Effect of Sugar Alcohols on Gut Function and Body Composition in Normal and Cecectomized Rats

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Abstract: The effects of two sugar alcohols on feed utilization, digesta retention, gut fermentation and serum lipid profiles were compared in normal and cecectomized rats to examine the possibility of the cecectomized rat as an experimental animal with relevance to humans. Semi-purified diets containing no sugar alcohol, 7% sorbitol or 7% lactitol were fed to normal and cecectomized rats for 16 days. The digestibility of the crude fat and the compositions of the carcass dry matter and crude fat were significantly decreased by feeding sugar alcohols in both groups, but the effects were relatively higher in the cecectomized rats than in the normal rats. Diarrhea, faster transit times and shorter retention times of digesta were noted in the cecectomized rats fed sugar alcohols, while the inverse results were observed in the normal rats fed similar diets. The concentration of cecal organic acids was increased in the normal rats, whereas the concentration of colonic organic acids was decreased in the cecectomized rats fed sugar alcohols, compared with their corresponding control groups. The concentration of serum total cholesterol was decreased in both the normal and cecectomized rats fed diets containing sugar alcohols. The tendencies for diarrhea, faster digesta transit and reduced body fat induced by the fermentable materials in the cecectomized rat have good relevance to the parallel effects of fermentable materials in humans, suggesting the possibility of using the cecectomized rat as a model to study some of the physiological effects of sugar alcohols in humans.

Key words: cecectomized rat, lactitol, mean retention time, sorbitol, transit time

Introduction

The anatomy of the digestive tract differs from animal to animal and depends on their feeding habits. Rodents are generally herbivores, although some, such as rats, are omnivores by nature [15]. Rats also display a basically non-wild tranquil behavior, and are easily acclimatized to new captive environments within a few days. Due to these characteristics, rats are widely used as experimental animals in scientific and medical research.

Although humans are an omnivorous species, there is an important difference between humans and rats in the physiology of the digestive tract. Rats possess a large
voluminous and non-sacculated cecum, which attaches to the gut at the junctions of the small intestinal ileum and the proximal colon. In the rat, it plays an important role in the storage, fermentation and utilization of indigestible and fermentable materials. It may also act as a “reservoir” of fluid during small intestinal hyper-secretion, and may play an important role in fluid conservation by storing secreted fluid [11]. In contrast, the sacculated colon in humans is the major site for retention of digesta and fermentation of indigestible and fermentable materials. In rats, fermentation of indigestible and fermentable materials takes place not only in the large cecum but also in the colon. The cecum of rats acts as a bypass storage unit between the ileum and the proximal colonic junction, but there is no such distinct feature in the large bowel of humans. Although rats are randomly used for human studies, these anatomical differences between the two species may limit the use of rats for studying the effects of fermentable functional food materials on the nutrition and physiology of humans.

The physiological and nutritional effects of indigestible and fermentable materials are also widely studied directly in human volunteers [3, 12, 17, 19], although excess consumption has laxative effects and large doses result in diarrhea in both humans and animals [4, 9, 30, 33]. Studies of the nutritional effects of functional food materials are more difficult in human subjects than in animals. It is also impossible to undertake wide-ranging studies in human subjects, as can be performed in animals. Under these circumstances, the possibility has been raised of using the cecectomized rat to study the nutritional effects of fermentable food materials in humans, because the digestive tract of a cecectomized rat is more analogous to the human digestive tract than that of an intact rat. However, very little is known about the different nutritional effects of fermentable food materials in normal and cecectomized rats [18], although removal of the cecum is a simple surgical procedure and cecectomy alone produces no major effects or morphological changes [24] in rats. Cecectomized rats recover rapidly, feed normally after surgery and have normal growth patterns [11]. Therefore, a comparative study of the effects of fermentable materials on the nutrition and physiology in normal and cecectomized rats and their relevance to human studies is important to justify their potential use as experimental animal models.

In the present study, the effects of one digestible and two fermentable materials on digesta retention, feed utilization, large gut fermentation, accumulation of body constituents and the serum lipid profile were compared between normal and cecectomized rats to investigate the possibility of using cecectomized rats as an experimental model animal for determining the physiological effects of sugar alcohols on humans.

### Materials and Methods

#### Animals

Thirty-two growing male Wistar rats (3 weeks old, Nippon SLC, Hamamatsu, Japan) were individually kept in stainless steel wire mesh bottom cages in an air-conditioned room at 23–25° C ambient temperature and 50–60% relative humidity. Light was controlled as 12 h on (0530–1730) and 12 h off (1730–0530). The rats were fed a commercial pellet diet (Labo MR Stock; Nihon Nosan Kogyo K.K. Ltd., Tsukuba, Japan) ad libitum with free access to tap water. After two weeks (5 weeks of age), when the body weight was 153.6 ± 11.3 g, 16 rats were randomly selected for cecectomy (described below). At 10 d after the surgery (the 11th day), the mean body weights of the cecectomized and normal groups were 233.1 ± 21.0 g and 242.8 ± 9.6 g, respectively. Of the 16 cecectomized rats, 14 were divided into 3 subgroups: 4 as the cecectomized control (CC) group, 5 as the cecectomized sorbitol (CS) group and 5 as the cecectomized lactitol (CL) group, with similar average body weights in each group. Of the 16 normal rats, 15 were randomly divided into 3 subgroups: 5 as the normal control (NC) group, 5 as the normal sorbitol (NS) group and 5 as the normal lactitol (NL) group, with similar average body weights in each group. Of the 16 cecectomized rats and one normal rat were sacrificed by diethyl ether anesthesia on the first day of the experiment. The whole gut was isolated and opened, and the contents were washed away with physiological saline. The washed gut was wiped with a paper towel and returned to the carcass. Each carcass was weighed and then preserved at −30° C for further analysis. This study was performed according to the rules and regulations for animal experiments of Okayama University.

#### Cecectomy

Surgery was performed via a mid-line abdominal incision under intra-peritoneal sodium pentobarbital
anesthesia (50 mg/ml; Dainippon Pharmaceutical Co. Ltd., Osaka, Japan), 40 mg/kg body weight. The cecum was lifted from the abdominal cavity and exteriorized on an alcohol-sterilized cotton drape; it was separated from the other intestines by cutting off the visceral peritoneum. A 4-0 silk ligature was placed around the junction between the cecum and the colon at the end of the ileum. After the ligature was secured and the ileocolonic passage confirmed, the cecum was resected, and the remaining exposed cecal mucosa was washed with physiological saline and 70% ethanol. The intestinal segment was then returned to the abdominal cavity. The abdominal muscle fascia and dermal incision were closed with a silk ligature. After surgery, the animals were immediately returned to their cages and allowed free access to the commercial pellet diet and tap water ad libitum. Within 6–7 h post-operation, all animals were awake and moving normally.

**Diet**

A digestible sucrose control and two fermentable materials were selected for both the normal and cecectomized groups. One fermentable material was a monosaccharide sugar alcohol (sorbitol; Nacalai Tesque Inc., Kyoto, Japan; Lot no. MOP 2028) and the other a disaccharide sugar alcohol (lactitol monohydrate; Wako Pure Chemical Ind. Ltd., Osaka, Japan; Lot no. APG 6984). The control diet was balanced with different essential food components, with the exception of sugar alcohol (Table 1). The diets containing sugar alcohol were prepared by replacing the 7% sucrose in the control diet with 7% sugar alcohol. After 10-d recovery, the experimental diets were provided to the animals (25 g/rat/d) for a 16-d experimental period. Moreover, nearly twice the usual amount of diet was supplied to all rats on the day prior to sacrifice to prevent possible starvation conditions for continuation of gut fermentation during the collection of samples.

**Food digestibility**

The food digestion trial period started on the 6th day of the experimental period and continued for 6 consecutive days. During this period, 25 g of diet was supplied daily per rat according to their corresponding diet groups. Feces were collected every day using the iron mesh at the bottom of each rat cage, dried at 60°C for 24 h and preserved at room temperature in separate plastic foil packs for further analysis.

**Digesta transit and retention**

A chromium mordanted cell wall constituent (Cr-CWC) fiber and cobalt ethylene diamine tetra acetate [Co(II)-EDTA] marker was used. The particle size of the prepared Cr-CWC marker was 250 µm to 840 µm in diameter. Chromium mordanted cell wall constituents (Cr-CWC) were prepared according to the description of Uden et al. (1980) [26]. A mixture of 0.1 g of Co(II)-EDTA and 0.2 g of Cr-CWC preparation was provided to each rat. After providing the marker, the feces of all rats were collected individually at 2 h intervals for the first 12 h, at 4 h intervals for the next 24 h and finally at 6 h intervals for the last 36 h. The transit time was determined as the time of the first appearance of the marker after a dose. The mean retention time of the digesta was calculated by the total collection method, as described by Coombe & Kay [8].

**Collection of blood, gut contents and carcass**

After completion of the experimental period, all rats were weighed and sacrificed by diethyl ether anesthesia. Eight to 10 ml blood from the jugular vein of each rat, the cecum from each normal rat and 2 cm of the proximal colon from each cecectomized rat were collected. The whole gut was then isolated and opened, and the contents were washed away with physiological saline. The washed gut was wiped with a paper towel and returned to the carcass. The cecum, colon and whole carcass were weighed and immediately preserved at −30°C for further analysis. The blood samples were

### Table 1. Composition of control and experimental diets on an air-dry basis

<table>
<thead>
<tr>
<th>Ingredients (g/kg)</th>
<th>Control</th>
<th>Sorbitol</th>
<th>Lactitol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk casein</td>
<td>250</td>
<td>250</td>
<td>250</td>
</tr>
<tr>
<td>Sucrose</td>
<td>280</td>
<td>210</td>
<td>210</td>
</tr>
<tr>
<td>Soybean oil</td>
<td>30</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>Lard</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Cellulose</td>
<td>20</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Corn starch</td>
<td>300</td>
<td>300</td>
<td>300</td>
</tr>
<tr>
<td>Vitamin premix (AIN 76)</td>
<td>20</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Mineral premix (AIN 76)</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Sorbitol</td>
<td>—</td>
<td>70</td>
<td>—</td>
</tr>
<tr>
<td>Lactitol</td>
<td>—</td>
<td>—</td>
<td>70</td>
</tr>
</tbody>
</table>

AIN: American Institute of Nutrition.
immediately refrigerated and then centrifuged at 3,000 rpm for 15 min. The serum was preserved at –30°C for subsequent analysis.

Analytical methods
The concentrations of Cr and Co in the ashed feces (550°C for 5 h) were determined by the method established by Williams et al. [31]. Analysis of Cr and Co in the treated samples was performed by flame atomic absorption spectroscopy (AAS 180-30; Hitachi Ltd., Tokyo, Japan).

The amounts of dry matter, crude protein, crude fat and crude ash in the diets, powdered feces and homogenized carcasses were determined by the methods of the Association of Official Analytical Chemists [2]. The amount of dry matter in the carcasses was determined by freeze-drying (EYELA, FD-81TA; Tokyo Rikakikai Co. Ltd., Japan).

The organic acid concentrations in the cecum and the colon contents were determined by high performance liquid chromatography (HPLC) (Column: 2 Shim-pack SCR-102H, Detector: Shimadzu CDD-6A; Shimadzu Corporation, Kyoto, Japan), and the pH of the homogenized cecum and colon contents was determined using a digital pH meter.

The concentrations of the serum total cholesterol, triglyceride (TG) and high-density lipoprotein (HDL) were determined by spectrophotometry (UV 1200; Shimadzu Corporation, Kyoto, Japan) using test kits from Wako Pure Chemical Company Ltd. (Osaka, Japan).

Calculations and statistical analysis
The apparent digestibility of each ingredient of the diet was calculated by the following formula:

\[
\text{Digestibility} = \frac{\text{amount ingested (g/d)} - \text{amount defecated (g/d)}}{\text{amount ingested (g/d)}}
\]

The ratios of dry matter, crude protein, crude fat and crude ash accumulated and consumed or absorbed in the carcass during the whole experimental period were determined by the following formulas:

Ratio of amount accumulated to amount consumed
\[
= \frac{\text{total amount accumulated}}{\text{total amount consumed}}
\]

Ratio of amount accumulated to amount absorbed
\[
= \frac{\text{total amount accumulated}}{\text{total amount absorbed}}
\]

Accumulation = amount in carcass after the experiment – amount in carcass before the experiment.

Data are presented as means and standard deviations, and were analyzed by two factorial (sugar alcohols and cecectomy) ANOVA. Statistical significance among the subgroups of each major group (normal and cecectomized) was verified by the Tukey-Kramer multiple range test (Statview, Version 5, SAS Institute Inc., USA). Differences were considered significant at p<0.05.

Results

Induction of diarrhea, feed intake, and body weight gain
Cecctomized rats with the diets containing sorbitol and lactitol suffered from diarrhea from the 2nd day of diet supplementation, whereas no diarrhea was observed for normal rats with the same diets. Feed intake and body weight gain were significantly (p<0.05) decreased by feeding sorbitol but not for cecctomy (Table 2).
Mean retention time (MRT) and transit time (TT) of digesta

The MRTs of cecectomized rats fed sugar alcohols were significantly shorter (p<0.05) than the control group. The MRTs of normal rats were relatively longer than their control group when they were fed the diets containing sugar alcohols (Fig. 1). The MRTs of the CS and CL groups were significantly (p<0.001 and p<0.01) shorter than the MRTs of the NS and NL groups, respectively. The TTs of cecectomized rats fed sugar alcohols were significantly (p<0.05) faster than the control group (Fig. 1), but no significant difference (p>0.05) was found in the normal rats fed the diets containing sugar alcohols. The TTs of the CC and CL groups were significantly (p<0.05 and p<0.01) faster than the NC and NL groups, respectively. Two factorial ANOVA tests revealed that TT was significantly (p=0.0007 for Cr, p=0.0002 for Co) faster for cecectomy than for sugar alcohols. The MRTs and TTs of both Cr-CWC and Co-EDTA markers were similar in this experiment.

Fecal nutrient concentrations and digestibility

The concentrations of crude protein in the feces of cecectomized rats were significantly lower than normal rats for cecectomy (p=0.0004), but no significant difference of crude protein concentration was found among individuals in the cecectomized and normal groups (Table 3). The crude ash concentration in the feces was significantly decreased (p<0.05) by sorbitol in normal rats and significantly (p<0.05) decreased by both sugar alcohols in cecectomized rats. The crude fat concentration in the feces of the cecectomized sorbitol group was significantly higher than the normal sorbitol group (p<0.001) and the cecectomized control group (p<0.05). Significant (p=0.002) interacting effects of sugar alcohols and cecectomy were found for increased fecal fat concentrations.

The crude protein digestibility was significantly (p=0.02) increased in the cecectomized groups fed sugar alcohols, and the digestibility of crude fat was significantly (p=0.0001) decreased by sugar alcohols although there were some interactions (p=0.004) (Table 3). Digestibility of crude protein was significantly (p<0.05) decreased by lactitol in normal rats and digestibility of crude fat was significantly (p<0.05) decreased by sorbitol in cecectomized rats but no significant effect among the other groups.

Carcass composition

The dry matter concentration in carcasses was significantly decreased (p=0.007) by sugar alcohols whereas in cecectomized rats it was significantly (p=0.04) higher than in normal rats (Table 4). Crude protein concentration was significantly (p<0.05) increased and crude fat concentration was significantly decreased by lactitol in cecectomized rats. No significant effect was found for the above parameters among normal rats. Crude protein concentration was significantly (p=0.02) increased by feeding sugar alcohols and crude fat concentration was significantly decreased by feeding sugar alcohols (p=0.002) and cecectomy (p=0.009). Crude ash concentration variations were insignificant in both cecectomized and normal groups.

Ratio of nutrient accumulated to nutrient consumed or absorbed in the carcass

The ratio of crude fat accumulated to consumed or
The ratio of dry matter accumulated to consumed or absorbed was significantly (p<0.05) lower in the cecectomized groups fed sugar alcohols than the control diet (Table 5). The ratio of dry matter accumulated to consumed or absorbed was significantly (p<0.0001 and p=0.0009) decreased by feeding sugar alcohol. The ratios of crude fat accumulated to consumed or absorbed were decreased by feeding sugar alcohols (p=0.001 and p=0.005) and cecectomy (p=0.006 and p=0.02). No significant difference for crude protein or crude ash was found among the groups.

Cecum and colon content analysis
During cecum and colon collection it was observed that the size of the cecum and colon of normal and cecectomized rats fed sugar alcohol contained more gas than their corresponding control groups. The weight of cecal tissue and the content of the rats fed sugar alcohols were significantly (p<0.05) higher than the control group (Table 6).

The pHs of the cecal content of the NS and NL groups were significantly (p<0.05) lower than the NC group, and the pH of the colon content of the CS group was significantly (p<0.05) lower than the CC group (Table 6).
Table 5. The effects of sugar alcohols on the ratio of nutrient accumulated to nutrient consumed or absorbed in the carcasses of normal and cecectomized rats after the 16-d experimental period

<table>
<thead>
<tr>
<th>Ratio</th>
<th>Normal</th>
<th>Cecectomized</th>
<th>Two factorial ANOVA test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Sorbitol</td>
<td>Lactitol</td>
</tr>
<tr>
<td>Dry matter</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acc : Con</td>
<td>0.13 ± 0.005</td>
<td>0.11 ± 0.026</td>
<td>0.12 ± 0.025</td>
</tr>
<tr>
<td>Acc : Abs</td>
<td>0.14 ± 0.006</td>
<td>0.12 ± 0.028</td>
<td>0.13 ± 0.027</td>
</tr>
<tr>
<td>Crude protein</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acc : Con</td>
<td>0.31 ± 0.026</td>
<td>0.30 ± 0.054</td>
<td>0.33 ± 0.027</td>
</tr>
<tr>
<td>Acc : Abs</td>
<td>0.32 ± 0.027</td>
<td>0.32 ± 0.056</td>
<td>0.34 ± 0.032</td>
</tr>
<tr>
<td>Crude fat</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acc : Con</td>
<td>1.07 ± 0.083</td>
<td>0.94 ± 0.24</td>
<td>0.88 ± 0.18</td>
</tr>
<tr>
<td>Acc : Abs</td>
<td>1.09 ± 0.076</td>
<td>0.97 ± 0.24</td>
<td>0.91 ± 0.19</td>
</tr>
<tr>
<td>Crude ash</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acc : Con</td>
<td>0.41 ± 0.079</td>
<td>0.51 ± 0.087</td>
<td>0.49 ± 0.14</td>
</tr>
<tr>
<td>Acc : Abs</td>
<td>0.63 ± 0.10</td>
<td>0.77 ± 0.10</td>
<td>0.81 ± 0.28</td>
</tr>
</tbody>
</table>

Acc: accumulated. Con: consumed. Abs: absorbed. Values are mean ± SD. No. of animals: 4 for cecectomized control and 5 for the other groups. NS: not significant. \(a\): p<0.05, \(b\): p<0.01, \(\star\): p<0.001. \(a\)\(b\) Mean values within a row with unlike superscripts letters are significantly different from each other (p<0.05). \(a\) For calculations, see materials and methods section.

Total organic acid and total SCFAs concentrations (\(\mu\)mol/g) in the colon content of cecectomized rats were significantly (p<0.001) lower than the total cecal organic acid and SCFAs concentrations (\(\mu\)mol/g) of normal rats, respectively (Table 6). Organic acid concentration in the cecal content of the NL group was significantly (p<0.05) higher than the NC group but no significant difference was found among the cecectomized groups; because of the large variation of data. Total SCFAs concentrations in the colon contents of the CS and CL groups were significantly (p<0.05) lower than the CC group.

The molar concentrations of different SCFAs were significantly modified by cecectomy. Especially, acetate, propionate, iso-butyrate, iso-valerate and n-valerate were significantly (p<0.001) higher in normal rats than in cecectomized rats fed the diets with sorbitol or lactitol (Table 6). Lactic acid concentration was significantly increased in cecectomized rats fed sugar alcohols compared to the control and corresponding normal rat groups. Formic acids and other organic acid concentrations were increased in the colon contents of cecectomized rats fed the diet containing sorbitol.

**Serum lipid profile**

The concentration of serum total cholesterol was decreased significantly (p=0.008) in both normal and cecectomized rats fed sugar alcohols compared to their corresponding control groups (Table 7). No significant differences of HDL concentrations were found among the groups. The concentration of TG was higher in normal but lower in cecectomized rats fed sugar alcohols than their respective control groups.

**Discussion**

It has been reported that excess consumption of sorbitol or lactitol has a laxative effect, and that large doses result in diarrhea in both humans and animals [4, 9, 30, 33]. Read et al. [22] reported that the tendency for diarrhea in response to a meal containing nonabsorbable carbohydrates depends more on the lack of colonic accommodation than on the rate of small intestinal transit. Soergel [25] reported that carbohydrate-induced diarrhea occurs when the amount of carbohydrate entering the colon exceeds its fermentation capacity. In this study, diarrhea only appeared in the cecectomized groups fed fermentable materials and not in the control groups. In addition, sugar alcohol fermentation production of lactic acid was significantly higher in the cecectomized rats fed sugar alcohols while most other organic acid concentrations were signifi-
Table 6. The effects of sugar alcohols on the weight, pH and organic acid concentration of cecum and colon content of normal and cecectomized rats, respectively, during the 16-d experimental period

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Cecetomized</th>
<th>Two factorial ANOVA test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Sorbitol</td>
<td>Lactitol</td>
</tr>
<tr>
<td>Cecum weight (g)</td>
<td>0.9 ± 0.2^a</td>
<td>1.6 ± 0.5^b</td>
<td>1.8 ± 0.4^b</td>
</tr>
<tr>
<td>Tissue</td>
<td>2.5 ± 0.8^a</td>
<td>5.5 ± 1.8^b</td>
<td>5.7 ± 1.9^b</td>
</tr>
<tr>
<td>Content</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Proximal colon weight (g)</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Tissue</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Content</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>pH</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Cecal content</td>
<td>7.6 ± 0.1^a</td>
<td>6.6 ± 0.3^b</td>
<td>6.3 ± 0.2^b</td>
</tr>
<tr>
<td>Colon content</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Organic acid concentration (µmol/g)</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

Or. Ac.: organic acids. SCFA: Short chain fatty acids (acetate, propionate, i-butyrate and n-butyrate). Values are mean ± SD. No. of animals: 4 for cecectomized control and 5 for the other groups. NS: not significant. *: p<0.05, **: p<0.01, ***: p<0.001. A, B and a, b, c Mean values within a row with unlike superscripts letters are significantly different from each other (p<0.05).

Table 7. The effects of sugar alcohols on the serum lipid profile of normal and cecectomized rats during the 16-d experimental period

<table>
<thead>
<tr>
<th>Concentration (mg/dl)</th>
<th>Normal</th>
<th>Cecetomized</th>
<th>Two factorial ANOVA test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Sorbitol</td>
<td>Lactitol</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>88.0 ± 23.0</td>
<td>66.0 ± 8.9</td>
<td>67.0 ± 13.1</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>46.0 ± 2.9</td>
<td>46.0 ± 7.3</td>
<td>50.0 ± 8.3</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>41.0 ± 25.2</td>
<td>20.0 ± 10.7</td>
<td>17.0 ± 5.2</td>
</tr>
<tr>
<td>Triglyceride</td>
<td>117.0 ± 42.6</td>
<td>157.0 ± 44.3</td>
<td>148.0 ± 38.1</td>
</tr>
<tr>
<td></td>
<td>82.9 ± 7.2</td>
<td>74.0 ± 8.5</td>
<td>64.1 ± 26.2</td>
</tr>
<tr>
<td></td>
<td>69.0 ± 7.9</td>
<td>52.0 ± 6.8</td>
<td>48.6 ± 11.5</td>
</tr>
<tr>
<td></td>
<td>26.0 ± 4.3</td>
<td>22.0 ± 8.6</td>
<td>21.3 ± 9.5</td>
</tr>
<tr>
<td></td>
<td>127.5 ± 12.5</td>
<td>111.0 ± 28.8</td>
<td>93.7 ± 28.6</td>
</tr>
</tbody>
</table>

HDL: high density lipo-protein. LDL: low density lipo-protein. Values are mean ± SD. No. of animals: 4 for cecectomized control and 5 for the other groups. NS: not significant. *: p<0.05, **: p<0.01. LDL cholesterol was determined by subtracting the HDL cholesterol value from total cholesterol value.

According to these studies, direct absorption of lactic acid from the gut is much slower than that of SCFAs. It is possible that a major part of the lactic acid is absorbed in the colonic mucosa of animals after conversion to SCFAs. However, due to the lack of the large intestinal fluid reservoir in the cecectomized rats.
fed sugar alcohols, lactic acid cannot be converted into SCFAs. As a result, the osmolality was increased in the colon. This could be the main reason why sorbitol and lactitol caused osmotic diarrhea in the cecectomized rats.

The retention and transit times of digesta, as well as intestinal or gastric emptying, are important determinants of the degree of intestinal digestion and absorption of dietary components. There were shorter MRTs and faster TTs for digesta in the cecectomized rats than in the normal rats due to the absence of the cecum and the limited accommodation in the colon, since a major portion (approx. 65%) of the diet from the small intestine usually travels to the colon through the cecum [14]. In normal rats, the diet travels through the cecum for further digestion and absorption. However, the time required for food to travel through the cecum is variable; the cecum never empties completely and only some of its contents travel on into the colon [14]. The significantly faster TTs and shorter MRTs of the cecectomized rats fed fermentable materials than the control rats revealed similar effects to those in the human digestive tract [7], while the inverse results were observed in the normal rats.

From many previous studies on humans and animals [12, 16, 21], it has been shown that sugar alcohols are extensively fermented by the cecal or colonic bacteria to SCFAs with increasing cecal size in rats [4, 33]. The heavier the cecum, the higher the amount of organic acids and the lower the pH of the cecal contents in normal rats fed the sorbitol and lactitol diets compared with those fed the control diet, demonstrating the stimulatory effect of sugar alcohols on cecal fermentation by cecal bacteria, as shown above. In contrast, the significantly lower concentrations of total colonic SCFAs in cecectomized rats fed the diets containing sugar alcohols than in those fed the control diet denotes that incomplete fermentation of sugar alcohols results in deficient availability or utilization of SCFAs [25]. The very limited fluid reservoir of the colon causes faster transit times and shorter retention times for digesta, which may be the reason why sugar alcohols cannot be fermented completely in the colon of the cecectomized rats. In other words, the composition and concentration of organic acids in the large gut digesta were largely modified by cecectomy.

Large intestinal fermentation of sugar alcohols increased fecal nitrogen excretion as well as decreasing urinary nitrogen excretion in pigs [28] and humans [5]. The significantly higher fecal crude protein excretion in the normal groups than in the cecectomized groups fed on the sugar alcohol diets might be due to increments of microbial protein connected with higher gut fermentation in this study. The lower values of fecal nitrogen excretion confirmed the lower fermentation of sugar alcohols in the cecectomized rats.

Sugar alcohol and diarrhea resulted in higher fecal fat excretion in both patients with liver cirrhosis [16] and normal humans [10]. In our study, it was found that fecal fat excretion was comparatively higher in the NS, NL and CL groups (177%, 194% and 260%, respectively) and significantly higher in the CS group (430%) compared to their corresponding control groups. Markedly higher fecal fat excretion was observed in the cecectomized groups than the normal groups fed sugar alcohols. In humans fed indigestible materials, it is thought that the increased fluid volumes within the small intestinal lumen might dilute the concentration of substrates involved in fat digestion, fat absorption or both, and finally that the increased fecal fat excretion, or faster transit due to the increased intestinal fluid volume might impair fat absorption by decreasing the contact time of the products of fat digestion with the small intestinal mucosal cells [13]. These possible mechanisms need to be considered with our results in the cecectomized rats. Increased fecal fat excretion as well as decreased fat digestibility means that the amount of absorbed energy was decreased in the rats fed sugar alcohols, since the digestibility of dry matter was similar among the groups (Table 3). This must be related to the body fat lowering effect of sugar alcohols in this study, since the effect was markedly larger in the cecectomized rats than in the normal rats (Table 4). The body fat lowering effect of fermentable materials in the cecectomized rats supports the results of human studies [16, 10]. Therefore, the body fat lowering effect of fermentable materials in the cecectomized rats shows that they display a similar effect for fermentable materials to that found in humans.

The significantly (p=0.008) decreased serum total cholesterol in normal rats fed sugar alcohols compared to the control group might be connected with higher cecal propionate concentrations found in this study, since propionate may have a hypocholesterolemic ef-
fect in normal rats [6]. No such effect of propionate was observed in a human study [29], although the serum triglyceride (TG) concentration was concomitantly increased with increasing propionate concentrations similar to the normal rats in our study. Although there was no difference in the colonic propionate concentration among the groups of cecectomized rats, the serum total cholesterol and TG concentrations were decreased by the addition of sugar alcohols. Therefore, there were no relationships between the serum total cholesterol and TG concentrations and the colonic propionate concentration. Propionate also has some different effects on lipid metabolism in humans and normal rats [29]. From the above contradictory explanation, it is difficult to summarize the similarities of the effects of SCFAs on lipid metabolism in humans and rats.

In summary, the results of this study show that the effects of sorbitol and lactitol on either digesta retention or gut fermentation differed between the normal and cecectomized rats, but the effects were similar for the two sugar alcohols. The tendency for diarrhea in the cecectomized rats, but not in the normal rats, fed sugar alcohol-containing diets denotes that cecectomized rats show a similar tendency for diarrhea after intake of sugar alcohols or diets with sugar alcohols to that observed for humans [20, 23]. The faster transit time of digesta in cecectomized rats fed sugar alcohols is also similar to the effect of fermentable materials in humans [7]. Furthermore, the body fat lowering effect of sugar alcohols in cecectomized rats is similar to that in humans [10, 16]. The results of this study support the possibility of using cecectomized rats for studying the physiological effects of sugar alcohols in humans, but further comparative studies between humans and cecectomized rats are required to confirm the actual possibility.

References


