tests were done in different groups of subjects, making comparisons between the sugars unreliable (MacDonald *et al*, 1978). Knowledge about the relative effects of sugars on plasma insulin is important because it has been suggested that fructose increases plasma insulin without increasing plasma glucose (Reiser *et al*, 1987). High plasma insulin concentrations and insulin resistance are associated with increased risk of cardiovascular disease (Pyörälä, 1978; Welborn & Wearne, 1979; Ducemetière *et al*, 1980; DeFronzo & Ferrannini, 1991). Therefore, our purpose was to determine the effect of various doses of glucose, sucrose, fructose and white bread on plasma glucose and insulin responses in normal subjects.

Methods

Eight normal, healthy human subjects (4 male, 4 female) were recruited for the study (mean±s.e.m. 25.4±4.5 years, range 21–33; body mass index 22.2±2.0 kg/m^2). All subjects were nonsmokers and were not taking any medications. The protocol was approved by the University of Toronto Human Subjects Review Committee and informed written consent was obtained from all subjects.

Subjects were studied on 13 separate occasions in the morning after 10–12 h overnight fasts. On each occasion they consumed, within 10 min a test meal containing 0 to 100 g available carbohydrate from bread, glucose, sucrose

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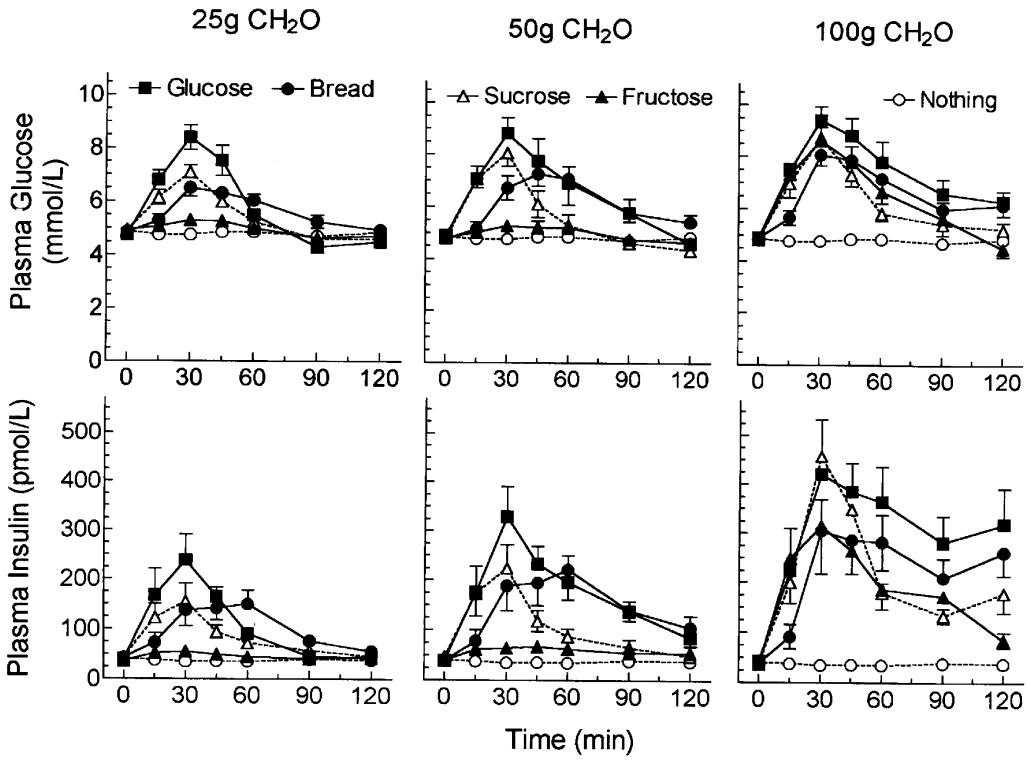

Figure 1 Plasma glucose (top) and insulin (bottom) responses after consuming 25 g (left), 50 g (centre) and 100 g (right) of carbohydrate from glucose, sucrose, fructose or white bread. The 100 g fructose meal consisted of 50 g fructose plus 50 g sucrose. The results for 0 g carbohydrate are shown on each panel. Points are means± s.e.m. for 8 healthy subjects. Statistical analysis was not done for the individual time points.

or fructose plus 500 ml of either tea or water (the drink chosen by each subject for the first test remained the same for all subsequent tests by that subject). The 13 different test meals consisted of the drink alone; 25, 50 and 100 g carbohydrate portions of white bread; 25, 50 and 100 g glucose (Bio-Health, Dawson Traders Ltd., Toronto, Ontario, Canada); 25, 50 and 100 g sucrose (Redpath Sugars, Division of Redpath Industries Ltd., Toronto, Ontario, Canada); 25 and 50 g fructose (Sweeten Less, Maximum Nutrition Inc., Toronto, Ontario, Canada); and 50 g fructose plus 50 g glucose. Fructose alone was not given at the 100 g dose because it was considered that this dose was likely to cause symptoms of malabsorption (Riby *et al*, 1993). The tests were grouped into 5 blocks: drink alone, glucose, fructose, sucrose and bread. The order of these blocks was randomized and the sequence of the test doses within each of the blocks alternated between ascending or descending order of carbohydrate dose.

Sugars were dissolved in the 500 ml drink of tea or water. To keep the total volume of all meals the same, the 25 and 50 g carbohydrate portions of bread were given with an additional 100 ml and 50 ml water, respectively, and an additional 150 ml water was drunk after the test meals without bread. White bread was baked in 250 g carbohydrate loaves containing 334 g all-purpose flour (Robin Hood, Maple Leaf Mills, Toronto, Ontario, Canada), 7 g sucrose, 6 g yeast, 4 g salt and 250 ml warm water using an automatic bread maker (model SD-BT2P, Matsushita Electronics Industries Co. Ltd, Japan). Loaves were cooled at room temperature for 1 h, weighed, and cut into 25 or 50 g carbohydrate portions (crust ends discarded), packed into plastic freezer bags and frozen. Prior to consumption, bread was thawed in a microwave oven.

Blood samples were drawn from a catheter placed into a forearm vein before the start of the test meal (time 0), and at 15, 30, 45, 60, 90 and 120 min after the start of eating. The catheter was kept open by injecting 3–5 ml normal saline after each blood sample. Saline was cleared from the catheter before blood sampling by withdrawing and discarding 1 ml. To facilitate blood taking, forearm blood flow was increased by warming subjects' hands in an electrically heated pad for ~5 min before each blood sample. Blood was drawn into 3 ml fluoro-oxalate tubes (Vacutainer, Beckton-Dickerson, Rutherford, NJ, USA) and kept refrigerated before centrifugation and removal of plasma, which was stored at −20°C prior to analysis of glucose (2300 Stat Glucose Analyzer, Yellow Springs Instruments, Yellow Springs, OH, USA) and insulin (Pharmacia Insulin RIA, Dorval, Quebec, Canada).

Results are expressed as means± s.e.m. Incremental areas under the glucose and insulin curves, ignoring any area below the fasting level (AUC), were calculated geometrically (Wolever *et al*, 1991). Glycaemic (GI) and insulinaemic (II) values were calculated by expressing the glucose and insulin AUC after the glucose, sucrose and fructose test meals as a percentage of the respective AUC after the same amount of carbohydrate from white bread.

Statistical analysis was performed by repeated measures analysis of variance using the Newman–Keuls method to adjust for multiple comparisons (Snedecor & Cochran, 1980). Values for one missing test were imputed using the method described by Snedecor & Cochran (1980). Nonlinear regression was performed using GraphPad Prism™ (GraphPad Software Inc, San Diego, CA, USA). Differences were considered statistically significant when $P<0.05$ (two-tailed).

Results

The 8 subjects completed all 13 tests, except for one subject who did not consume 50 g fructose because he experienced severe symptoms of malabsorption (flatulence, abdominal cramps and diarrhoea) after consuming 25 g fructose. Five of the other 7 subjects experienced mild symptoms of malabsorption at the fructose 50 g dose level.

The plasma glucose and insulin response curves after the 13 different tests are shown in Figure 1, and the incremental areas under the curves in Table 1. After the 0 g carbohydrate test meal, the plasma glucose and insulin AUC were 1.4 ± 0.6 mmol min/l and 0.2 ± 0.1 nmol min/l, respectively. Plasma glucose and insulin responses increased as the dose of carbohydrate consumed increased. For each carbohydrate source, the mean AUC after the 100 g dose was significantly greater than after 25 g (Table 1) with the response for the 50 g dose being intermediate. However, the dose–response curves for plasma insulin were steeper than those for plasma glucose. The mean AUC of plasma insulin increased nearly linearly as the dose of carbohydrate increased from 0 to 100 g, with a 4-fold increase in carbohydrate intake (25–100 g) resulting in a 3.95-fold increase in insulin AUC (mean for glucose, bread, sucrose). By contrast, the rate of increase glycaemic responses became less as the dose of carbohydrate increased. Doubling carbohydrate intake from 25 to 50 g was associated with a 68% increase in glucose AUC, while a further 2-fold increase in carbohydrate from 50 to 100 g resulted in only a 37% increase in glucose AUC. Thus, the relationship between plasma glucose and insulin responses was not linear (Figure 2).

The order of the mean glucose and insulin AUC at each dose of carbohydrate was glucose>bread>sucrose>fructose, except at 100 g where the fructose/glucose mixture produced similar responses to sucrose. The differences between carbohydrate sources were not always significant at every dose. However, the glucose and insulin responses of bread were significantly less than those of glucose at 100 g; the glucose and insulin responses after sucrose were significantly less than after glucose at 100 g; fructose elicited significantly lower glucose responses than all the other carbohydrate sources at 25 and 50 g, and a significantly lower insulin response than bread and glucose at 50 g.

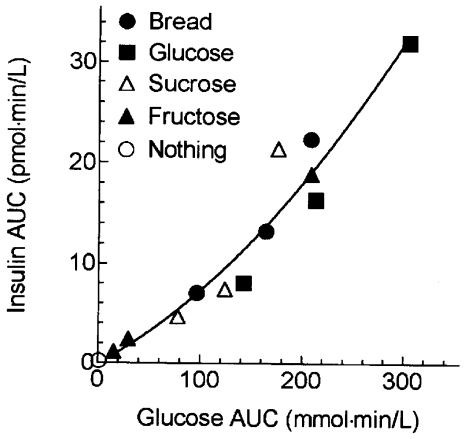

Figure 2 Relationship between incremental areas under the plasma glucose and insulin reponses after consuming various amounts of carbohydrate from glucose, white bread, sucrose or fructose. Points are means ± s.e.m. for 8 healthy subjects. Nonlinear regression using a polynomial model was used to generate the line which represents the formula: $I = 0.0576\,G + 0.000165G^2 - 0.0968$ where I = insulin AUC and G = glucose AUC ($r^2 = 0.929$).

The glycaemic (GI) and insulinaemic index (II) values of the sugars are shown in Table 2. The mean GI and II values of glucose, 149 ± 16 and 147 ± 18, respectively, were significantly greater than that of bread (100) ($P = 0.017$ and $P = 0.038$). The GI and II values of sucrose, 87 ± 6 and 83 ± 7, were less than those of bread, but the differences just missed statistical significance ($P = 0.087$ and $P = 0.0503$, respectively). The GI and II values of fructose, 16 ± 4 and 22 ± 3, were significantly less than bread ($P < 0.001$). There were no significant differences between the GI and II values of any of the sugars, with the overall mean GI for the 9 different sugar-containing test meals (94%) being virtually identical to the overall mean II (92%; $P = 0.79$).

Discussion

The results show that the plasma glucose and insulin responses of healthy subjects after consumption of different sugars are influenced by both the source and amount of carbohydrate tested. Glucose elicited the highest plasma glucose and insulin responses, followed by white bread, sucrose and fructose. For each source of carbohydrate, plasma glucose and insulin responses increased as the amount of carbohydrate consumed increased. However, the increase in plasma glucose response area tended to flatten off as carbohydrate intake rose from 50 to 100 g, whereas plasma insulin response areas continued to increase in a nearly linear fashion. The pattern of glucose and insulin dose–response curves observed here for different sugars is very similar to that previously observed for different starchy foods (Wolever and Bolognesi, 1996).

The glycaemic index values for glucose and sucrose from this study, 149 and 87, respectively, are similar to previously published values (Foster-Powell & Brand Miller, 1995). The glycaemic index value for fructose (16) was half the mean value of four studies, (32 ± 2)(Foster-Powell & Brand Miller, 1995), which may be because of a higher than normal prevalence of malabsorption among our subjects. It is well known that fructose is poorly absorbed (Riby *et al*, 1993). In a series of 103 subjects given 50 g oral fructose in water, 26 (25%) experienced symptoms (Truswell *et al*, 1988). In the present study, 6 of 8 subjects (75%) experienced symptoms of malabsorption during the fructose tests, a prevalence 3 times that found by Truswell *et al*, (1988) ($P = 0.008$).

High plasma insulin concentrations are associated with insulin resistance and increased risk for coronary heart disease (DeFronzo & Ferrannini, 1991) and it is believed that fructose and sucrose may raise plasma triglycerides, at least in part, because they elicit high plasma insulin responses that stimulate hepatic lipogenesis (Frayn & Kingman, 1995). Several studies have compared the glycaemic effects of sugars with those of starchy foods (Foster-Powell & Brand Miller, 1995) but many of these did not include a measure of insulin. There are surprisingly few studies that have determined the blood glucose and insulin raising effects of sugars in normal subjects and none of these can be used to compare the insulinaemic effects of sugars and starches. MacDonald *et al*, (1978) measured glycaemic and insulinaemic responses after 4 different doses of glucose, sucrose, fructose and sorbitol. However, different subjects tested the different sugars so reliable comparisons of the

Table 1 Incremental areas under the plasma glucose and insulin repsonse curves after different doses of sugars and white bread in normal subjects

	25 g	*50 g*	*100 g*
Plasma glucose (mmol min/l)			
Glucose	142.2± 21.9^{cde}	212.7± 37.6^{e}	304.0± 48.3^{f}
Bread	96.3± 8.4^{c}	164.0± 27.6^{de}	207.6± 26.1^{e}
Sucrose	78.1± 4.5^{bc}	123.8± 17.7^{cd}	175.2± 21.3^{de}
Fructose	15.3± 4.9^{a}	29.8± 11.6^{ab}	207.8± 25.3^{e}*
Plasma insulin (nmol min/l)			
Glucose	8.1± 1.6^{abc}	16.3± 2.7^{cd}	32.0± 5.9^{e}
Bread	7.0± 1.6^{abc}	13.3± 2.3^{bcd}	22.3± 5.0^{d}
Sucrose	4.7± 1.0^{ab}	7.4± 1.9^{abc}	21.4± 3.6^{d}
Fructose	1.2± 0.2^{a}	2.4± 0.4^{a}	18.9± 3.6^{d}*

Values are means ± s.e.m.
^{abc}Means sharing the same letter superscript are not significantly different. Superscript a indicates no significant difference from the reponse to 0 g carbohydrate. Means with different letter superscripts are significantly different ($P<0.05$).
*Test meal was 50 g fructose plus 50 g glucose.

Table 2 Glycaemic and insulinaemic indices of glucose, sucrose and fructose at different levels of carbohydrate intake

	25 g	*50 g*	*100 g*	*Mean*
Glycaemic index (%)				
Glucose	146.9± 18.3	136.6± 22.0	162.8± 28.2	148.8± 15.8
Sucrose	85.5± 8.5	83.3± 14.9	93.5± 14.2	87.4± 6.3
Fructose	15.7± 4.9	16.4± 5.5	109.4± 14.9*	16.1± 4.2
Insulinaemic index (%)				
Glucose	152.0± 29.9	126.3± 14.0	161.6± 20.4	146.6± 18.2
Sucrose	73.4± 7.0	57.5± 11.2	117.2± 14.9	82.7± 7.3
Fructose	22.9± 7.6	20.6± 4.1	100.9± 14.0*	21.8± 3.4

Values are means± s.e.m.
*Test meal was 50 g fructose plus 50 g glucose. This value is not included in the mean for fructose.

effects of the sugars relative to each other is not possible, and, no starchy food was included.

Crapo *et al*, (1976) compared the glycaemic and insulinaemic effects of 100 g sucrose with those of 50 g glucose and 50 g starch from rice and potato. They found that the plasma glucose response after sucrose was similar to that after glucose and potato, but the plasma insulin response after sucrose was greater than after glucose and potato. The present results are consistent with those of Crapo *et al*, (1976) in that 100 g sucrose tended to elicit lower plasma glucose and greater plasma insulin responses than 50 g glucose (Table 1). Similarly, Reiser *et al*, (1987) found that when 1.75 g/kg fructose was consumed 20 min after consuming test meals containing 1.0 g/kg glucose or 0.9 g/kg starch, plasma insulin increased in the absence of a rise in plasma glucose. The results of these studies imply that sucrose and fructose elicit larger insulin responses than would be expected from their glycaemic responses. However, the design of these studies was flawed because the sucrose and fructose test meals contained a much larger amount of carbohydrate than the glucose and starch test meals. The present results show that an increase in carbohydrate intake results in a larger percentage increase in the insulinaemic response than in the glycaemic response. This suggests that the insulinogenic effect of fructose demonstrated by Reiser *et al*, (1987) was due to the additional amount of carbohydrate in the test meal rather than to a specific insulinogenic effect of fructose.

The relationship between glucose and insulin responses was similar for sucrose, fructose, bread and glucose (Figure 2), and the GI values of sucrose, glucose and fructose were not significantly different from their II values (Table 2). This suggests that sugars do not produce inappropriately high postprandial insulin responses, that is, the insulin response elicited by sucrose and fructose is no different from that which would be expected from a starchy carbohydrate food with the same GI. Nevertheless, consumption of sucrose or fructose may increase postprandial insulin concentrations if total carbohydrate intake is increased or if the sugar replaces starch of a lower GI. However, sucrose and fructose have lower GI values than many common starchy foods, and highly refined starches have glycaemic responses similar to glucose (Foster-Powell & Brand Miller, 1995). Replacing refined starch with an equal amount of sucrose in processed foods (such as sweetened breakfast cereals) may actually reduce their blood glucose and insulin responses (Brand Miller & Lobbezoo, 1994).

We conclude that, in normal subjects, as carbohydrate intake is increased from 0 to 100 g, plasma insulin responses increase at a greater rate than plasma glucose responses. The plasma insulin response elicited by glucose, sucrose or fructose is similar to that which would be expected from a starchy food with the same glycaemic index. Since we studied only normal subjects, these conclusions may not apply to individuals with impaired glucose tolerance or diabetes.

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