**Human Nutrition and Metabolism**

**D-Tagatose, a Stereoisomer of D-Fructose, Increases Hydrogen Production in Humans without Affecting 24-Hour Energy Expenditure or Respiratory Exchange Ratio**

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**ABSTRACT** In growth studies on rats, the ketohexose D-tagatose has been shown to contribute no net metabolizable energy, and a pronounced thermic effect of the sugar has been suggested to account for the absence of energy. In a double-blind and balanced cross-over design, we measured 24-h energy expenditure in eight normal weight humans in a respiration chamber during the consumption of 30 g D-tagatose or 30 g sucrose/d. Metabolic measurements were performed before and after a 2-wk adaptation period with a 30-g daily intake of the test sugar. Total 24-h energy expenditure and hour-by-hour profile were unaffected by the test sugar. The nonprotein respiratory exchange ratio (RERnp) was similar during consumption of D-tagatose and sucrose. However, the effect on RERnp due to CO₂ produced by fermentation of D-tagatose could not be quantified in this study. A significant increase in 24-h H₂ production (35%) during D-tagatose administration suggests a substantial malabsorption of the sugar. We found no effects of the 2-wk adaptation period on the measured gas exchange variables. Significantly lower fasting plasma insulin and triglyceride concentrations were observed during D-tagatose administration compared with the sucrose period. No effects of D-tagatose on body weight and composition were seen, but the perception of fullness 2.5 h after the sugar load was greater with D-tagatose. In conclusion, this study does not suggest a pronounced thermic effect of D-tagatose, and other mechanisms seem to be required to explain its lack of net energy. J. Nutr. 128: 1481–1486, 1998.

**KEY WORDS:** D-tagatose • energy expenditure • fermentation • humans • hydrogen

Low energy bulk sweeteners are sugars or sugar alcohols that can be used as additives in the manufacture of low energy foods. Unlike intense sweeteners, low energy bulk sweeteners have a sweetening effect that is lower than or comparable to that of sucrose; thus, a greater volume of the sweetener is required. This is often useful in the manufacture of artificially sweetened food products. The low energy content of bulk sweeteners is often due to malabsorption, and daily consumption may therefore be limited by gastrointestinal side effects such as flatulence and diarrhea (Koutsou et al. 1996). It has been suggested that D-tagatose, a stereoisomer of fructose, is absorbed to a greater extent than most other low energy bulk sweeteners, while still having a lower net energy content than sucrose (Levin et al. 1995). If this is true, then the gastrointestinal side effects of D-tagatose should be less because less of the sugar may be assumed to reach the large intestine, causing osmotic diarrhea and gas production from fermentation. The finding of a 68% recovery by breath of [14C] from [14C]-labeled D-tagatose given orally to adapted rats, (Levin et al. 1995) suggests that a substantial proportion of D-tagatose can be absorbed and metabolized in the body. However, the expiratory [14CO₂] may, in fact, have derived from absorbed and subsequently metabolized fermentation products of D-tagatose (short-chain fatty acids, SCFA) or directly from bacterial degradation of D-tagatose. A recent study in pigs concluded that a maximum of 26% of ingested D-tagatose is absorbed at the level of the distal part of the small intestine (Johansen et al. 1997). This observation implies that the lack in net energy of D-tagatose reported from growth studies in rats (Levin et al. 1995, Livesey and Brown 1996) may be explained in part by malabsorption.

When D-tagatose enters the liver, it is metabolized in much the same way as D-fructose. First, it is phosphorylated by keto-hexokinase and then cleaved by aldolase B to enter glycolysis at the level of dihydroxy-acetone phosphate and D-glyceraldehyde (van den Berghe 1975). Therefore D-tagatose probably has a metabolizable energy comparable to that of D-fructose.
If most of it is absorbed, it should therefore be expected to have a strong thermic effect to account for its putative lack of net energy. A third possibility is that D-tagatose may impair the absorption of other macronutrients. This possibility has not as yet been examined.

In this study, we investigated whether the intake of D-tagatose is associated with a marked thermogenesis both acutely and after a 14-d adaptation period, because exposure to nonabsorbed carbohydrates over a period of time may increase the fermentation capacity of the gut flora (Briët et al. 1995). Hydrogen and methane excretion were measured to detect any increase in fermentation when D-tagatose was administered. We took advantage of the study design to see whether the 15-d D-tagatose administration had an effect on liver function and blood lipids, which may be detectable in the fasting state.

MATERIALS AND METHODS

Five Caucasian female subjects (weight 66.3 ± 2.9 kg, height 169.0 ± 2.3 cm, age 26.2 ± 2.63 y) and three Caucasian male subjects (weight 74.4 ± 3.9 kg, height 183.7 ± 0.8, age 25.0 ± 3.4 y), recruited through advertisements in local newspapers, took part in the study. Only nonsmokers were included in the study. Before inclusion, all candidates were screened for adverse responses (nausea or diarrhea) to D-tagatose. A single dose of 30.0 g of D-tagatose was administered at the screening. One candidate was excluded due to diarrhea; another subject was excluded because he felt uncomfortable with the indirect calorimetry procedure, although his symptoms probably did not relate to D-tagatose. The study protocol was approved by the Municipal Ethical Committee of Copenhagen and Frederiksborg, Denmark.

Metabolic measurements were performed over a 24-h period on d 1 and 15 of each study period in which either 30.0 g of D-tagatose or 30.0 g sucrose was consumed in the breakfast meal. The study protocol is randomized crossover design, with the subjects functioning as their own controls. The subjects and investigators did not know which of the test sugars was being consumed during the respective study periods. The tests of the two sugars were separated by a washout period of > 2 mo.

During the 2-wk intervention periods, the test sugar was administered in the form of the sugar in a piece of cake (test sugar, egg, butter, wheat flour, soy flour, desiccated coconut, cream and baking powder), supplied every weekday at the department. The subjects were allowed to eat the cake at any time during the day. The subjects otherwise consumed their own home-cooked food ad libitum. On weekends and special occasions, the subjects were supplied with cake to last a few days. The subjects were supplied with a fixed diet prepared by a metabolic kitchen during the four metabolic test days and the day preceding each of these tests. In an attempt to standardize 24-h energy and macronutrient balances, the prepared diet was identical for all of the 8 d. The daily energy content was individually calculated from the fat-free mass of the subjects by using an algorithm based on indirect calorimetry measurements in healthy subjects performed previously at our department (Klausen et al. 1997). Fat-free mass was determined by measurements of weight, height and bioimpedance by using an algorithm presented by Heitmann (1990). The macronutrient composition of the diet was 50, 37 and 13 energy% carbohydrate, fat and protein, respectively. The controlled diet consisted of a continental breakfast (rye and wheat breads, butter, cheese, raspberry jam and orange juice), a lunch (rye and wheat breads, butter, salted ham, liver paste, cottage cheese with ham, cucumber, apple and fruit juice) and supper (goulash made with beef, onion, tomato puree, carrot, cream, cornflour, served with rice and an apple).

On each metabolic test day, respiratory gas exchange was measured over a 24-h period in a metabolic chamber from 0900 to 0900 h (Astrup et al. 1990). In addition to oxygen uptake and carbon dioxide production, we measured the production rates of hydrogen by nondispersive infrared absorption (URAS 3G, Hartmann & Braun AG, Frankfurt, Germany) and of methane by an electrochemical sensor (STATOX-S, Computer Monitors Sensor Technology GmbH, Frankfurt, Germany). Total urine was collected for the following three periods: daytime (900–1830 h), post-supper (1830–2300 h) and night (2300–0900 h), and analyzed for total nitrogen excretion to calculate O2 and CO2 exchange not derived from protein oxidation. Protein oxidation was achieved by assuming that 6.25 g of protein was combusted per gram of nitrogen excreted in the urine (Brouwer 1965). Energy expenditure (EE) and nonprotein respiratory exchange ratio (RERnp) are presented as hour-by-hour profiles based on the assumption that nitrogen excretion was constant over each of the urine-sampling intervals. In four tests, hour-by-hour recordings of hydrogen production were lost due to a temporary sampling failure in the software. Data from the corresponding tests with the other test sugar were removed from the presentations and analyses. The calculation of EE does not take the formation of H2 and CH4 into account because the maximum recorded H2 and CH4 production within 1 h in any one experiment was 240 and 72 mL, respectively. Using the calculations of Poppitt et al. (1996), this corresponds to a reduction in EE of 1.15 and 0.19 kJ h−1, respectively, or only ~0.3 and 0.05% of measured EE.

Subjects spent the night preceding each 24-h measurement in the respiratory chamber to become familiarized with the environment and to ensure that they were at ease when the experiment commenced. Each metabolic experiment was performed according to the same schedule. Breakfast, lunch and supper were served at 0900, 1230 and 1830 h, respectively. A piece of cake containing the test sugar, identical to that given on the other days of the intervention period, was eaten immediately after lunch. The subjects were in bed between 2300 and 0900 h. Five periods of light exercise during the daytime (a bicycling session at 75 W for 10 min at 0930, 1330 and 1730 h, and short walking sessions at 1100 and 1530 h) were included in the program. The subjects were otherwise free to follow their own daily routine, but they were not allowed to take additional exercise. A radio, a television, a video and a telephone were available in the chamber and could be used freely during daytime and evening. During the stay in the chamber, the subjects completed a questionnaire 2.5 h before the load. Urine collections (24-h) from the metabolic study periods: daytime (900–1830 h), post-supper (1830–2300 h) and night (2300–0900 h), and analyzed for total nitrogen excretion to calculate O2 and CO2 exchange not derived from protein oxidation. Protein oxidation was achieved by assuming that 6.25 g of protein was combusted per gram of nitrogen excreted in the urine (Brouwer 1965). Energy expenditure (EE) and nonprotein respiratory exchange ratio (RERnp) are presented as hour-by-hour profiles based on the assumption that nitrogen excretion was constant over each of the urine-sampling intervals. In four tests, hour-by-hour recordings of hydrogen production were lost due to a temporary sampling failure in the software. Data from the corresponding tests with the other test sugar were removed from the presentations and analyses. The calculation of EE does not take the formation of H2 and CH4 into account because the maximum recorded H2 and CH4 production within 1 h in any one experiment was 240 and 72 mL, respectively. Using the calculations of Poppitt et al. (1996), this corresponds to a reduction in EE of 1.15 and 0.19 kJ h−1, respectively, or only ~0.3 and 0.05% of measured EE.

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In the morning, immediately before commencement of each chamber measurement, body weight, height and bioimpedance were assessed to estimate fat-free mass, and supine blood pressure was measured. Shortly after termination of the gas exchange measurements, ~21 h after the preceding dose of the test sugar, blood samples were taken from the fasting subject after 10 min supine rest. Blood was analyzed for glucose and lactate by enzymatic methods (Bergmayer 1974), insulin (RIA, Pharmacia and Upjohn, Copenhagen, Denmark), triglycerides (enzymatic test, Boehringer Mannheim Denmark, Erpharm, Hörsholm), total cholesterol (HPTL chromatography, Boehringer Mannheim), HDL cholesterol (enzymatic test, Boehringer Mannheim), Sugiuchi et al. 1995) and urate (by microbial uricase and a peroxidase-catalyzed chromogenic process; Town et al. 1985). To test a possible effect of D-tagatose on liver function, we measured alkaline phosphatase (EC 3.1.3.1) (Boehringer Mannheim; Recommendations of the German Society for Clinical Chemistry 1970) and γ-glutamyl transferase (EC 2.3.2.2; Deutsches Arzneibuch der DDR 1968). In two subjects, serum was also analyzed for D-tagatose (capillary gas chromatography after deactivation of hydroxy groups; Jansen et al. 1986) to test whether the sugar remained detectable in blood 21 h after the load. Urine collections (24-h) from the metabolic study were analyzed for D-tagatose and urate to calculate their excretion rates. Additional analyses of fasting blood and 24-h urine collections from d 7 or 8 of the period were performed. The blood data for d 7 of one subject were excluded because she was not fasting when the samples were taken.

Statistics. The effects of treatment and day on EE, RERnp and H2 production were tested by three-way ANOVA, with treatment, day and subject as categoric variables. Possible effects of treatment on the hour-by-hour profiles of RERnp were tested by the split-plot
**TABLE 1**

Body weight and composition in eight fasting subjects in the morning after the first and last days of a 15-d period of consumption of 30 g D-tagatose or sucrose.\(^1,2\)

<table>
<thead>
<tr>
<th></th>
<th>d 1</th>
<th>d 15</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Body weight, kg</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sucrose</td>
<td>69.2 ± 2.9</td>
<td>69.6 ± 2.9</td>
<td>0.39</td>
</tr>
<tr>
<td>D-Tagatose</td>
<td>69.2 ± 2.8</td>
<td>69.3 ± 2.7</td>
<td>0.64</td>
</tr>
<tr>
<td><strong>Fat mass, kg</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sucrose</td>
<td>15.9 ± 2.1</td>
<td>16.2 ± 2.0</td>
<td>0.38</td>
</tr>
<tr>
<td>D-Tagatose</td>
<td>15.6 ± 1.9</td>
<td>15.5 ± 2.0</td>
<td>0.45</td>
</tr>
<tr>
<td><strong>Fat-free mass, kg</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sucrose</td>
<td>53.3 ± 3.3</td>
<td>53.4 ± 3.0</td>
<td>0.76</td>
</tr>
<tr>
<td>D-Tagatose</td>
<td>53.6 ± 3.0</td>
<td>53.7 ± 3.0</td>
<td>0.51</td>
</tr>
</tbody>
</table>

\(^1\) Values are means ± SEM, \(n = 8\).

\(^2\) Differences between d 1 and 15 were tested separately for each treatment by two-way ANOVA with day and subject as factors.

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RESULTS

Body weight, fat-free mass, fat mass and blood pressure did not change significantly from d 1 to 15 (Table 1), and the across-period changes in weight and body composition were not found to be influenced by the nature of the test sugar (\(P > 0.25\)).

No differences between D-tagatose and sucrose tests were found in 24-h EE (D-tagatose vs. sucrose, d 1: 8843 ± 471 vs. 8852 ± 492 kJ, \(P = 0.96\); d 15: 8787 ± 466 vs. 8916 ± 522 kJ, \(P = 0.29\)). D-tagatose did not produce a d 1–15 change in 24-h EE (\(P = 0.58\)). The hour-by-hour profiles across the 24-h measuring periods were very similar for all four tests (Fig. 1). Protein oxidation did not differ between D-tagatose and sucrose tests on a 24-h basis (D-tagatose vs. sucrose: 1.18 ± 0.71 vs. 1.17 ± 0.73 MJ, \(P = 0.96\)), and no test sugar × day interactions were seen. Twenty-four hour RER\(_{np}\) was unaffected by the nature of the test sugar, before and after, accounting for actual energy balance as a covariate by ascribing the same energy value to D-tagatose and sucrose. No significant test sugar × day interaction on RER\(_{np}\) could be demonstrated, which otherwise would have suggested a possible long-term influence of D-tagatose on relative CO\(_2\) production. Furthermore, no differences between sucrose and D-tagatose were found in hour-by-hour profiles of RER\(_{np}\) at d 1 or 15 (\(P > 0.15\) by split-plot procedure, Fig. 2). Furthermore, RER\(_{np}\) did not show any response to treatment when a 5-h period after the test sugar load (1300–1800 h) was analyzed separately.

Total 24-hour hydrogen production was ~35% higher for D-tagatose than for sucrose, both when administered acutely and after the 14-d adaptation period (Table 2). This was solely attributable to an increased hydrogen production during the daytime, particularly during the 5-h period after the load (Table 2, Fig. 3).

Hydrogen production was significantly increased after D-tagatose from between 1300 and 1400 h, i.e., as early as 0.5–1.5 h after the load. The difference in hydrogen production between D-tagatose and sucrose tests during the 5-h post-load period varied substantially among subjects (from −10 to 254 mL on d 1, and from 84 to 266 mL on d 15).

One subject had a high 24-h methane production, which was 835 mL on d 1 and 692 mL on d 15 in the D-tagatose tests, and 409 and 519 mL in the corresponding sucrose experiments, respectively. The maximum observed 24-h methane production in the remaining subjects was 60 mL. With one single exception, the remaining subjects all had a higher 24-h hydrogen production in each of the four tests than did the methane-producing subject. Hydrogen production over a 24-h period remained significantly higher in D-tagatose tests after omission of the methane-producing subject from the analyses.

When D-tagatose was administered, 24-h urinary excretion

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**FIGURE 1** Profiles of energy expenditure (EE) over a 24-h period in eight human subjects measured in a respiration chamber during consumption of 30 g D-tagatose or sucrose on the d 1 and 15 of an adaptation period with a daily intake of 30 g of the sugar.
was tested against sucrose separately for each of the three sampling occasions. However, when observations from the 3 d were merged into one analysis using a split-plot procedure, lower concentrations of insulin and triglycerides after D-tagatose were significant (insulin: D-tagatose vs. sucrose, d 1: 55.2 ± 4.0 vs. 64.4 ± 6.5; d 7: 59.3 ± 5.7 vs. 91.8 ± 20.8; d 15: 54.1 ± 3.9 vs. 58.2 ± 4.6 pmol/L, P = 0.05; triglycerides: D-tagatose vs. sucrose, d 1: 1.20 ± 0.13 vs. 1.38 ± 0.19; d 7: 1.37 ± 0.13 vs. 1.41 ± 0.17; d 15: 1.46 ± 0.22 vs. 1.70 ± 0.39 mmol/L, P = 0.04). Urinary urate excretion over a 24-h period from the chamber experiments tended to be increased by D-tagatose (D-tagatose vs. sucrose: 2.61 ± 0.18 vs. 2.29 ± 0.20 mmol, P = 0.09). No significant interactions between the nature of the sugar and point of time in the experimental period were found for urate excretion or any of the blood parameters. Of the four different perceived appetite scores, fullness 2.5 h after dinner was the only score that seemed to be affected by the nature of the test sugar, showing an increase with D-tagatose from 39 to 52% (P = 0.02). This response was similar on d 1 and 15.

No severe gastrointestinal symptoms were recorded during the calorimetry measurements. There were three cases of moderate rumbling in the stomach, one case of loss of appetite, two cases of moderate and one case of strong distension, all observed when D-tagatose was administered. Symptom scores could not be analyzed statistically due to the small number of observations and their skewed distribution. However, there were no obvious improvements or deteriorations in recorded symptoms from d 1 to 15 during the D-tagatose intervention or during the control period.

DISCUSSION

A pronounced thermogenic effect of D-tagatose has previously been proposed to explain the lack of net energy of the sugar when added to the basal diet seen in growth studies in rats (Levin et al. 1995, Livesey and Brown 1996). This was not confirmed by the present human study. In the rat studies, the daily load of D-tagatose was ~10% of gross energy, which

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**TABLE 2**

<table>
<thead>
<tr>
<th>Day</th>
<th>Sucrose</th>
<th>D-Tagatose</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>24-hour</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>580 ± 57</td>
<td>782 ± 85</td>
<td>0.002</td>
</tr>
<tr>
<td>15</td>
<td>567 ± 81</td>
<td>782 ± 58</td>
<td>0.002</td>
</tr>
<tr>
<td>0900–2300 h</td>
<td>1</td>
<td>429 ± 47</td>
<td>534 ± 88</td>
</tr>
<tr>
<td>15</td>
<td>339 ± 87</td>
<td>642 ± 58</td>
<td>0.004</td>
</tr>
<tr>
<td>2300–0900 h</td>
<td>1</td>
<td>126 ± 17</td>
<td>196 ± 63</td>
</tr>
<tr>
<td>15</td>
<td>132 ± 32</td>
<td>125 ± 17</td>
<td>0.81</td>
</tr>
<tr>
<td>1300–1800 h</td>
<td>1</td>
<td>126 ± 24</td>
<td>231 ± 53</td>
</tr>
<tr>
<td>15</td>
<td>91 ± 24</td>
<td>286 ± 43</td>
<td>0.004</td>
</tr>
<tr>
<td>1800–2300 h</td>
<td>1</td>
<td>234 ± 39</td>
<td>218 ± 32</td>
</tr>
<tr>
<td>15</td>
<td>185 ± 69</td>
<td>267 ± 450</td>
<td>0.06</td>
</tr>
</tbody>
</table>

1 Values are means ± SEM, n = 8 for 24-h data, n = 7 and n = 5 for subperiods on d 1 and 15, respectively.
2 Differences between treatments are tested separately for each day by two-way ANOVA with treatment and subject as factors.

of the sugar in the different subjects and on the different days ranged between 0.2 and 1.6 g, corresponding to 0.7 and 5.3% of daily dose, respectively. No D-tagatose was found in the urine from the sucrose tests. Urinary D-tagatose excretion did not vary significantly over the three D-tagatose days (d 1 vs. d 7 vs d 15: 0.67 ± 0.13 vs. 0.56 ± 0.12 vs. 0.71 ± 0.16 g/d). There was a positive relationship in D-tagatose excretion between d 1 and 7 and between d 1 and 15 (r = 0.88, P < 0.02 by Spearman rank correlation), indicating a consistency within each subject in the amount of D-tagatose excreted. Plasma concentration of D-tagatose was below the detection limit of 0.05 mmol/L in blood samples from the two subjects whose blood concentrations were analyzed. No significant differences were found in alkaline phosphatase, γ-glutamyl transpeptidase, urate, blood lipids, glucose or insulin when D-tagatose

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**FIGURE 2** Profiles of nonprotein respiratory exchange ratio (RERnp) over a 24-h period in eight human subjects measured in a respiration chamber during consumption of 30 g D-tagatose or sucrose on d 1 and 15 of an adaptation period with a daily intake of 30 g of the sugar.
is about twice the relative dose used in this study. Therefore it cannot be excluded that an increased energy expenditure compared with sucrose would have been disclosed with a higher load. However, the 30-g dose was chosen as a level that most humans could tolerate without unacceptable gastrointestinal symptoms. Furthermore, if the putative lack of net energy of D-tagatose were due solely to thermogenesis, an increase of ~5% in 24-h EE would be anticipated in this study. If most of this increase can be expected to occur within a few hours after the load, it should be above the detection limit based on calculations of within-subject variation of repeated measurements previously performed in our respiration chambers (Toubro et al. 1995). The 24-h indirect calorimetry tests were performed on d 1 of D-tagatose administration and after a 15-d period with regular intake to examine the possibility that an adaptation might increase the thermic effect of the sugar as a consequence of an improved recovery of its energy was examined. Repeated exposure of the colon to nonabsorbed carbohydrates may alter the intestinal flora and increase its capacity to ferment the carbohydrate (Briet et al. 1995), thus rendering a greater part of its energy available as absorptive SCFA. Moreover, studies with intravenous infusion of different SCFA suggest that they may be more thermogenic than glucose (Chiolerò et al. 1993). In this study, total 24-h EE and hour-by-hour profiles of EE were very similar before and after the 2-wk intervention period, which does not indicate an increased energy expenditure as a consequence of adaptation (Fig. 1).

A significant increase of ~35% in hydrogen production was seen with D-tagatose compared with sucrose, with similar responses on d 1 and 15. This indicates that a substantial part of the consumed D-tagatose escapes absorption and is fermented in the large intestine. This is in agreement with a recent study in pigs, suggesting that the digestibility of D-tagatose does not exceed 26% (Johansen and Jensen 1997). The average increase of ~200 mL in the present study corresponds to 6.7 mL/g D-tagatose. This is between the values of 1.9 mL/g (obtained by ventilated hood; Bond and Levitt 1972) and 13.5 mL/g (obtained in a respiration chamber study; Christl et al. 1992) after ingestion of the nonabsorbable disaccharide lactulose. The higher values obtained from whole-body calorimetry studies may be due to the recovery of hydrogen in the flatus because <50% of H$_2$ produced from rapidly fermented sugars may be excreted by the breath (Christl et al. 1992). Moreover, the amount of total hydrogen excretion is always subject to a pronounced interindividual variation which, in fact, makes it questionable to compare data concerning hydrogen production from different studies. The large between-subject variation in hydrogen release is probably due to ecological differences of the large intestine, resulting in different quantities of H$_2$ being eliminated by the formation of different organic substances. The observation in this study that the only subject who produced appreciable amounts of methane had a low H$_2$ excretion may reflect this mechanism. Comparing total 24-h H$_2$ and CH$_4$ production, or their hour-by-hour profiles over the days, did not give any indication that a possible change in fermentation capacity had occurred because no significant differences from d 1 to 15 were observed.

Surprisingly, an increased H$_2$ production was found with D-tagatose within 1.5 h after the administration of the test sugar, and the increase seemed to be similar on d 1 and 15. The most likely explanation for the early peak in H$_2$ excretion after lunch is that the meal caused a protrusion of previously ingested food into the cecum, initiating its fermentation, rather than it being a result of fermentation of the lunch per se. This would be a result of a reflex stimulation of the ileum, which therefore should be more pronounced after D-tagatose. If so, a greater osmotic effect of D-tagatose might be involved. A very short delay of 1.5 h between ingestion of sugar alcohols and the appearance of an augmented H$_2$ excretion compared with sucrose has previously been reported (Lee et al. 1994).

Several factors may compromise the applicability of RER as a measure of substrate partitioning when increased fermentation occurs. The formation of 1 mol of H$_2$ spares 0.5 mol O$_2$ consumption and should therefore be accounted for when calculating energy expenditure and metabolic respiratory quotient (RQ) from RER (Poppitt et al. 1996). However, an increase in H$_2$ production of ~200 mL/d induced by D-tagatose
is trivial compared with a daily $O_2$ uptake of $\sim 400$ L. More unpredictable is the $CO_2$ production associated with the formation of SCFA. An equation developed for the fermentation of hexoses in the colon of individuals with no methane production proposes that 1.68 mol $CO_2$ is produced for each mole hexose degraded (Grimble et al. 1988). The fermentation of 25 g D-tagatose/d would add 5.2 L $CO_2$ or $\sim 1.5\%$ to the measured $CO_2$ production. In methane producers, $CO_2$ is produced only in an amount that is equimolar to the degraded hexose (Miller and Wolin 1979). In addition to the $CO_2$ produced by the fermentation, the various SCFA being formed are oxidized by the body at different RQ, e.g., the RQ of acetic acid and butyric acid are 1.00 and 0.80, respectively.

The actual effect of colonic fermentation of nonabsorptive sugars on whole-body $CO_2$ production and the implications for the assessment of substrate oxidations have been addressed in two studies, both using lactulose. An excessive $CO_2$ production of 63 mL/g lactulose was found when 60 g lactulose was added to a natural sugar solution given to fasting subjects (Heresch et al. 1995). Ritz et al. (1993) found 212 mL/g excessive $CO_2$ on administration of 20 g lactulose. Both studies concluded that the observed increase in $CO_2$ production would be sufficient to invalidate the calculation of substrate oxidations from respiratory gas exchange. The effect of $CO_2$ produced by fermentation may be even greater in 24-h experiments using a respiration chamber compared with these short-term ventilated hood studies in which some of the $CO_2$ produced may have accumulated in the colon or escaped the ventilated hood through flatus.

No effects of the D-tagatose on weight, fat mass or fat-free mass were found. However, assuming that D-tagatose contributed no net energy and that no compensation in energy intake occurred, this would result in a relative energy deprivation of 30 g x 17 kJ/(g x d) x 14 d = 7.1 MJ. A decline in body energy stores of this size would probably not be reflected in a detectable change in body weight. On the other hand, the maintained body weight contradicts a massive anorectic effect of D-tagatose.

In conclusion, previous suggestions that the ketohexose D-tagatose should have a pronounced thermogenic effect to explain its apparent lack of net energy could not be confirmed in this human study. However, an increased $H_2$ production indicates that a substantial part of the sugar is malabsorbed. Data on RER are inconclusive because a possible decrease in metabolic RQ caused by a reduced carbohydrate availability for oxidation may have been masked by the extra $CO_2$ produced by the increased fermentation under D-tagatose substitution of sucrose.

ACKNOWLEDGMENTS

We thank Charlotte Kostecki for the preparation of the experimental diet. We are also indebted to Anne Raben and Christina Cuthbertson of the Research Department of Human Nutrition, to Hans Bertelsen of MD Foods Ingredients, Denmark and to Albert Bär of Bioresco, Switzerland, who assisted with the preparation of the experimental protocol and manuscript.

LITERATURE CITED


