

## **The effects of lactulose-sweetened yoghurt on the rate of gastric emptying and intestinal transit in healthy human volunteers**

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**Summary:** A non-invasive, radioisotopic method was utilised to study the effects of a lactulose-sweetened yoghurt product on gastric emptying and intestinal transit. Healthy human volunteers were given <sup>99m</sup>Tc-DTPA-labelled lactulose yoghurt before and after adaptation to the product. A control group received a similarly labelled glucose solution. Gastric emptying and intestinal transit were evaluated by scintigraphy. The mean half-time for gastric emptying for glucose was  $39.8 \pm 3.4$  min and for lactulose yoghurt,  $31.3 \pm 11.0$  min. After 10 days' adaptation, the corresponding value for lactulose yoghurt was  $25.2 \pm 8.2$  min. Intestinal transit time was faster after lactulose yoghurt than after glucose solution and did not change during adaptation. The observed effects indicate that lactulose yoghurt may be beneficial in the treatment of chronic constipation using dietary methods.

**Zusammenfassung:** Um die Wirkung eines mit Lactulose gesüßten Joghurts auf die Magenentleerung und den intestinalen Transit zu untersuchen, wurde eine nicht invasive Methode gewählt, bei der radioaktive Isotope zum Einsatz kamen. Gesunde, freiwillige Probanden erhielten einen mit <sup>99m</sup>Tc-DTPA markierten Lactulose-Joghurt (vor und nach Adaptation an das Produkt). Als Kontrolle diente eine ähnlich markierte Glucose-Lösung. Magenentleerung und intestinaler Transit wurden scintigraphisch gemessen. Die mittlere Halbwertszeit für die Magenentleerung nach Gabe der Glucose-Lösung betrug  $39,8 \pm 3,4$  Minuten, nach Verzehr des Lactulose-Joghurts waren es  $31,3 \pm 11,0$  Minuten. Nach 10tägiger Adaptation lag der entsprechende Wert für den Lactulose-Joghurt bei  $25,2 \pm 8,2$  Minuten. Die intestinale Transitzeit war nach Gabe des Lactulose-Joghurts kürzer als nach Einnahme der Glucoselösung und änderte sich während der Adaptation nicht. Die beobachteten Wirkungen zeigen, daß Lactulose-gesüßter Joghurt ein gutes Mittel bei der diätetischen Behandlung der chronischen Verstopfung sein könnte.

**Schlüsselwörter:** Lactulose; Joghurt; intestinaler Transit; Magenentleerung; chronische Verstopfung

**Key words:** lactulose; yoghurt; intestinal transit; gastric emptying; chronic constipation

### **Introduction**

Lactulose is a carbohydrate sweetener which is not absorbed by the small intestine. Lactulose has been indicated to be a useful agent for treating chronic constipation (3, 9). However, high lactulose doses can

cause transient diarrhoea. It has been suggested that the diarrhoeogenic effect of polyols is more marked when given in liquid form than in solid form (8). This has been attributed to more rapid emptying of the stomach after liquid than solid food ingestion. Osmotically induced peristalsis is also believed to be reduced by solid meals with concomitant lengthening of their time of passage through the small intestine. However, in previous studies we have indicated (6, 7) that xylitol solutions may decrease gastric emptying when compared to glucose.

We decided to utilise a non-invasive, radioisotopic method for the measurement of gastric emptying time (2, 4) to study the effects of a lactulose-sweetened yoghurt product on gastric emptying and intestinal transit. This yoghurt product was designed to act as a laxative food product for the dietary treatment of constipation. Also, the effects of continuous lactulose yoghurt consumption on the rate of gastric emptying were studied. This study was completed to improve understanding of the mechanisms by which lactulose-sweetened yoghurt may relieve chronic constipation and also to observe any adaptive changes in longer continuous consumption of the product.

## Materials and Methods

The radioisotope marker  $^{99m}\text{Tc}$ -technetium-DTPA (Solco Nuclear, Switzerland) was prepared from a commercial kit and utilised as described by Christofides et al. (2). 100  $\mu\text{Ci}$  of the radiomarker was mixed with lactulose yoghurt or glucose solution immediately prior to use. Scintigraphy was completed using a gamma camera (General Electric, Maxicamera 500, Autotune ZS) coupled with a computer (General Electric STAR Data Processing System) and a Polaroid camera. Data were recorded on magnetic disc.

Pictures of gastric emptying were recorded at a speed of one frame per 60 s. Results were analysed using STAR Data Processing Software capable of constructing time/activity curves generated from the region of interest over the stomach. The target area was determined by an external medical physicist. The effective half-time of gastric emptying was determined assuming mono-exponential behaviour of gastric emptying of sugar solutions, as indicated by Kim (4) and others (1, 5). One exponential function was then fitted to the data, using a Fortran program solving a non-linear, least-squares problem. An attempt to fit a two-exponential curve to the data was also made but abandoned as unsuitable.

Lactulose-containing yoghurts were produced utilising lactose-hydrolyzed fat-free milk and *Lactobacillus acidophilus* starter bacteria. The final product was prepared to contain 9.0 % lactulose syrup with a 67 % lactulose content (Duphalac).

The study group consisted of six healthy male volunteers who had not been introduced to lactulose yoghurt prior to the study. Five volunteers were utilised as a control group. On two occasions after an overnight fast (12 h) the test group volunteers were seated in front of the gamma camera and given 150 ml of test yoghurt containing lactulose. The test yoghurts were given 10 days apart and consumed within 2 min. After the first test, the volunteers were asked to consume 150 ml of lactulose yoghurt for breakfast and lunch every day for 10 days until the second test was completed. After an overnight fast (12 h) the control group were served a test drink of similar volume but consisting of water and 30 g glucose.

After consumption of the test drink or test yoghurt, gastric emptying was measured every 60 s for 50 min from the ingestion. Thereafter, static pictures were taken of the whole lower gastrointestinal tract area with the subjects standing in the front of the gamma camera. These were taken to delineate intestinal transit of the marker.

Table 1. Calculated biological half-time of gastric emptying after oral ingestion of lactulose-sweetened yoghurt prior to and after prolonged lactulose yoghurt consumption. A 30-g glucose solution served as a control. The data used for one exponential curve fitting are included.

Test substance/Group	Subject	A	$k \times 10^{-3}$	$t_{1/2}/\text{min}$	Unpleasant effects
Lactulose yoghurt given to volunteers	1	127	-0.526	22.0	flatulence
	2	116	-0.461	25.1	flatulence
	3	106	-0.240	48.2	—
	4	111	-0.444	26.0	flatulence
	5	100	-0.273	42.3	flatulence
	6	122	-0.476	24.3	flatulence
Lactulose yoghurt given to after 10 days of daily lactulose yoghurt consumption (300 ml/day)	1	106	-0.393	29.4	—
	2	122	-0.553	20.9	—
	3	131	-0.592	19.6	flatulence
	4	123	-0.686	16.9	flatulence
	5	104	-0.461	25.1	—
	6	117	-0.294	39.3	—
A solution containing 30 g glucose given to normal volunteers	1	80	-0.269	43.0	—
	2	71	-0.296	39.0	—
	3	105	-0.276	41.8	—
	4	71	-0.337	34.3	—
	5	123	-0.283	40.8	—

The control volunteers were given the glucose drink and similar procedures to those with the test yoghurt group were followed. The study was approved by the Hospital Oncology Clinic Ethical Committee.

## Results

All volunteers found lactulose yoghurt pleasant to consume and continued the required consumption throughout the study.

The mean half-life (mean  $\pm$  standard deviation) of gastric emptying for glucose was  $39.8 \pm 3.4$  min. For lactulose yoghurt without prior consumption, the mean half-life was  $31.3 \pm 11.0$  min and after a continuous 10-day consumption, the corresponding value was  $25.2 \pm 8.2$  min. Individual values and mono-exponential curve fitting data are summarized in Table 1. The data for intestinal transit indicated that 50 min after lactulose yoghurt ingestion, the radioactivity from the marker had clearly reached the most distal parts of the colon in five of the volunteers. Similar intestinal transit was observed even after 10 days of regular lactulose yoghurt consumption. In glucose controls the radioactivity still remained in the small intestine area after the test.

In the first test and during the first couple of days of lactulose yoghurt consumption, five out of six volunteers had cases of flatulence and even meteorism, but these were gradually diminished during lactulose yoghurt consumption. At the end of the study period, all volunteers were able to tolerate the product without side effects. A small, but not significant, increase in the number of faecal productions was observed during lac-

tulose yoghurt consumption. No cases of diarrhoea were observed during the study.

## Discussion

Initially the effect of lactulose yoghurt on gastric emptying was similar to that of glucose solution. After 10 days of regular lactulose yoghurt consumption, gastric emptying was slightly faster, indicating that some physiological adaptation to lactulose yoghurt may have occurred. However, in both test situations, lactulose yoghurt that left the stomach rapidly traversed the small intestine and reached the distal colon within 50–60 min. This phenomenon did not appear to be influenced by the continuous lactulose yoghurt consumption and it is therefore assumed that no physiological intestinal adaptation occurred during the 10-day period. By comparison, the controls receiving a glucose solution had the marker radioactivity still in the small intestinal area 50–60 min after the test. No adaptation to glucose solutions was utilised since all volunteers were thought to be adapted to large amounts of glucose in their normal diet.

To our knowledge, no previous data have been published on the rate of gastric emptying and intestinal transit after lactulose-containing yoghurt products. However, earlier work has clearly documented gastrointestinal discomfort and even diarrhoea after large oral doses of lactulose (3, 9). Our results indicate that up to 15 g lactulose consumed daily in yoghurt did not appear to cause any diarrhoea in healthy human volunteers. However, cases of flatulence and meteorism were observed, but these disappeared even though gastric emptying was slightly increased during prolonged lactulose yoghurt consumption. Lactulose yoghurt appeared to act as a mild laxative, increasing the number of faecal productions in healthy volunteers and no adaptation to lactulose yoghurt was observed during the 10-day consumption period. Additionally, the ingested *Lactobacillus acidophilus* bacteria may utilise added lactulose in the colon lowering the pH and promoting the laxative action of the test yoghurt. Our result seems to indicate that, compared to glucose, lactulose yoghurt and its prolonged consumption may increase gastric emptying. Lactulose yoghurt also significantly decreased the intestinal transit time of the marker presumably by increasing intestinal motility. However, stimulating of peptide hormones, as in the case of xylitol (7) may also occur and needs to be further studied. The observed effects, which did not disappear during prolonged lactulose yoghurt consumption, may be beneficial in the treatment of chronic constipation using dietary methods rather than laxative pharmaceuticals.

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