**Short communication**

**Human gut microbiota does not ferment erythritol**

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Erythritol, a naturally occurring polyol, is gaining attention as a bulk sweetener for human nutrition. Industrially, it is produced from glucose by fermentation. From various studies it is known to be non-cariogenic. Moreover, it is rapidly absorbed in the small intestine and quantitatively excreted in the urine. Only about 10% enters the colon. Earlier *in vitro* experiments showed that erythritol remained unfermented for a fermentation period of 12 h. In order to investigate whether fresh human intestinal microbiota is able to adapt its enzyme activities to erythritol, a 24 h lasting fermentation was carried out under well-standardised *in vitro* conditions. For comparison maltitol, lactulose and blank (faecal inoculum only) were incubated as well. Fermentation patterns were established by following total gas production, hydrogen accumulation, changes in pH value, SCFA production and substrate degradation. Taking all fermentation parameters into account, erythritol turned out to be completely resistant to bacterial attack within 24 h, thus excluding an adaptation within that period. Since under *in vivo* conditions more easily fermentable substrates enter the colon continuously, it seems very unlikely that erythritol will be fermented *in vivo*.

**Erythritol: Maltitol: Lactulose: *In vitro* fermentation**

Polyols (sugar alcohols) are being used as bulk sweeteners in human nutrition. Maltitol, sorbitol, lactitol, mannitol, isomalt and xylitol have a long history of use. Until some time ago erythritol was only available in Japan. However, recently erythritol has been launched on the American market and it obtained a positive evaluation from the European Commission’s Scientific Committee of Food (2003), opening the doors for future use in Europe. Erythritol, a four-carbon sugar alcohol, occurs widely in nature and also in foods like wine, beer, mushroom, pear, grape and soy sauce (Bernt *et al.* 1996). Industrially, it is produced from glucose by an osmophilic yeast (Goossens & Röper, 1994). Subsequent separation and purification yield a crystalline product with a purity of 99%. Erythritol is not metabolised by oral micro-organisms. *In vitro* incubation with a range of *Streptococci* species showed that neither lactic acid nor other organic acids are produced. Additionally, *Streptococci* were unable to grow on erythritol as sole C-source (Kawanabe *et al.* 1992).

In man, up to 90% of erythritol is rapidly absorbed in the small intestine by passive diffusion. It is distributed widely through tissues but its metabolism is minimal. Being poorly reabsorbed by the kidneys it is quantitatively excreted in the urine (Bernt *et al.* 1996). Neither plasma glucose nor insulin levels are affected by oral erythritol intake (Borret *et al.* 1996; Ishikawa *et al.* 1996). Mean glycaemic and insulinaemic indices of 0 and 2, respectively, have been reported (Livesey, 2003). Moreover, no effect on NEFA homeostasis has been observed (Ishikawa *et al.* 1996). All these observations indicate that erythritol is neither entering carbohydrate- nor fat-metabolic pathways. Compared to other polyols ingested in comparable amounts, erythritol leads to clearly lower osmotic pressures and to rarely any gas production (Oka & Okazaki, 1996). This is due to the fact that only a small fraction of erythritol enters the colon. Theoretically, each gram of polyol being completely absorbed is fully available as energy, whereas total fermentation would result in an energy contribution of approximately 50% via SCFA that are absorbed by the colonic epithelium (Livesey, 2003). Based on both the negligible metabolism and the small amount reaching the large intestine, the energy value of erythritol was confirmed to be less than 0.9 kJ/g by the European Commission’s Scientific Committee on Food (2003).

The relatively small unabsorbed fraction of erythritol enters the colon, where it may be subject to fermentation by the colonic microbiota (Bernt *et al.* 1996). Early animal experiments (Noda & Oka, 1992) suggest that 10% of supplied erythritol may be susceptible to fermentation in rats. Data from human faecal inoculate are scarce. Hiele *et al.* (1993) studied the metabolic fate of 25 g 13C-labelled orally ingested erythritol in six healthy human volunteers. No increase in breath 13CO2 and H2 was observed, indicating that the polyol absorbed is neither metabolised endogenously nor by colonic bacteria. Indeed, a high proportion of erythritol...
(84·1 (SE 3·3) %) was recovered unchanged from urine, leaving the possibility that the remainder was either excreted with faeces or converted to non-oxidised compounds by colonic bacteria. In order to check the latter possibility, the authors performed an in vitro fermentation experiment under strict anaerobic conditions, using fresh faecal microbiota from six volunteers. After 6 h the H₂ concentration was measured in the headspace of the vials. No H₂ production from erythritol was observed. The authors concluded that erythritol is not metabolised by human faecal bacteria but raised the point that some metabolism may occur after a longer adaptation period. In another, non-published experiment (Barry et al. 1992), erythritol was introduced in fermentation flasks placed in a water bath at 38°C. For this experiment a fresh human inoculate from three healthy volunteers was used. Gas and SCFA production as well as erythritol disappearance were monitored during the 12 h lasting fermentation period. Neither gas nor SCFA were produced and the polyl was recovered virtually completely after fermentation. Therefore, the authors concluded that erythritol is non-fermentable.

Since both known in vitro experiments using fresh human faecal microbiota showed no degradation of erythritol within 12 h, the aim of the present study was to prolong the fermentation period to 24 h and thus to check whether colonic bacteria are able to adapt their enzyme activities within this period. For comparison, maltitol was chosen as a second substrate. This disaccharide-type polyl is characterised by a lower absorption, but a higher fermentation rate (approximately 40 and 60 %, respectively) compared to erythritol (Livesey, 2003), thus being expected to be better fermentable. In addition, lactulose as a very easily fermentable substrate and a blank (faecal inoculum only) were included to standardise the experiment.

Materials and methods

Substrates

Erythritol and maltitol (purity on DM basis: ≥99·8 % and ≥99·0 %, respectively) were obtained from Cerestar-Cargill R&D Center (Vilvoorde, Belgium). Lactulose was purchased from Fluka Chemie (Buchs, Switzerland) and was ≥98·0 % pure.

Methodology

In vitro fermentation was carried out by applying a well-standardised batch technique (Lebet et al. 1998). Incubations were performed under strictly anaerobic conditions with a mixture of freshly collected human faeces of four non-methanogenic individuals. Duplicate samples were taken at 0, 6 and 24 h. HgCl₂ was used to stop fermentation. pH, total gas, H₂ and SCFA production in an acidified aliquot of the supernatant were determined as described in the standard procedure. The residues were freeze-dried and ground in a ball mill. To determine substrate disappearance residual polyols were quantified by HPLC, based on ISO International Standard (1998) method 10504.

Results

Total gas production and H₂ accumulation can be followed in Fig. 1(A and B). Values obtained for lactulose (easily fermentable substrate as positive control) and blanks (endogenous fermentability of inoculum as negative control) were found to be in agreement with overall mean values obtained with the same fermentation system. Compared to the blank, virtually no additional gas was produced when fermenting erythritol. Moreover, no H₂ accumulation could be observed. Maltitol showed a clearly lower total gas production during the first 6 h as well as an intermediate H₂ accumulation compared to lactulose. By the end of the incubation, however, almost identical amounts in total gas were produced.

Fig. 1. Total gas production (A), hydrogen accumulation (B) and substrate disappearance (C) during in vitro fermentation of erythritol (●) compared to maltitol (▲), lactulose (○) and blank (□). For details of procedures, see p. 644. Values are means of duplicates with standard deviation <5 % (except where indicated: *10 %).
Erythritol is not fermented in man

Table 1. Changes in pH values and SCFA production during in vitro fermentation of erythritol compared to maltitol, lactulose and blank*
(Values are means of duplicate samples; standard deviation < 5% except where indicated)

<table>
<thead>
<tr>
<th>Sample time (h)</th>
<th>pH</th>
<th>Total Acetate</th>
<th>Propionate</th>
<th>Butyrate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blank</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>6·75</td>
<td>65·3</td>
<td>35·6</td>
<td>7·2</td>
</tr>
<tr>
<td>6†</td>
<td>6·85</td>
<td>122·7</td>
<td>73·9</td>
<td>13·2</td>
</tr>
<tr>
<td>24</td>
<td>6·83</td>
<td>163·2</td>
<td>94·0</td>
<td>27·5‡</td>
</tr>
<tr>
<td>Erythritol</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>6·64</td>
<td>70·1</td>
<td>41·4</td>
<td>8·3</td>
</tr>
<tr>
<td>6</td>
<td>6·83</td>
<td>122·9§</td>
<td>70·4§</td>
<td>17·0§</td>
</tr>
<tr>
<td>24</td>
<td>6·83</td>
<td>165·7</td>
<td>89·3</td>
<td>21·6§</td>
</tr>
<tr>
<td>Maltitol</td>
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</tr>
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<td>0</td>
<td>6·62</td>
<td>66·4</td>
<td>33·2</td>
<td>9·9</td>
</tr>
<tr>
<td>6</td>
<td>6·68</td>
<td>369·7</td>
<td>256·3</td>
<td>27·5</td>
</tr>
<tr>
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<td>5·95</td>
<td>1196·0</td>
<td>828·6</td>
<td>115·3</td>
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<tr>
<td>Lactulose</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
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<td>79·0</td>
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<td>7·6</td>
</tr>
<tr>
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<td>6·15</td>
<td>1012·5</td>
<td>778·9</td>
<td>50·7</td>
</tr>
<tr>
<td>24</td>
<td>6·05</td>
<td>1113·0</td>
<td>852·9</td>
<td>64·7</td>
</tr>
</tbody>
</table>

*For details of procedures, see p. 644. †Single values. ‡Standard deviation <10%. §Standard deviation >10%.

When looking at changes in pH values and SCFA production (Table 1), similar observations were made. Erythritol and blanks did not differ in any parameter, whereas maltitol and lactulose reached similar end values. As also seen for gas production, SCFA formation and thus pH drop was found to be considerably slower for maltitol compared to lactulose within the first 6 h of fermentation. Although the total SCFA production reached comparable end values for both substrates, it has to be mentioned that qualitative differences were observed. Significantly higher amounts of propionate and butyrate were produced from maltitol.

Substrate disappearance can be followed in Fig. 1(C). Erythritol turned out to be completely resistant to the attack by the colonic microbiota during the 24 h of fermentation. In contrast, maltitol degradation was found to be linear but complete within that period. Lactulose disappearance was not determined in the present study. However, its complete degradation within 6 h was shown in earlier experiments (Arrigoni et al. 2004).

Discussion

Gas production from erythritol turned out to be negligible. Similar in vitro results were also observed by Hiele et al. (1993), who showed that H2 formation by faecal bacteria after 6 h of incubation with erythritol was not higher than after the blank incubation. Moreover, Barry et al. (1992) reported neither total gas nor H2 production over a fermentation period of 12 h. The fact that gas production from maltitol is retarded compared to that from lactulose is in accordance with in vivo results by Storey et al. (1998). They found significantly lower breath H2 values (cumulated over a period of 6 h after ingestion) from maltitol. SCFA production as well as the concomitant pH drop reflects the observations made for gas production. No published data are available for total SCFA production from erythritol. However, the changes in pH values observed in the present study confirm observations made by Barry et al. (1992) for both erythritol and maltitol. As can be seen from substrate disappearance data, erythritol turned out to be completely resistant to the attack by faecal bacteria, a fact which has already been reported for a period of 12 h (Barry et al. 1992). However, the present experiment showed that erythritol is even not susceptible to the colonic microbiota within 24 h. The nearly linear degradation of maltitol is in accordance with results obtained by Barry et al. (1992), who also found a retarded metabolism of the substrate.

Taking all fermentation parameters into account, it can be stated that erythritol as a sole substrate is completely non-fermentable by freshly collected human faecal microbiota within a period of 24 h. Based on the currently obtained data, the contribution to daily energy intake by gut fermentation of erythritol after oral intake in man is considered to be nil. For verification in vivo, a complete balance study would be required. Erythritol determination in faeces is rather simple, but a quantification of the absolute amount entering the colon is very complex. Although its total resistance to faecal bacterial fermentation in vivo is not definitively proven, it seems very likely that erythritol is excreted unchanged in man. The latter is supported by the fact that undigested dietary substrates as well as endogenous sources enter the colon continuously in considerable amounts (Gibson et al. 1996), most of them being more easily fermentable.

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References


