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Small intestinal transit and digestibility of lactitol in Wistar rats

Transitzeit und Verdaulichkeit von Lactit im Dünndarm von Wistarratten

Summary The study was conducted to evaluate if the recovery of lactitol and its cleavage products varied when different doses of this disaccharide sugar alcohol (150 and 1 200 mg/kg body weight, respectively) were given by gastric gavage to unadapted male rats. Phenol red added to the test solution as marker dye served to determine the intestinal transit and distribution areas. Marker transit revealed that the test substance did not reach the cecum in all series. Gastric emptying was more retarded after the high dose. Administration of low doses did not alter intestinal transit and luminal volume as compared to control animals. But a much larger luminal volume was found in the third intestinal quarter after the high doses, although the marker transit through this segment was equal under all experimental conditions. The total gastrointestinal recovery of lactitol at 63.2 (± 3.9) and 75.5 (± 4.5) % was significantly different ($p < 0.001$) 1 hour after administration of 150 mg and 1200 mg/kg body weight, respectively. Only free sorbitol was detected in the gastrointestinal contents in both dosage groups. Based on these results and correcting the values for marker recovery (85 % in both groups), it is reasonable to assume that the maximum amount of lactitol that can be hydrolyzed and absorbed by the small intestine is 11.2 and 25.2 %, respectively, and not zero. In conclusion, the caloric availability of lactitol is dose-dependent and should be determined under normal conditions in which the laxative threshold is not exceeded.

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Zusammenfassung Die Untersuchung wurde durchgeführt um festzustellen, ob sich nach intragastraler Gabe unterschiedlicher Dosen (150 mg bzw. 1 200 mg/kg Körpergewicht) von Lactit an nichtadaptierte männliche Ratten die Wiederfindung dieses Disaccharidalkohols und seiner Spaltprodukte verändert. Das den Versuchslösungen als Marker zugesetzte Phenolrot diente zur Bestimmung der Darmpassage und der Verteilungsräume. Die Markerpassage zeigte, daß die Testsubstanz bei allen Versuchsserien das Caecum nicht erreicht hat. Die Magenentleerung war nach der hohen Dosis mehr verzögert. Gabe von niedrigen Dosen veränderte nicht die Darmpassage und das luminale Volumen im Vergleich zu Kontrolltieren. Jedoch konnte nach den hohen Dosen eine viel stärkere luminale Volumenzunahme im 3. Viertel des Dünndarms festgestellt werden, obgleich der Markertransit durch diesen Abschnitt unter allen Versuchsbedingungen gleich war. Die gesamte intestinale Wiederfindung für Lactit war 1 Stunde nach Gabe von 150 mg und 1 200 mg/kg Körpergewicht mit 63,2 (± 3,9) bzw. 75,5 (± 4,5)% signifikant ($p < 0.001$) verschieden. In den Magen-Darm-Inhalten konnte bei beiden Dosisgruppen nur freier Sorbit nachgewiesen werden. Auf der Basis dieser Ergebnisse und korrigiert auf die Markerwiederfindung (85 % in beiden Gruppen) kann

vorausgesetzt werden, daß maximal 11,2 bzw. 25,6 % und nicht 0 % Lactit im Dünndarm hydrolysiert und absorbiert werden können. Es wird gefolgert, daß die energetische Nutzung von Lactit dosisabhängig ist und nur unter normalen Bedingungen, bei denen die laxative Toleranzschwelle nicht überschritten wird, bestimmt werden sollte.

Key words Sugar substitute – lactitol – transit time – flow rate – absorption – small intestine

Schlüsselwörter Zuckeraustauschstoff – Lactit – Transitzeit – Flußrate – Absorption – Dünndarm

Introduction

Lactitol (4-0-β-D-galactopyranosyl-D-sorbitol) is a hydrogenated disaccharide sugar alcohol being proposed as a low-energy, full-bulk, alternative carbohydrate sweetener. An energy value of approximately one-half that of sucrose (8 kJ/g) has been calculated by the factorial approach on the assumption that lactitol is not hydrolyzed and absorbed by the small intestine and completely fermented in the colon (1, 5, 15, 17). Factors that influence sugar alcohol absorption and digestion include the quantity consumed and whether the sugar alcohols are ingested as part of a mixed meal. High intake of sugar alcohols decreases the rate of gastric emptying but concomitantly shortens transit time (and absorption time), thus, decreasing net energy value. As shown previously, consumption of small amounts of sugar alcohols such as isomalt and maltitol results in slower intestinal transit time and less osmotic effect, favoring intestinal digestion and absorption, and, thus, increasing the energy value (3, 6, 11, 12). Consequently, the aim of the present study was to investigate whether different doses also have an effect on small intestinal transit and digestibility of lactitol.

Material and methods

Male juvenile Wistar rats weighing on average (± sd) 105 ± 7 g were fasted overnight for 16 h with free access to drinking water and prevention of coprophagy (12). Lactitol dihydrate (Lacty^R, CCA Biochem (1)) was administered by gastric gavage as a 1.5 ml bolus per 100 g body weight (= b.w.) in a hypotonic electrolyte (14) containing 0.075 % (w/v) phenol red (Merck) as a marker dye.

Lactitol was tested in two dosages, 150 mg/kg b.w. and 1 200 mg/kg b.w., each in n = 6 animals; control rats (n = 9) received blank electrolyte solution and marker only.

After a one-hour digestion time and no access to drinking water, the rats were sacrificed after anaesthetization (14). As quickly as possible, the whole gastrointestinal tract was removed and subdivided into stomach, small intestine, cecum, and colon. Additionally, the small intestine was separated into the first half, the third- and the distal quarter.

Gastrointestinal contents were collected in centrifuge tubes by washing the segments thoroughly by means of a syringe with about 10 ml of cold saline (20 ml in the case of the first half of the small intestine). To collect possible residues, the stomach was cut open and rinsed and the intestinal segments were squeezed accurately. The specimens were centrifuged (15 min, 30000 x g, 4 °C) and the supernatants were analyzed colorimetrically for phenol red and by HPLC technique for lactitol, galactose, and sorbitol (10,12). It was taken into account that Lacty^R contains about 10% water.

Intestinal transit was determined for each segment of the small intestine by relating the quantity of marker which had left a segment to the amount which had entered it during the experimental time (20).

Quantitation of the gastrointestinal contents was performed by weighing the organs before and after sample gaining, assuming that 1 g of intestinal content would correspond to 1 ml of luminal volume.

Student's paired t-test was used to determine significant differences ($p<0.05$); experimental results are indicated as means with their standard deviations.

Results

The mean gastrointestinal recovery of phenol red was 85 ± 3 % with no difference between the experimental groups.

As shown in Table 1, about 90 % of the administered marker had left the stomach of the animal within the first hour after ingestion; gastric emptying tended to be retarded when the high dose of lactitol was tested. Moreover, as compared to the blanks and the low-dosed series, transit through the first half of the small intestine was significantly delayed under 1200 mg lactitol/kg b.w. (Table 1). No significant differences were revealed with regard to transit through the third small intestinal quarter. Since phenol red was not found in any of the rat's ceca or large intestines after the experimental time, transit through the distal quarter of the small intestine was defined as zero in all series (Table 1).

Gastrointestinal volume under the different experimental conditions 1 hour after gavage is shown in Table 2. While under a low dose of lactitol it significantly exceeded the control value in the fourth quarter of the small intestine only, it was substantially higher in the whole gastrointestinal tract when 1 200 mg lactitol/kg b.w. was administered. The main increase was noted for the first half of the small gut.

Table 1 Gastric emptying and marker transit; Effect of different doses of lactitol on gastric emptying and marker transit through small intestinal segments after a 1 h digestion time indicated by the percentage of phenol red which had left the respective gastrointestinal compartment in relation to the amount which had entered it during the 1 h digestion time. [a]marks a significant difference versus the controls and [b]versus the 150 mg/kg b.w. group

Initial dose of lactitol [mg/kg b.w.]	Percentage of stomach emptying and marker transit			
	Stomach	First half	Third quarter	Distal quarter of the small intestine
0	94.1 ± 2.6	90.9 ± 17.4	15.6 ± 19,4	0
150	94.2 ± 5.0	92.3 ± 4.9	30.4 ± 17.1	0
1200	87.6 ± 8.9	70.5 ± 11.7 a,b	29.1 ± 6.1	0

Table 2 Gastrointestinal volume; Effect of different doses of lactitol on luminal volume of the stomach and of different small intestinal segments of rats 1 h after intragastric administration of different doses of lactitol. Significant differences are indicated as noted for Table 1

Initial dose of lactitol [mg/kg b.w.]	Gastrointestinal volume [ml]			
	Stomach	First half	Third quarter	Distal quarter of the small intestine
0	0.25 ± 0.07	0.15 ± 0.14	0.22 ± 0.10	0.18 ± 0.12
150	0.24 ± 0.08	0.28 ± 0.08	0.27 ± 0.08	0.34 ± 0.10 a
1200	0.42 ± 0.10 a,b	0.90 ± 0.24 a,b	0.80 ± 0.15 a,b	0.54 ± 0.12 a,b

Table 3 Recovery rate; Percentage of gastrointestinal recovery of different doses of lactitol and of its cleavage products galactose and sorbitol 1 h after intragastric administration to rats. Significant differences are indicated as noted for Table 1

Initial dose of lactitol [mg/kg b.w.]	Percentage of recovery i) lactitol; ii) free galactose; iii) free sorbitol			
	Stomach	First half	Third quarter	Distal quarter of the small intestine
150	i) 0.5 ± 1.3 ii) 0 iii) 0	3.3 ± 3.9 0 0	41.7 ± 8.3 0 1.3 ± 1.4	17.7 ± 10.2 0 0.3 ± 0.5
1200	i) 4.8 ± 3.4 b ii) 0 iii) 0.1 ± 0.1 b	20.3 ± 8.6 b 0 0.6 ± 0.4 b	36.2 ± 6.3 0 1.0 ± 0.4	14.2 ± 4.8 0 0.3 ± 0.2

One hour after administration, total gastrointestinal recovery of lactitol was 63.2 ± 3.9 % and 75.5 ± 4.5 % with 150 and 1200 mg/kg b.w. respectively. This is a significant difference ($p < 0.001$). Corrected for the phenol red recovery (85 %, see above), this would correspond to 74.4 and 88.8 % recovery. The relative recovery of lactitol and liberated cleavage product sorbitol in the gastrointestinal segments is shown in Table 3. The portion of lactitol still recovered in the rats' stomachs was significantly higher when 1 200 mg lactitol/kg b.w. was administered; a comparable result was revealed for the upper half of the small intestine where liberated sorbitol was also recovered. Moreover, free sorbitol was analyzed in the distal parts of the small gut for both doses, and traces were found in the stomachs of the high-dosed group. Free galactose was not detected in the gastrointestinal contents in both experimental series (Table 3). No lactitol or cleavage products were detected by HPLC in the negative control animals.

Discussion

Lactitol has been reported a poor substrate for mammalian small gut mucosal enzymes (7, 16) and fermentative degradation by the microflora of the large intestinal tract was supposed to be the main route of its digestion (4, 17, 18). The resulting microbial metabolites such as short-chain fatty acids and lactate (15, 19) may be absorbed, delivering some of the calories of the disaccharide sugar alcohol to the host. Assuming an extensive metabolism of lactitol by the colonic flora, only about 50 % of the theoretical energy content of this sugar substitute was supposed to be utilized by humans (5, 17).

As demonstrated more recently (6,11–13,20), the rat model and the marker technique used in this study are well suited to discriminate clearly between small intestinal digestion and fermentation processes in the large gut and can furnish information on gastrocecal transit. However, since this investigation used only a single point of time to determine digestion and transit of the test substance, transit time could not be described by a mathematical model as published previously (11) but had to be calculated as indicated for Table 1. Transit time and volume of intestinal fluids are important determinants of the degree of digestion in the small intestine: increasing excessively, both parameters have the potential to reduce degradation and absorption by limiting the substrate contact with the mucosal surface (2, 9).

One of the most pronounced physiological effects of sugar substitutes is their dose-related influence on gastrointestinal osmoregulation and net water movement, and diarrhea due to osmosis limits the extent of consumption (12, 14, 17, 18).

Under the nonphysiologically high and osmotic active load of 1 200 mg lactitol/kg b.w., which corresponded exactly to the laxative threshold of 1.2 g/kg b.w. per day in normal human subjects (18), the transit of marker through the proximal half of the small intestine was delayed (Table 1). A similar effect was also revealed in rats with high doses of the disaccharide sugar alcohols isomalt and maltitol (11,12). Apparently, peristalsis did not sufficiently accelerate the flow rate in this intestinal segment to transport the intraintestinal volume which was drastically higher in relation to the controls in a normal transit time (Table 2). An explanation would be that during the first hour after ingestion any possible increase in flow rate may be compensated by a concomitant and proportional increase of luminal volume (2).

Nevertheless, the flow rate was obviously substantially encouraged in the third intestinal quarter, which, related to its length, contained nearly double the volume as compared to the first half of the small intestine (Table 2): the marker transit through this segment was equal under all experimental conditions (Table 1) but compared to the controls and the low-dosed series, a much larger volume was carried to the distal quarter of the small gut under 1 200 mg lactitol/kg b.w. (Tables 1 and 2). It can be assumed that such a huge volume entering the terminal ileum at a high flow rate would have the potential to easily overcome the ileocecal valve, since the dilatation capacity of the ileum is limited (2). Thus, by elimination of the physiological "ileal brake" (9), substantial fractions of undigested material (Table 3) can escape absorption and undergo colonic fermentation. Consequently, a more pronounced reduction of potential energy yield would occur (3, 5, 8, 17). However, probably due to the relatively short experimental digestion time of 1 h, this effect could not observed in this experiment.

In contrast, the administration of 150 mg/kg b.w. did not alter intestinal transit or the luminal volume in a comparable manner (Tables 1 and 2). This would explain the more effective small intestinal degradation and absorption of this small dose as indicated by the lower percentage of recovery in our experiments (Table 3). It is, therefore, reasonable to assume from our results corrected for the marker recovery that the maximum amounts of lactitol that can be hydrolyzed and absorbed by the small intestine are 11.2 and 25.6 %, respectively, and not zero as estimated by the Dutch Nutrition Council (3, 17).

In conclusion, as already shown for other disaccharide sugar alcohols (6, 11, 12), the caloric availability of lactitol is also dose-dependent and must be determined under conditions of realistic low amounts of consumption which should not exceed the laxative threshold.

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