Metabolic response to lactitol and xylitol in healthy men

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ABSTRACT  Sugar alcohols are used in food products, yet their metabolic effects in humans are poorly known. We examined plasma glucose, insulin, and C-peptide responses and changes in carbohydrate and lipid oxidation after the ingestion of 25 g lactitol, xylitol, or glucose. Eight healthy, nonobese men were studied after an overnight fast. After the ingestion of lactitol or xylitol, the rise in plasma glucose, insulin, and C-peptide concentrations was less than after the ingestion of glucose (P < 0.02), with no difference between the two polyols. With the glycemic index of glucose as 100, the indexes of xylitol and lactitol were 7 and −1, respectively. A reactive hypoglycemia was observed 3 h after glucose ingestion, but not after the ingestion of sugar alcohols. There were no significant changes in the carbohydrate or lipid oxidation as determined by indirect calorimetry after the ingestion of sugar alcohols. After glucose ingestion, the rise in carbohydrate oxidation was nearly significant (P = 0.07). In conclusion, lactitol and xylitol cause smaller changes than does glucose in plasma glucose and insulin concentrations and thermogenic response. A small hormonal response and the lack of a thermogenic effect may be beneficial when these sugar alcohols are used in food products. The small glucose and insulin responses also suggest that lactitol and xylitol are suitable components of the diet for diabetic patients.


KEY WORDS  Xylitol, lactitol, sugar alcohols, insulin, glucose, thermogenesis, diabetes

INTRODUCTION

Because of their physiologic properties, such as a sweetening power, low caloricity, and reduced energy content, sugar alcohols are widely used as sugar substitutes in various food products. The lower energy derived from sugar alcohols is due to the fact that they are only partially absorbed from the digestive tract. A large proportion of ingested xylitol reaches the distal part of the gut, where the end products of its metabolism by bacteria are the volatile fatty acids, such as acetate, propionate, and butyrate (1, 2). Most of the volatile fatty acids are absorbed from the gut and are further utilized in mitochondria for production of acetyl-CoA, thus, contributing to energy homeostasis in humans.

Among the major sugar alcohols used in the food industry are xylitol and lactitol. Xylitol, a five-carbon polyol, is metabolized primarily in the liver, where it is converted through an insulin-independent pathway to glucose-6-phosphate. Because of its slow conversion to glucose, the rises in blood glucose and insulin concentrations are only modest after either oral or intravenous xylitol administration in healthy humans (3, 4). Thus, under conditions of insulin deficiency xylitol can be used as a sugar substitute because of its partially insulin-independent metabolism. Xylitol has the same sweetness as sucrose. Lactitol is a dimeric sugar alcohol that is not absorbed in the small intestine and is degraded by the colonic flora when it reaches the colon (5). Thus, the metabolism of lactitol takes place entirely by fermentation in the lower gut. Lactitol has a low energy value (9.4 kJ/g) (6), which makes it particularly interesting for the production of reduced-energy food products. To what extent lactitol can elicit a plasma glucose or insulin response is poorly known. Neither is it known to what extent energy expenditure differs after the ingestion of different sugar alcohols in healthy humans. This information is important because sugar alcohols are used in food products for specific groups, such as diabetic or obese persons, to facilitate their weight-loss efforts. Consequently, the present study was designed to examine the effects of xylitol or lactitol ingestion on plasma glucose and insulin and the thermogenic response in humans.

SUBJECTS AND METHODS

Subjects

We studied eight healthy, nonobese male volunteers with a mean age of 25 ± 1 y and body mass index (in kg/m²) of 22.1 ± 0.5. None of the subjects took any medication and they had been consuming weight-maintaining diets with 200–250 g carbohydrate/d for ≥ 3 d before the study. All subjects were informed about the nature, purpose, and possible risks of the study before giving their consent to participate. The study protocol was approved by the Ethical Committee of the Helsinki University Hospital.

Procedure

The subjects were studied in the postabsorptive state after an overnight (10–12 h) fast. An indwelling catheter was inserted in an antecubital vein for blood sampling. After two baseline

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1 From the Helsinki University Central Hospital, Department of Medicine, Helsinki.
2 Supported by the Finnish Academy of Science and Yrjö Jahnsson Foundation.
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4 Received August 8, 1996. Accepted for publication November 13, 1996.
blood samples were obtained, the subjects ingested within 2–3 min 250 mL of a solution containing either 25 g glucose, 25 g xylitol, or 26.25 g lactitol monohydrate, which contains 4.9% water of crystallization and is equivalent to 25 g lactitol dry weight. Blood samples were drawn at 30-min intervals for the next 180 min. Plasma glucose was determined with the glucose oxidase method using a Beckman glucose analyzer (Fullerton, CA). Serum insulin was measured by a double-antibody radioimmunoassay (Pharmacia, Uppsala, Sweden) (7) and the serum C-peptide concentration was determined with a radioimmunoassay (8). For the determination of carbohydrate, lipid, and protein oxidation and energy expenditure, indirect calorimetry (Deltatrac Metabolic Monitor; Datex, Helsinki) was performed with subjects in the basal state (between −40 and 0 min) and from 60 to 120 min after the glucose or sugar alcohol ingestion as described previously (9, 10). The constants used to calculate glucose, lipid, and protein oxidation and energy expenditure from the respiratory exchange data were given previously (9). Each subject participated in all three studies. The studies were done in a randomized order at 1-wk intervals and in a single-blind fashion so that the subject was unaware of the substance he was given.

Statistical analysis

Comparisons between the paired items were made by using the Wilcoxon rank-sum test (SYSTAT; Systat Inc, Evanston, IL). In addition, analysis of variance (ANOVA) for repeated measures was used to analyze the differences between the treatments. In the ANOVA for repeated measures, Greenhouse-Geisser adjustment was used to avoid excessive type I error. The values are given as means ± SEMs.

RESULTS

In the basal state, plasma glucose and serum insulin and C-peptide concentrations were not significantly different in any studies (Figures 1–3). The rise in plasma glucose was significantly greater 30 and 60 min after the ingestion of glucose than after ingestion of sugar alcohols (P < 0.02). A small but significant elevation (7% of the magnitude seen after glucose ingestion) was also seen after the ingestion of xylitol. No change from baseline was observed after the lactitol load (Figures 1–3). At 150 and 180 min, the plasma glucose concentration was below baseline and it was lower than after the ingestion of the sugar alcohols (P < 0.05). When analyzed with

![Figure 1](https://example.com/fig1.png)

**FIGURE 1.** Plasma glucose response after the ingestion of glucose (■), lactitol (○), or xylitol (▪). *Significantly different from baseline, P < 0.05–0.01. x ± SEM; n = 8.

![Figure 2](https://example.com/fig2.png)

**FIGURE 2.** Serum insulin response after the ingestion of glucose (■), lactitol (○), or xylitol (▪). *Significantly different from baseline, P < 0.05–0.01. x ± SEM; n = 8.

![Figure 3](https://example.com/fig3.png)

**FIGURE 3.** Serum C-peptide response after the ingestion of glucose (■), lactitol (○), or xylitol (▪). *Significantly different from baseline, P < 0.05–0.01. x ± SEM; n = 8.

ANOVA for repeated measures, the plasma glucose curve was significantly different after glucose ingestion than after both lactitol and xylitol ingestion (P < 0.01 in both). When the glucose curve after xylitol ingestion was compared with that of lactitol, no significant difference was found. The C-peptide curve after xylitol ingestion differed from that for lactitol or xylitol (P < 0.01 in both) and the curve after xylitol ingestion differed from that of lactitol (P = 0.03). The insulin curve after glucose ingestion differed from those for xylitol and lactitol (P < 0.01 for both).

The areas under the plasma glucose and insulin curves were significantly lower after lactitol than after xylitol ingestion and both of these were lower than after the ingestion of glucose (P < 0.01). The reactive hypoglycemia was not observed after the sugar alcohols. When the glycemic index is calculated as an increment under the plasma glucose curve and the value after glucose ingestion is taken as 100, the glycemic index of xylitol is 7 ± 7 and of lactitol is 1 ± 7.

There were no significant changes in carbohydrate or lipid oxidation after the ingestion of lactitol or xylitol (Figure 4). After glucose ingestion, the rise in carbohydrate oxidation was nearly significant (P = 0.07), and the fall in lipid oxidation was significant compared with after xylitol ingestion.

None of the subjects had abdominal pain or diarrhea during the study and all of them completed the three studies.

DISCUSSION

The postprandial rise in plasma glucose and insulin concentrations in healthy humans depends on the size and quality of
the meal, particularly on the amount of carbohydrate ingested. This is well appreciated by the modern food industry, particularly when confectionery or diet food is prepared. The use of sugar alcohols as sweeteners is increasing in these food products. In the present study, we examined blood glucose, insulin, and the thermogenic response to the sugar alcohols lactitol and xylitol compared with those of glucose. All the current tests were performed with small doses (25 g) to avoid any abdominal discomfort, which the sugar alcohols can cause in large amounts (11). None of the subjects had any symptoms, indicating that the amount used here can be given as a single dose.

There was no change in glucose or insulin response after lactitol, confirming that lactitol is not absorbed by the small intestine and is metabolized in the colon (12). After the ingestion of xylitol, plasma glucose, insulin, and C-peptide concentrations increased slightly, but the glucose response was only 7% and insulin and C-peptide response was 20–25% of that after glucose ingestion. The small plasma glucose response after the ingestion of xylitol and the lack of any response after lactitol indicate that a very small amount of xylitol is converted to glucose, and that lactitol is not converted at all. This was confirmed by comparing plasma insulin responses. Three hours after glucose ingestion there was a reactive hypoglycemia, probably caused by a high insulin response. This did not occur after the ingestion of sugar alcohols. Because lactitol caused no insulin response and the response after xylitol was very small, no reactive hypoglycemia was observed after these sugar alcohols.

The polyols were administered in liquid form to fasting subjects. Under these conditions, the transit time is more rapid than when they are eaten with a solid meal (13, 14). However, the experimental conditions were equal in all studies and, thus, a rapid transit time had a similar effect on both sugar alcohols and glucose.

The energy value of sugar alcohols depends primarily on the percentage of ingested carbohydrate, including the original sugar alcohols and their hydrolysis products, which are absorbed in the small intestine, and how they are metabolized after absorption (15). In the current study, there was no significant change in total energy expenditure after the ingestion of lactitol or xylitol compared with the basal value. The only increment of borderline significance was a rise in carbohydrate oxidation with a simultaneous decrease in lipid oxidation after the ingestion of glucose. This was probably mediated by an increase in plasma insulin concentration after the glucose load. Unchanged thermogenesis after the ingestion of sugar alcohols may be due to the fact that the dose (25 g/250 mL water) was small, and the amount of hydrolysis products that were absorbed in the small intestine was also small. In addition, the low energy value of lactitol (9.4 kJ/g) (6) compared with that of glucose (16.5 kJ/g) may contribute to the lack of any significant thermogenic effect. However, xylitol yields the same amount of energy (16.5 kJ/g) (16) as glucose, so the slow conversion to glucose-6-phosphate may be responsible for the lack of thermogenic effect. These data indicate that a single dose of sugar alcohols as given here does not cause any changes in carbohydrate or lipid oxidation or in the net energy balance. Because glucose and lipid metabolism are related (15), we measured the oxidation of both glucose and lipids simultaneously. Because the insulin response was very different after glucose and sugar alcohol ingestion and insulin is important in the regulation of lipolysis, we measured lipid oxidation after the ingestion of each of these compounds.

Avoiding the perturbations of glycemic and thermogenic response by the ingesting sugar alcohols may have several practical implications. First, they will not cause a hyperglycemic response in insulin-deficient diabetic patients. Second, the lack of thermogenesis and heat production by the meal may reduce postprandial sweating, which can be a problem in some individuals.

In the current study, the sugar alcohols were given in pure form. Thus, our results are directly applicable only to the pure forms of xylitol and lactitol. However, if polyols were mixed with flavoring or essential oils and sweeteners (eg, with protein and fat such as in chocolate) we would not anticipate any major differences from the results in the present study, because the doses of sugar alcohols would be smaller in food products than in the current study (17, 18).

Taken together, the present study confirms the potential metabolic advantages of the use of xylitol and lactitol as carbohydrate energy sources in the diet. Compared with glucose, the advantages associated with these sugar alcohols are lower energy content, smaller fluctuations in blood glucose and insulin responses, and smaller thermogenic effects. Because of their very low glycemic indexes (19), they may be considered suitable components of diets for diabetic patients.

The expert technical assistance of Elisa Kostamo is acknowledged.

REFERENCES


