

ORIGINAL ARTICLE

Gastrointestinal tolerance of erythritol and xylitol ingested in a liquid

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Objectives: To determine and compare the gastrointestinal (GI) responses of young adults following consumption of 45 g sucrose, 20, 35 and 50 g xylitol or erythritol given as a single oral, bolus dose in a liquid.

Design: The study was a randomized, double-blind, placebo-controlled study.

Subjects: Seventy healthy adult volunteers aged 18–24 years were recruited from the student population of the University of Salford. Sixty-four subjects completed the study.

Interventions: Subjects consumed at home without supervision and in random order, either 45 g sucrose or 20, 35 and 50 g erythritol or xylitol in water on individual test days, while maintaining their normal diet. Test days were separated by 7-day washout periods. Subjects reported the prevalence and magnitude of flatulence, borborygmi, bloating, colic, bowel movements and the passage of faeces of an abnormally watery consistency.

Results: Compared with 45 g sucrose, consumption of a single oral, bolus dose of 50 g xylitol in water significantly increased the number of subjects reporting nausea ($P < 0.01$), bloating ($P < 0.05$), borborygmi ($P < 0.005$), colic ($P < 0.05$), watery faeces ($P < 0.05$) and total bowel movement frequency ($P < 0.01$). Also 35 g of xylitol increased significantly bowel movement frequency to pass watery faeces ($P < 0.05$). In contrast, 50 g erythritol only significantly increased the number of subjects reporting nausea ($P < 0.01$) and borborygmi ($P < 0.05$). Lower doses of 20 and 35 g erythritol did not provoke a significant increase in GI symptoms. At all levels of intake, xylitol produced significantly more watery faeces than erythritol: resp. 50 g xylitol vs 35 g erythritol ($P < 0.001$), 50 g xylitol vs 20 g erythritol ($P < 0.001$) and 35 g xylitol vs 20 g erythritol ($P < 0.05$).

Conclusions: When consumed in water, 35 and 50 g xylitol was associated with significant intestinal symptom scores and watery faeces, compared to the sucrose control, whereas at all levels studied erythritol scored significantly less symptoms. Consumption of 20 and 35 g erythritol by healthy volunteers, in a liquid, is tolerated well, without any symptoms. At the highest level of erythritol intake (50 g), only a significant increase in borborygmi and nausea was observed, whereas xylitol intake at this level induced a significant increase in watery faeces.

Sponsorship: Cerestar R&D Center, Vilvoorde, Belgium.

European Journal of Clinical Nutrition advance online publication, 20 September 2006; doi:10.1038/sj.ejcn.1602532

Keywords: erythritol; xylitol; gastrointestinal tolerance; glycaemic index; laxation

Introduction

Polyols are widely used to replace sugars in foods, especially confectionery, because of their low energy content, non-cariogenicity and their potential to help reduce glycaemic and insulinaemic responses, when substituted for sugars. However, when ingested in excessive quantities,

most polyols may cause undesirable, sometimes stressful gastrointestinal (GI) symptoms (Zumbe *et al.*, 2001). Although transient, such symptoms may invite unnecessary medical visits, especially in children. Erythritol is a naturally occurring four-carbon polyol. It is industrially produced using a fermentation process. Having a sweetness approaching 60–80% that of sucrose, it has sensorial and functional properties that allow the formulation of low-calorie and diet beverages (as well as other applications such as chewing gum, mints and chocolate (Goosens and Röper, 1994; de Cock, 1999; de Cock and Bechert, 2002)).

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Received 22 May 2006; accepted 5 July 2006

Erythritol is rapidly absorbed in the upper intestine by a concentration-dependent diffusion process (Schiweck and Ziesenitz, 1996) and has no effect on plasma glucose and insulin (Ishikawa *et al.*, 1996; Bornet *et al.*, 1996a, b). Erythritol is only minimally fermented in the oral cavity by *Streptococcus mutans* (Kanwanabe *et al.*, 1992) and not fermented in the colon (Arrigoni *et al.*, 2005). As a result, erythritol has an estimated energy value of 0 kcal/g (de Cock and Bechert, 2002; Arrigoni *et al.*, 2005), compared to 4 kcal/g for sucrose (Paul and Southgate, 1978). After oral intake, most erythritol is excreted with urine, excretion being 60–78% of an oral dose after 24 h (Bornet *et al.*, 1996a, b) and 90% after 48 h (Munro *et al.*, 1998) have been observed. Thus, in contrast to other monosaccharide and disaccharide polyols, only small amounts of ingested erythritol remain unabsorbed in the intestinal tract. Acute doses of up to 25 g erythritol are reported not to lead to excess intestinal fermentation (Hiele *et al.*, 1993). Nausea, borborygmi, bloating, flatulence and soft faeces following consumption of 0.4 and 0.8 g/kg body weight (BW) erythritol by healthy subjects were observed by Bornet *et al.* (1996b). However, these GI responses were not significantly different from those following ingestion of equivalent doses of sucrose. Tetzloff *et al.* (1996) observed that a daily dose of 1 g/kg BW erythritol (mean intake 78 g/day), ingested in small portions throughout the day, during 5 consecutive days, was well tolerated and did not cause untoward GI disturbances compared with an equivalent dose of sucrose. Based on regression analysis, Oku and Okazaki (1996) concluded that the maximum dose of erythritol not causing laxation is 0.80 g/kg BW for females and 0.66 g/kg BW for males. This figure should be seen as an approximation, as linear regression may overestimate the cutoff point due to the binomial nature of the data.

Xylitol is a naturally occurring monosaccharide – pentitol polyol – with a wide range of applications in sugar-free confectionery (Pepper and Ollinger, 1988). Because of its non-cariogenic properties (Maguire *et al.*, 2000), xylitol is often the polyol of choice in sugar-free chewing gum (Zumbe *et al.*, 2001). Diarrhoea, flatulence and bloating have been reported by Dubach *et al.* (1969) in adults following consumption of xylitol, although no dose dependency was noted. In another study by Culbert *et al.* (1986) in which participants consumed 30–100 g xylitol per day, a dose-dependent effect was observed. Although erythritol and xylitol have similar physicochemical properties and are being used in a wide variety of food applications, little is known about their comparative GI tolerance, especially when consumed at higher doses in liquid. The latter has received recent interest related to the advice of some expert groups to reduce overall daily glycaemic responses by substituting rapidly available carbohydrates for low glycaemic sweeteners. This paper investigates the GI tolerance of young adults (18–24 years) given 400 ml drinks, containing either 45 g sucrose or 20, 35 and 50 g of erythritol or xylitol.

Methods

Subjects

Seventy healthy, non-adapted volunteers, 34 males and 36 females, aged between 18 and 24 years, were randomly recruited from the student population of the University of Salford. The purpose and nature of the proposed studies were explained to volunteers who provided written consent and were free to leave the study at any time and for any reason. Studies were approved by the Salford Health Authority Regional Ethics Committee. Potential recruits were included according to the procedures as described by Lee and Storey (1999). Body mass indices (mean \pm s.d.) were 24.54 ± 4.46 and 22.34 ± 2.60 kg/m² for males and females, respectively. Five male subjects failed to complete the study. Of these, three dropped out because of illnesses unrelated to the study and two because of adverse GI effects following consumption of xylitol containing test products. All female subjects completed the study satisfactorily. Subjects received remuneration for travel expenses and the inconvenience of participating in studies.

Test materials

Test materials were provided as 400 ml orange-flavoured non-carbonated drinks (2 \times 200 ml glass bottles), containing either sucrose, erythritol or xylitol (Table 1). All drinks were supplied by Cerestar R&D, Vilvoorde, Belgium. Differences in sweetness intensity were corrected to 11.25 sucrose equivalent value for all test drinks with the use of aspartame. Test drinks were identified by one of seven different code numbers, the identities of which were not revealed to the investigators or subjects until completion of the study.

Study design and restrictions

The study was a randomized, double-blind, placebo-controlled study. Subjects consumed test drinks separated by 7-day washout periods, while maintaining their customary, normal diet. Product allocation was randomized according to a Latin square design. Dietary restrictions (e.g. no prior consumption of polyol-containing products) were enforced according to Lee and Storey (1999). Subjects consumed test drinks according to choice, either as a mid-morning or mid-

Table 1 Composition of test drinks (g per 400 ml)

Test drink	Sucrose	Erythritol	Xylitol
1	45	—	—
2	—	20	—
3	—	35	—
4	—	50	—
5	—	—	20
6	—	—	35
7	—	—	50

afternoon drink, after having consumed a normal breakfast or lunch. Drinks were consumed within 15 min. Subjects were requested not to consume any food or drinks in the 2-h period following consumption of test drinks, except for up to 300 ml water to quench thirst. Each subject was individually debriefed 24 h after consumption of each test drink to determine adherence to dietary restrictions and consumption regimen, and to assess GI responses.

GI symptoms

Subjects were given printed sheets on which to record the incidence and magnitude of GI responses and details of their bowel movements for the 24-h period following consumption of test products. Notifiable responses were nausea, borborygmi, colic, bloating and flatulence. Each response was ranked on a hedonic scale, where 0 indicated 'normal' function, 1 indicated 'slightly more symptom than usual', 2 indicated 'noticeably more symptom than usual' and 3 indicated 'considerably more symptom than usual'. Subjects recorded the number of bowel movements to pass faeces of normal, hard or watery consistency, where watery faeces were defined as those of an abnormally watery consistency (loss of firm shape owing to high water content). Information regarding faecal volume was not collected.

Statistics

Symptom responses were classified as categorical, and considered to be non-parametric. GI responses following consumption of different test drinks were compared by 2×2 contingency table analysis (χ^2) according to the methods of McNemar (1947). The binomial test was used when the expected frequency in each cell of the contingency table was less than 5. χ^2 was used to test for differences in the occurrence of multiple symptoms following consumption of products. Symptom scores following consumption of test drinks were derived by summing each subject's GI responses, where 0 = normal, 1 = 'slightly more symptom than usual', 2 = 'noticeably more symptom than usual' and 3 = 'considerably more symptom than usual'. The frequency of bowel movements to pass normal, watery and hard faeces were analysed by one-way analysis of variance, followed by Dunnett's *post hoc* test to locate differences in case of an overall significant treatment effect.

Results

Sixty-five subjects completed the study. In one subject, part of the GI symptoms reporting was incomplete. Accordingly, analysis was carried out on 64 subjects where appropriate. Table 2 shows the number of subjects experiencing GI symptoms following consumption of drinks containing 45 g sucrose and 20, 35 and 50 g erythritol or xylitol. Compared with 45 g sucrose, consumption of 20 g xylitol was associated

with a significant increase in the number of subjects reporting nausea ($P < 0.01$) and consumption of 35 g xylitol resulted in a significant increase of the number of subjects reporting watery faeces. Intake of 50 g xylitol was associated with a significant increase in the number of subjects reporting nausea ($P < 0.01$), bloating ($P < 0.05$), borborygmi ($P < 0.01$), colic ($P < 0.05$) and watery faeces ($P < 0.005$). In contrast, consumption of 50 g erythritol was associated with only a significant increase in the number of subjects reporting nausea ($P < 0.01$) and borborygmi ($P < 0.05$).

Table 3 shows the frequency of all bowel movements to pass normal, watery and hard faeces in the 24 h following consumption of test drinks. Compared with 45 g sucrose, consumption of 50 g xylitol significantly increased total bowel movement frequency ($P < 0.01$). At all levels of intake, xylitol produced more watery faeces than erythritol: resp. 50 g xylitol vs 35 g erythritol ($P < 0.001$), 35 g xylitol vs 20 g erythritol ($P < 0.05$) and 50 g xylitol vs 20 g erythritol ($P < 0.001$).

Symptom scores were dose dependent following consumption of increasing doses of xylitol and erythritol (Figure 1). Consumption of 50 g erythritol and xylitol was associated with a significant increase in the mean symptom score ($P < 0.001$ in both cases), compared with 45 g sucrose. Consumption of 35 g xylitol was also associated with a significant increase in the mean symptom score compared with 45 g sucrose ($P < 0.005$). However, 20 and 35 g erythritol and 20 g xylitol did not significantly increase mean symptom scores. There was a significant difference in mean symptom scores following consumption of 20, 35 and 50 g xylitol compared with equivalent doses of erythritol ($P < 0.025$, < 0.05 and < 0.005 , respectively).

Few subjects experienced more than three symptoms following consumption of any test drinks. However, consumption of 50 g xylitol was associated with a significant increase in the number of subjects experiencing three or more GI symptoms compared with 45 g sucrose ($P < 0.001$).

Discussion

GI symptoms following consumption of polyols, including abdominal pain and increased laxation, are well documented, but less so for xylitol and erythritol (Livesey, 2001; Zumbe *et al.*, 2001). Some factors affecting tolerance include the dose of polyol ingested, type of polyol (be it monosaccharide, disaccharide or polysaccharide), the medium of ingestion, consumption pattern, the individual GI tolerance of the individual and composition of the colonic flora (Cummings *et al.*, 2001; Marteau and Flourie, 2001). Disaccharide polyols such as isomalt are generally better tolerated than monosaccharide polyols such as sorbitol, which exerts a greater osmotic load in the GI tract (Zumbe and Brinkworth, 1992; Lee *et al.*, 1994). The dose of sorbitol and xylitol in confectionery is usually less than 20 g, presumably to limit adverse GI effects (Zumbe *et al.*, 2001).

Table 2 GI symptoms in the 24 h following consumption of test drinks containing 45 g sucrose and 20, 35 and 50 g erythritol or xylitol (number of subjects reporting symptoms, $n = 65^a$)

Symptom ^b	45 g Sucrose	20 g Erythritol	20 g Xylitol	35 g Erythritol	35 g Xylitol	50 g Erythritol	50 g Xylitol
<i>Nausea (n = 64)</i>							
0	58	54	47	50	49	44	43
1	3	8	14**	8	11	10	4
2	3	2	2	5	4	6	15
3	0	0	1	1	0	4	2
Total	6	10	17*	14	15	20*	21**
<i>Bloating (n = 64)</i>							
0	53	55	53	50	45	45	41
1	8	9	7	11	16	13	14
2	3	0	3	3	3	5	8
3	0	0	1	0	0	1	1
Total	11	9	11	14	19	19	23*
<i>Borborygmi (n = 64)</i>							
0	49	48	42	51	42	40	31
1	13	14	16	9	14	12	22
2	2	2	4	1	5	8	8
3	0	0	2	3	3	4	3
Total	15	16	22	13	22	24*	33**
<i>Colic (n = 64)</i>							
0	56	58	54	50	53	48	44
1	5	5	5	9	7	9	11
2	3	1	4	4	3	7	8
3	0	0	1	1	1	0	1
Total	8	6	10	14	11	16	20*
<i>Flatulence (n = 64)</i>							
0	46	52	47	50	45	44	40
1	14	10	12	11	15	15	16
2	4	2	5	2	4	5	7
3	0	0	0	1	0	0	1
Total	18	12	17	14	19	20	24
<i>Watery faeces (n = 65)</i>							
None	56	60	51	54	43	46	37
1 ^c	7	5	10	7	10	9	10
2	1	0	4	3	6	5	8
3+	1	0	0	1	6	5	10
Total	9	5	14	11	22*	19	28**

Abbreviation: GI, gastrointestinal.

^aSixty-five subjects completed the study. In one subject, part of the GI symptoms reporting was incomplete. Accordingly, analysis was carried out on 64 subjects where appropriate.

^b0 = Normal (no more symptom than usual), 1 = slightly more symptom than usual, 2 = Noticeably more symptom than usual and 3 = considerably more symptom than usual.

^cNumber of bowel movements to pass watery faeces. Symptom responses were classified as categorical, and considered to be non-parametric. GI responses following consumption of test drinks were compared by 2×2 contingency table analysis (χ^2) according to the methods of McNemar (1947). The binomial test was used when the expected frequency in each cell of the contingency table was less than 5. χ^2 was used to test for differences in the occurrence of multiple symptoms following consumption of products.

*Significant increase in number of subjects experiencing symptom compared to 45 g sucrose, * $P < 0.05$, ** $P < 0.01$.

Although both xylitol and erythritol have a high osmotic potential in the GI tract, consumption of xylitol in this study was associated with significantly more subjects experiencing GI symptoms, increased laxation and elevated symptom scores compared with equivalent doses of erythritol.

Molecular size is important with respect to the extent of polyol absorption in the small intestine (Livesey, 1992). Sorbitol has a molecular weight of 182, which is close to the limit for passive diffusion in the upper intestine (Dwivedi,

1978), xylitol a molecular weight of 152 and erythritol 122 (Zumbe *et al.*, 2001). Thus, the low molecular weight of erythritol may explain its rapid absorption in the upper intestine leaving little unabsorbed to provoke osmotically induced GI symptoms.

Human studies have shown that 60–90% of ingested erythritol is rapidly absorbed across the small intestine, the majority excreted unmetabolized in the urine and only small amounts excreted in faeces (Hiele *et al.*, 1993; Bornet *et al.*,

Table 3 Frequency of bowel movements to pass normal, watery and hard faeces in the 24 h following consumption of test drinks containing 45 g sucrose, 20, 35 and 50 g erythritol or xylitol/mean (s.d.) (*n* = 65)

	45 g Sucrose	20 g Erythritol	20 g Xylitol	35 g Erythritol	35 g Xylitol	50 g Erythritol	50 g Xylitol
Normal faeces	1.06 ± 0.87	1.03 ± 0.84	0.92 ± 0.83	1.05 ± 0.88	0.89 ± 0.81	0.89 ± 0.81	0.75 ± 0.70
Watery faeces	0.20 ± 0.61	0.08 ± 0.27	0.28 ± 0.57	0.28 ± 0.77	0.66 ± 1.13*	0.62 ± 1.22	1.09 ± 1.7**
Hard faeces	0.03 ± 0.17	0.03 ± 0.17	0.11 ± 0.47	0.06 ± 0.24	0.05 ± 0.21	0.06 ± 0.30	0.15 ± 0.40
Total bowel movements	1.29 ± 0.99	1.14 ± 0.94	1.31 ± 0.96	1.38 ± 1.16	1.60 ± 1.13	1.57 ± 1.26	2.00 ± 1.62**

*Significant increase (analysis of variance) in bowel movement frequency compared to 45 g sucrose, ***P* < 0.01.

Other observed differences (Dunnett's *post hoc* test) 20 g erythritol vs 50 g erythritol (*P* < 0.05), 20 g erythritol vs 35 g xylitol (*P* < 0.05), 20 g erythritol vs 50 g xylitol (*P* < 0.001), 35 g erythritol vs 50 g xylitol (*P* < 0.001) and 20 g xylitol vs 50 g xylitol (*P* < 0.001).

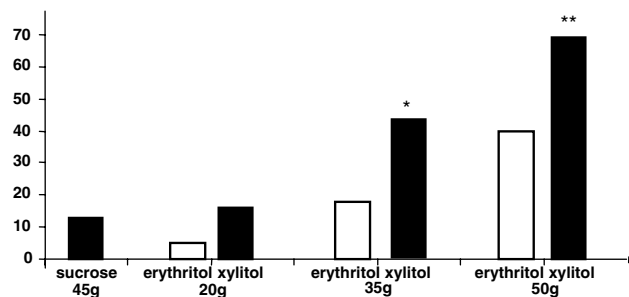


Figure 1 Number of bowel movements by the total study group (*n* = 65) to pass watery faeces in the 24 h following consumption of a bolus dose of 400 ml orange flavoured drinks containing 45 g sucrose or 20, 35 and 50 g erythritol or xylitol. *Significant increase in the number of bowel movements to pass watery faeces compared to 45 g sucrose, **P* < 0.05, ***P* < 0.01.

1992, 1996a,b; Noda *et al.*, 1994). However, estimates for upper intestinal absorption and urinary excretion of erythritol in these studies are dependent on the urinary collection period. Munro *et al.* (1998) consider that between 24 and 48 h at least 90% of ingested erythritol is excreted, leaving 10% for potential microbial fermentation in the large bowel. Thus, 24-h urine sampling may underestimate absorption because the remainder is excreted between 24 and 48 h. In comparison, little information is available regarding the extent of small intestinal absorption of xylitol, although Asano *et al.* (1973) estimate that only 50% of a 30 g daily dose is absorbed in the upper intestine.

In this study, consumption of 35 g xylitol resulted in watery faeces and 50 g xylitol was associated with a significant increase in all symptoms, except flatulence. In contrast, intake of 50 g erythritol provoked only mild nausea and borborygmi. These results suggest that a higher fraction of ingested xylitol passes into the large bowel provoking more symptoms owing to osmotic and fermentation related effects. Table 3 shows the pronounced osmotic effect of 50 g xylitol, with bowel movement frequencies to pass watery faeces of 1.09 ± 1.70 and faeces of normal consistency of 0.75 ± 0.70 (mean ± s.d.). This suggests that during xylitol consumption, watery faeces were passed at the expense of faeces of a normal consistency.

Nausea is not uncommon following polyol consumption. Ingestion of erythritol, sorbitol, lactulose, maltitol and D-

tagatose have reportedly caused nausea in some subjects, presumably due to high fluid influx into the upper intestinal lumen (Lanthier and Morgan, 1985; Lederle *et al.*, 1990; Beaugerie *et al.*, 1991; Oku and Okazaki, 1996; Bornet *et al.*, 1996a; Lee and Storey, 1999).

Figure 1 clearly shows that laxation scores were dose dependent following consumption of single doses of erythritol and xylitol. However, Tetzloff observed that when 1 g/kg BW was ingested in portions spread over the day, no GI disturbances were observed with erythritol, compared with an equivalent amount of sucrose (Tetzloff *et al.*, 1996). These results are broadly in keeping with results of this study, confirming that 20 and 35 g erythritol provoke no significant GI responses and up to (or at least) 50 g erythritol is associated with only mild nausea and borborygmi and laxation. However, it is important to emphasize that occurrence of GI symptoms following consumption of polyols is influenced by the time over which they are consumed. Ingesting small amounts over time has been shown to result in less symptoms than consuming the same amount as one single bolus (Storey *et al.*, 2002).

Although this study was not designed to derive a precise laxative threshold for erythritol (the maximum dose at which no individual responds with laxation), in terms of g/kg BW intake, an approximate figure for comparison with other studies that did define such a threshold may be derived. Consumption of 50 g erythritol did not significantly increase the number of subjects passing watery faeces. This dose equates to 0.78 ± 0.19 g/kg BW (mean ± s.d.), based upon the body mass of subjects in this study, which is close to the laxative threshold level as determined by Bornet *et al.* (1996b) and Oku and Okazaki (1996). Compared to placebo, 35 g xylitol provoked a significant increase in the number of subjects passing watery faeces and at all levels of intake xylitol induced more GI distress than erythritol. Interestingly, recent results of 24 h *in vitro* fermentation studies, using human faecal inoculum and measuring substrate disappearance as well as fermentation products, have shown that erythritol is not fermented (Arrigoni *et al.*, 2005). Accordingly, at moderate doses erythritol is not expected to have a substantial impact on GI symptoms such as abdominal colic and flatulence.

Overall the data of this study show that when consumed as a liquid in a drink, erythritol is not associated with the

occurrence of multiple symptoms, whereas consumption of 50 g xylitol provoked a significant increase in the occurrence of both osmotic and fermentative intolerance symptoms. We conclude that consumption of up to 35 g erythritol by healthy volunteers, in water, is tolerated well, without any symptoms. The highest level of intake, 50 g, provoked only significant increases in borborygmi and nausea.

Acknowledgements

We acknowledge Dr P Scarf (Director, Centre for Operational Research and Applied Statistics at the University of Salford) for initial advice on statistical methodology.

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