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Erythritol Is More Effective Than Xylitol and Sorbitol in Managing Oral Health Endpoints

Peter de Cock  ¹, Kauko Mäkinen,² Eino Honkala,² Mare Saag,³ Elke Kennepohl,⁴ and Alex Eapen ⁵[Show more](#)**Academic Editor:** Athena Papas**Published:** 21 Aug 2016

Abstract

Objective. To provide a comprehensive overview of published evidence on the impact of erythritol, a noncaloric polyol bulk sweetener, on oral health. *Methods.* A literature review was conducted regarding

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acceptance by consumers for use in a wide variety of food products [3, 6].

While known for its nutritional and technological benefits, erythritol has also been shown to exert a number of beneficial oral health effects (summarized in Table 1). Specifically, the noncariogenicity of erythritol was established first in rats by a group of researchers in 1992 [7].

Table 1

Summary of *in vitro* and *in vivo* bacterial (dental plaque) growth inhibition studies with erythritol.

Inclusion of erythritol in studies aimed at investigating the effects of polyols on dental caries followed the logical scientific process: other common polyols, notably xylitol and sorbitol, both of which are commonly used as sugar replacers in food products, had for dozens of years been studied as potential caries-preventive agents. Inventions related to erythritol manufacturing and comprehensive safety conclusions of the metabolic effects of erythritol have marked its gradual advent in the real world of consumers. The palette of polyol sweeteners has been expanding and may be nearing completion, since the number of physiologically acceptable polyol sweeteners can be considered limited. Erythritol may be regarded as a welcome addition to this palette.

The present review deals with erythritol primarily from the oral health perspective.

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the dose at which xylitol did not show a laxative effect in adults under the same severe conditions was about 0.3 g/kg bw [34]. It is anticipated that the exposure to erythritol *via* oral healthcare products will be very low at approximately 0.1 g/kg body weight per day, which is only 10% of the reported well-tolerated dose in humans [24].

4. Erythritol Suppresses Harmful Bacteria and Reduces Biofilm (Dental Plaque)

Erythritol was investigated for its potential to inhibit the growth of bacteria in dental plaque (i.e., a biofilm of microbial accumulations, particularly *S. mutans*) [8–11, 13, 14, 16, 17], as summarized in Table 1 and described below.

Mäkinen et al. [8, 9] conducted 2 preliminary xylitol, erythritol, and sorbitol comparison studies looking at their effects on saliva and plaque levels of *S. mutans*. In the first study [8], 2 groups of 15 subjects (mean age of 30.3 ± 17.1 years) were given either xylitol- or erythritol-containing chewable tablets (10 tablets/day) for a period of 2 months with a daily polyol intake of 5.2 g. Xylitol, but not erythritol, showed a statistically significant reduction of dental plaque and saliva and plaque levels of *S. mutans*. In the second study [9], subjects also were given chewable tablets (10 tablets/day) that contained xylitol ($n = 26$), sorbitol ($n = 24$), xylitol-erythritol ($n = 22$), or sorbitol-erythritol ($n = 23$) for up to 64 days. Total daily polyol consumption was 5.4 g/day (mixtures contained 2.7 g/day of each polyol). A significant reduction in plaque and saliva counts of *S. mutans* was demonstrated for xylitol alone and for the 1 : 1

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shown in Figures 1 and 2, respectively. Notably, the erythritol group not only had a significantly lower

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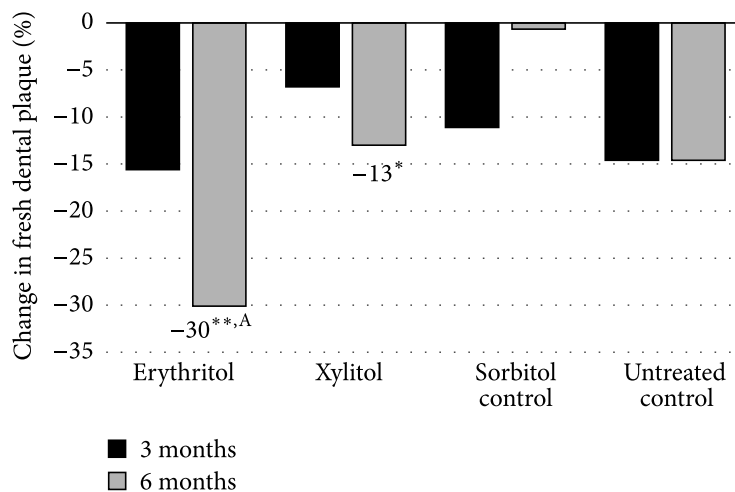
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however, is higher at the same osmolarity. There is an additional growth-reducing effect of erythritol that xylitol, sorbitol, and maltitol do not have. This may be associated with the ability of erythritol to easily pass the cell membrane passively and suppress growth via several pathways as suggested by Hashino et al. [16] where it interferes in some of the enzymatic pathways involved in the growth of *S. mutans*. Figure 4 provides a useful insight into how big the differences in growth reduction is between the polyols tested at the same weight/volume concentrations. To reduce the absorbance to, for example, 1, the gram amount of maltitol required to reduce growth to that level is about 7x higher compared to erythritol and for xylitol; it is about 3x higher.



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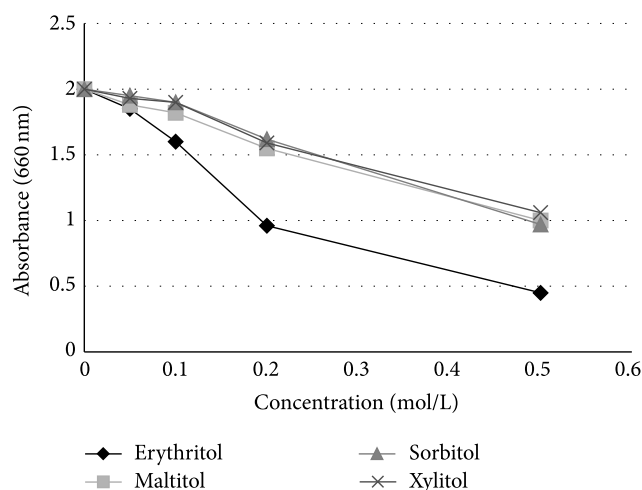
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■ Saliva
□ Plaque

Figure 2

Percent change in salivary and plaque *S. mutans* score against baseline over a 6-month period in a teenage cohort consuming erythritol-, sorbitol-, or xylitol-containing chewable tablets. Adapted from Mäkinen et al. [10].
** $p < 0.001$ when compared to baseline using a paired t -test.


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 Erythritol  Sorbitol
 Maltitol  Xylitol

Figure 4

Effect of polyol concentration (g/100 mL) on growth of *S. mutans* (strain 267-S) after 5 hours. Adapted from Mäkinen et al. [10] and Mäkinen [36].

Of interest was the observation that erythritol seemed to inhibit the growth of *S. mutans* by a mechanism that differs from that of xylitol. Normally, xylitol-dependent inhibition of bacterial growth has appeared throughout the entire growth phase, whereas erythritol also inhibited—quite distinctly—the growth of some *S. mutans* strains during later growth phases. Both polyols were considered to have significant utility value in limiting the incidence of dental caries.

In addition to its inhibition of the growth of *Streptococcus*, erythritol was found to decrease the adherence of polysaccharide-forming oral streptococci (14 strains tested: *S. mutans* (9), *S. sanguinis* (2), *S. salivarius* (2), and *S. sobrinus* (1)) in an *in vitro* study investigating the growth inhibition and adherence of cells to a smooth glass surface by 2 or 4% erythritol and xylitol [11]. Both erythritol and xylitol, at a concentration of 4%, significantly reduced the glass surface adhesion of most of the polysaccharide-forming streptococci tested; *S. mutans* 10449 and *S. sobrinus* OMZ 176 were not affected. Growth inhibition was considered not to be associated with the magnitude of the decrease in adherence (for erythritol there was a trend ($p = 0.12$) toward an association) indicating that cell adherence was *via* a

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inhibitory effects of erythritol at a concentration of 10% on *S. mutans* were also reported by Søren et al. [15]

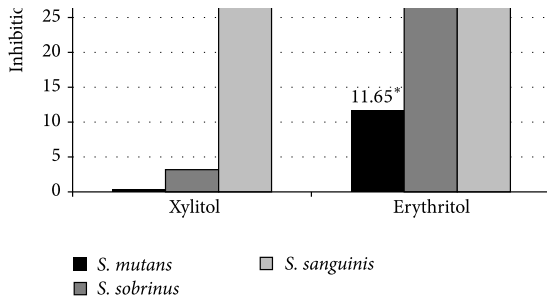
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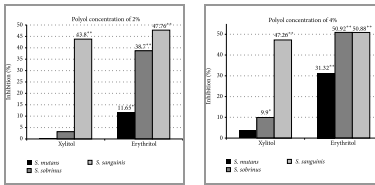
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(a)



(a)

(b)



Figure 5

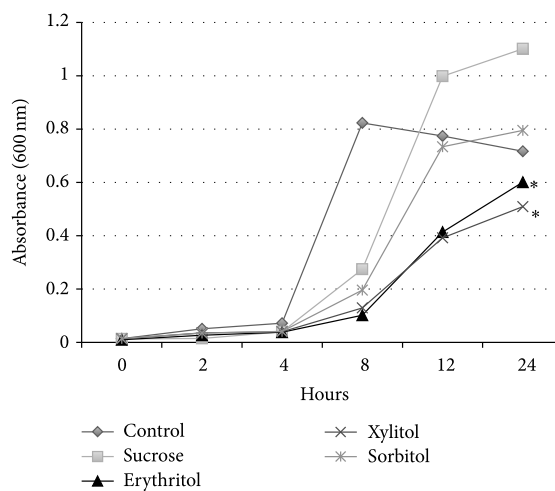
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control (water) or sorbitol (see Figure 6(b)). Erythritol and xylitol both significantly decreased the expression of 3 GTF genes and 1 FTF gene ($p < 0.05$) compared to sucrose. The decreases seen with erythritol also were significantly decreased when compared with sorbitol and untreated control (see Figure 6(c)). Since erythritol inhibited the growth of *S. mutans*, reduced adhesion of *S. mutans* to smooth surfaces, and decreased the expression of genes involved in sucrose metabolism, the authors considered erythritol to have anticariogenic potential.



(a)

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the only, long-term human caries trial using erythritol alone (no mixture with other polyols) was executed by Tartu University Institute of Stomatology in Tartu, Estonia, in 2008–2011 [37].

This study resulted from theoretical considerations that the relative effect of three common polyols (i.e., erythritol, xylitol, and sorbitol) on the incidence and propagation of dental caries should differ and reflect the number of hydroxyl groups present in the polyol molecules [38]. Preliminary results obtained with erythritol in animal caries [7] and some oral biologic processes in humans [8–10] were encouraging and, therefore, the Tartu polyol double-blind randomized controlled prospective intervention trial was developed to compare the long-term usage of erythritol and xylitol candies with sorbitol candies in children.

At the start of the trial, 485 first and second grade school children (~8-9 years of age) from 10 schools were randomly divided into erythritol ($n = 165$), xylitol ($n = 156$), and sorbitol (control, $n = 164$) groups. By the end of the 3-year trial, 374 children remained in the study [37]. Those leaving the trial were not at school on examination days, changed schools, or did not wish to continue to participate in the study.

Teachers provided the children with four small chewable tablets containing erythritol, xylitol, or sorbitol to consume three times each school day (about 200 school days per year) resulting in a calculated daily polyol consumption level of about 7.5 g. The children were educated on oral hygiene and provided with a toothbrush and fluoride toothpaste every 6 months with a recommendation to brush their teeth more than once a day. For assessment, the children were assigned to one of 4 trained dental examiners and underwent double-blind clinical examinations at the start of the trial (baseline) and at 12, 24, and 36

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Erythritol Xylitol
 Sorbitol

Figure 7

Percentage of tooth surfaces developing into enamel or dentin caries, percentage of enamel caries developing into dentin caries, and percentage of surfaces with an increase in caries score (increase in caries score is transition from any caries score to increase in score of 1 or more) over a 3-year period in a child cohort consuming erythritol-, sorbitol-, or xylitol-containing candies. From Honkala et al. [37]. *** $p < 0.001$ when compared to sorbitol using Fisher's exact test (two-tailed).

In 2014, 3 years following cessation of the polyol interventions, 364 of the children were reevaluated using the same procedures (ICDAS examination) used during the 3-year intervention study (Falony et al., manuscript submitted). No significant differences in decayed, missing, and filled teeth and surfaces between the intervention groups were noted; however, in the erythritol group, percentages of surfaces developing enamel/dentin caries or dentin caries or subject to dentist intervention were still reduced compared to the other groups (see Figure 8). Consequently, habitual usage of erythritol candies in this child cohort showed a slower and lower caries development compared to the xylitol and sorbitol groups.


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when compared to sorbitol using Fisher's exact test (two-tailed) *** $p < 0.001$ when compared to sorbitol

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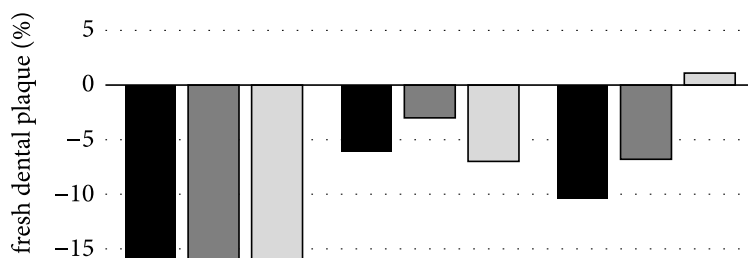
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erythritol with a reduction tendency at the 2-year examination, as shown in Figure 7. No such changes were found in groups receiving sorbitol or xylitol. Chemical analysis indicated that usage of the three polyols had no significant or consistent effect on the plaque levels of protein, glucose, glycerol, or calcium. However, after three years, the plaque of erythritol-receiving subjects contained significantly ($p \leq 0.05$) smaller levels of acetic acid and propionic acid than that of subjects who had received xylitol or sorbitol. The plaque levels of lactic acid partly followed this same general pattern. The consumption of erythritol was also generally associated with significantly ($p < 0.05$) lower counts of salivary and plaque *S. mutans*. The use of these polyols had no significant effect on salivary *Lactobacillus* levels. Three months after the end of the trial, a fourth group of children ($n = 162$) was evaluated as an additional comparison group within the same age groups. In this comparison group, mean salivary *S. mutans* counts were significantly higher than in the erythritol and xylitol groups ($p = 0.014$ and 0.034 , resp.), but not the sorbitol group. Taken together, these results suggested that habitual consumption of erythritol reduced the involvement of several oral biologic factors that have normally been associated with the initiation and propagation of dental caries. Consequently, these results were in congruence with the clinical caries observations reported by Honkala et al. [37].



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show that xylitol outperformed sorbitol. In terms of demonstrable effectiveness, there are some

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Furthermore, (1) the polyol tablets had to be consumed at schools within a relatively short duration of the day, as stipulated by the school hours (children left school latest at 2 pm); (2) chewing gum used in most xylitol studies is a much better salivary flow stimulant [46] compared to the compressed tablets used in the Honkala et al. [37] study, which used tablets purposely to focus as much as possible on the pharmacological effects of the polyols; (3) the exposure to the school children was a very mild intervention that did not take place during weekends and vacations meaning that intervention was only for about 200 days per year; and (4) erythritol has a lower solubility and molecular weight than xylitol and, therefore, erythritol dissolves more slowly most likely resulting in longer exposure and diffuses faster and deeper into the dental plaque where it can better exercise its impact on microbes like *S. mutans*.

The results from Honkala et al. [37], Runnel et al. [40], and Falony et al. (manuscript submitted) investigations indicate that erythritol did show statistically significant differences from the other two polyols in terms of caries development and oral biologic processes. In these studies, erythritol turned out to be a potential caries-preventing dietary sucrose substitute with higher efficacy compared to sorbitol and xylitol.

Some reports have claimed nonefficaciousness of erythritol as a caries-limiting agent. Closer examination of the study designs involved has revealed serious generalizations and shortcomings. For example, in a review of a double-blind, cluster-randomized clinical trial in school children (~10 years of age) conducted by another group of researchers [41], Duane [47] commented that there was no evidence of caries reduction in a school xylitol and erythritol lozenge program. However, the overall length of the intervention period may have been too short (± 190 intervention days in 9 months or ± 380 intervention days in 21 months), while the frequency of use (3x per school day) and the amount of xylitol (4.7 g) and

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causing less pain for patients [53]. Since erythritol has similar abrasive properties and particle size to

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operator treated control sites with curettes until all subgingival deposits were removed. All remaining dentition was treated using standard supportive periodontal therapy. Based on a visual analog scale, patient's tolerance was significantly better for sites treated with erythritol than those without. There were no differences in clinical outcomes between subgingival air-polishing with erythritol or traditional scaling except that patients tended to prefer air-polishing. More recently, Hägi et al. [54] published the results of a similar study, but over a period of 6 months, in which subjects underwent treatment at baseline and 3 and 6 months with subgingival low abrasive erythritol powder using an air-polishing device or repeated scaling and root planing at study sites identified at baseline as bleeding on probing positive sites with probing pocket depth of ≥ 0.4 mm but no detectable calculus. At baseline and 6 months, plaque index, bleeding on probing, probing pocket depth, clinical attachment level, and subgingival plaque were evaluated. In the 38 patients completing the study, both treatments produced significant reductions in bleeding on probing and probing pocket depth and increases in clinical attachment level. There were no statistically significant differences between the treatment groups.

In another study, subgingival air-polishing with erythritol containing 0.3% chlorhexidine was compared to ultrasonic debridement at 3-month intervals for up to 12 months [55]. Fifty patients with 6,918 sites were examined at start of the study (baseline) and served as their own controls (i.e., one side was treated with erythritol air-polishing and one side with ultrasonic debridement). At the 12-month examination, there was no difference between the treatments with respect to the presence or absence of a probing depth >4 mm and the frequencies at $>1,000$ and $>100,000$ cell/mL of 6 microorganisms (*Porphyromonas gingivalis*, *Aggregatibacter actinomycetemcomitans*, *Tannerella forsythia*, *Treponema denticola*, *Prevotella intermedia*, and *Parvimonas micra*). However, at 12 months, erythritol-treated sites were less frequently positive for *Aggregatibacter actinomycetemcomitans* at $>1,000$ cell/mL, with counts never

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From all other polyols, it has the smallest molecular size as this polyol is of the lowest type and it is the first polyol to be commercially produced by fermentation, a natural process [1]. Its unique metabolic profile renders it to be noncaloric, nonglycemic, noninsulinemic, and very well tolerated. It has been consumed by animals and humans for ages as small quantities of erythritol occur widely in microorganisms, algae, fermented foods, lichens, mushrooms, many fruits and vegetables, and also animal and human tissues [5, 20, 57].

Unlike all other polyols including sorbitol and xylitol, ingested erythritol is rapidly and almost completely absorbed from the small intestine, not metabolized, and excreted unchanged in the urine [32]. Depending on the quantity ingested, approximately 10% of ingested erythritol may reach the colon [5]. Its high systemic bioavailability has been linked to additional health benefits for people with diabetes by reducing arterial stiffness and improving small vessel endothelial function [18].

Owing to its sweet taste and high digestive tolerance, erythritol is well suited to replace sugar pound-for-pound in foods without replacing any calories thereby significantly reducing the energy density of those foods. All dental and oral biological studies carried out to date have suggested erythritol to be noncariogenic. Erythritol is being used as a sweetener in dentally safe confectionery items, desserts, tabletop sweeteners, beverages, and many other sugar-free and calorie-reduced foods. Erythritol is authorized for use in foods in more than sixty countries and is included in the GSFA-list (General Standard for Food Additives) of the *Codex Alimentarius* under INS number 968.

The noncariogenicity of erythritol was first investigated and established in rats in 1990 [7, 58] and soon after in 1996 in humans [59]. Early studies demonstrated that erythritol limits the growth, lactic acid production, and plaque formation of *S. mutans* (serotypes a-h) [58] and a number of other streptococci

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The results reported in these three publications showed that erythritol has caries preventing activity with

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production of glucans and fructans.

(iii) Decrease in *in vitro* biofilm formation and *in vivo* dental plaque weight.

Certain exposure conditions should be met in order to benefit from the caries-preventing activity of erythritol. The two short term studies by Mäkinen et al. in 2001 and 2002 [8, 9] that did not show plaque reduction used an intervention period of 2 months and used very fragile tablets that fragmented and dissolved in the mouth rapidly resulting in an exposure time of 1 to 2 minutes. The total daily dose of erythritol in both studies was 5.1 g and 2.7 g in 2001 and 2002, respectively. In addition, these tablets contained low use levels of erythritol: 39.5% and 24.5% in 2001 and 2002, respectively. The short exposure time combined with the rather low use level and low total daily dose of erythritol, as well as the short intervention period of 2 months, has likely contributed to the absence of a plaque reducing effect in these two studies. The caries study by Hietala-Lenkkeri et al. 2012 [41] that did not show caries-preventive effects of erythritol and xylitol used lozenges containing 49.4% erythritol that were consumed 3 times daily resulting in a total dose of 4.5 g erythritol daily. The actual intervention duration was 9 and 18 months in the 2 groups investigated who were, respectively, examined 39 and 27 months after termination of the intervention. In addition, the study was done in an area with low caries prevalence: average DMFT for 12-year-olds was 0.8 in comparison with the average for Finland which is 1.2. This, and the rather low use level and low total daily dose of erythritol, as well as the short intervention period of maximally 18 months and the absence of a clinical examination immediately after the intervention, has likely contributed to the absence of a caries reducing effect in this study.

The erythritol candies used in the human studies published by Mäkinen et al. [10], Runnel et al. [40], Honkala et al. [37], and Falony et al. (manuscript submitted) were conducted with pressed

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The present review summarizes the oral health benefits of erythritol use as demonstrated by a reduction in

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distinction among polyols.

Competing Interests

The authors Peter de Cock and Alex Eapen are employees of Cargill. The author Elke Kennepohl is a consultant to Cargill. The authors Kauko Mäkinen, Eino Honkala, and Mare Saag have no competing interests to declare.

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