IN BRIEF

- Xylitol is one of a number of non-sugar sweeteners approved for use in foods and other items, in many countries.
- It is well-established that xylitol is non-cariogenic.
- Xylitol in chewing gum is anti-cariogenic as are other polyols in chewing gum.
- Xylitol exhibits dental health benefits which are superior to other polyols in all areas where polyols have been shown to have an effect.
- The inhibition of mother/child transmission of cariogenic oral flora leading to reduced caries development in young children is caries-preventive.
- Xylitol's specific effects on oral flora and especially on certain strains of mutans streptococci add to its caries-preventive profile and give it a unique role in preventive strategies for dental health.

Xylitol and caries prevention — is it a magic bullet?

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Several recent publications have focused discussion on the value of xylitol in caries prevention. Some reviewers have concluded that xylitol has a unique active role in caries prevention, while other reviewers have been more cautious saying that the case is not yet proven. Chewing xylitol gum is certainly effective at preventing caries development compared with chewing sugared gum or not chewing any gum. Xylitol gum appears to be more effective than sorbitol gum or combinations of xylitol and sorbitol. One recent trial suggested that the effectiveness of eating a xylitol candy could be similar to that of chewing xylitol gum: this is valuable as it would remove the necessity of disposing of spent gum; it has also been suggested that xylitol has a positive action in addition to the favourable effect of chewing. A further recent publication reported substantial reductions in caries development in children whose mothers had chewed xylitol gum. The main explanation appears to be that xylitol changed the plaque flora of the mothers so that transmission of cariogenic oral micro-organisms from mother to child was reduced. Further developments in this field are awaited, but at present we may conclude that xylitol exhibits dental health benefits which are superior to other polyols in all areas where polyols have been shown to have an effect. In addition, xylitol's specific effects on oral flora and especially on certain strains of mutans streptococci add to its caries-preventive profile and give it a unique role in preventive strategies for dental health.

Thirty years ago, there was no information on the effect of xylitol on dental caries. Since then, some 270 articles have been published describing clinical studies and investigations into possible mechanisms for xylitol's seemingly remarkable efficacy. The first of these studies was the Turku sugar studies conducted between 1972 and 1974[1] at a time when caries experience was very high in northern Europe, and in Finland which is a major xylitol producer. Xylitol production is now over 10,000 tonnes per year, mainly going to confectionery manufacturers and the pharmaceutical and oral hygiene industries.

While there is no doubt that xylitol is non-cariogenic and the cariostatic effect of xylitol chewing gum is well accepted, the existence of an active anti-caries role of xylitol *per se* remains controversial. More recently, remarkable results have emerged from a trial where development of dental caries was much lower in children whose mothers had chewed xylitol gum when their children were young (beginning at three months of age) during the so-called 'discrete window of infectivity' from mother to child (between 19 –31 months of age), compared with control children.[2,3,4]

For many years, many thousands of Finnish children have participated in caries preventive programmes which involved chewing xylitol gum in school.[5,6] Disposal of spent gum has been seen as a draw-back for such community programmes by public health authorities in many countries and it was of considerable interest that, in a recently published trial, the caries preventive effectiveness of chewing xylitol sweets was observed to be similar to that of xylitol chewing gum.[7]

Because of these recent events, it was thought to be useful to summarise the evidence concerning 'is xylitol a magic bullet?'

Xylitol is one of a number of non-sugar sweeteners permitted for use in foods.[8] It is found naturally in some foods but it is mass-produced principally from sustainable xylan-rich hardwood sources such as birch and beech wood — a process first reported over a hundred years ago. Chemically, it is a pentitol which is a five-carbon polyol. In this, it differs from other common polyols such as sorbitol and mannitol, which contain a six-carbon ring. It was

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Table 1 Sweeteners approved for use in foods in the UK

Bulk sweeteners[1]	Intense sweeteners
Sorbitol	Saccharine
Mannitol	Acesulfame K[2]
Hydrogenated glucose syrup[2]	Aspartame[2]
Isomalt[2]	Thaumatin[2]
Xylitol[2]	Cyclamate[4]
Lactitol[3]	Neohesperidine DC[4]
Maltitol[5]	

[1]also known as nutritive sweeteners
[2]permitted in 1983
[3]permitted in 1988
[4]permitted in 1995
[5]permitted in 1996

approved for use in foods in the UK in 1983 (Table 1) as one of several non-sugar sweeteners.[8] The Department of Health COMA report on 'Dietary sugars and human disease' gave encouragement to their use.[9] Presently in the UK, consumption of xylitol is about 1,000 tonnes per year, principally in chewing gums, confectionery, toothpaste and medicines.

Many clinical trials have shown that chewing sugarless gum leads to substantial caries prevention, with xylitol-containing gums being particularly effective. Chewing sugarless gum increases saliva flow considerably and thus fast flowing saliva with its high pH and high concentration of calcium and phosphate aids remineralisation of dental enamel and resists caries development. It has also been observed in such trials with xylitol-containing gums that the bacterial flora of plaque changes with the more cariogenic bacteria becoming less frequent. Some research has suggested that xylitol has a unique, positive role in preventing dental caries,[10,11] while other research workers refute xylitol's unique action suggesting that the caries-preventive effects of xylitol chewing gum can be explained adequately by the favourable action of chewing gum alone.[12] One of the main purposes of this review is to summarize the evidence upon which these arguments rest. Other purposes of this review are to describe progress in the so-called 'mother and child' study[4] and to compare the effectiveness in caries prevention of xylitol with other bulk non-sugar sweeteners. The intense non-sugar sweeteners listed in Table 1 will not be discussed.

TERMS USED TO DESCRIBE XYLITOL'S ACTION.

When considering the literature, it is important that the terminology used to describe xylitol's effects is accurate and consistent. Acidogenicity and fermentability are essentially terms used to describe findings from *in vitro* experiments and *in vivo* studies other than clinical trials, whereas cariogenicity, non-cariogenic and anti-cariogenic are clinical terms. It is clear from the literature that some authors have interpreted a number of definitions relating to these cariological and bacteriological terms in slightly different ways, which have led to some difficulties interpreting the findings of some studies. The terms 'cariostatic', 'anti-cariogenic' and 'anti-caries' have all been used when discussing dental therapeutic claims of xylitol, as have 'active' and 'passive' effects. For the purposes of this review, the properties of non-fermentability and non-cariogenicity will be classed as passive effects while active caries-preventive (or caries-inhibitory) effects will include the terms bacteriostatic and cariostatic. Only a reversal in the caries process, that is the remineralisation of a carious lesion, will be described as a therapeutic or anti-cariogenic effect.

EVIDENCE FROM CLINICAL TRIALS

Evidence of the effect of xylitol and other sweeteners on dental caries comes from many different types of study – laboratory incubation experiments, *in vivo* plaque pH and enamel slab caries experiments, and animal experiments. The best form of evidence, though, is from clinical trials – particularly randomised clinical trials (RCTs) where subjects are randomly allocated to treatment groups and they and their assessors do not know the group identity of the subject. Often it is not possible for a subject to be unaware of the treatment he or she is receiving and allocation to groups sometimes has to be done on a school or community basis rather than on an individual basis.

Clinical trials involving xylitol and other polyols can be divided into three main designs: total substitution of normal dietary sugars for xylitol, partial substitution, and supplementation of normal dietary sugars with xylitol or other polyols. A few of the clinical trials using partial substitution or supplementation have involved confectionery but most have studied the effects of chewing gums containing xylitol and/or sorbitol. A few trials which have looked at supplementation with xylitol have involved toothpastes or mouthrinses.

• Total substitution studies

The Turku sugar studies are one of the milestones of dental caries research.[1] The main study tested the effect of almost total substitution of normal dietary sugars with xylitol on development of dental caries over two years in adults. This long-term clinical trial was a great organisational feat since it involved the special manufacture and distribution of over a hundred food products. The daily consumption of xylitol was about 50 g per day. While the sucrose and fructose groups developed caries during the two-year study, little caries developed in the xylitol group. There have been some criticisms of the study, especially regarding its design, since allocation to the various test groups was based mainly on personal preference, and the nature of the study excluded the possibility of it being 'blind'.[12] In addition, groups varied with respect to their sweetener intake and possibly their dental health awareness.

The caries data for buccal surfaces[13] and approximal[14] surfaces of teeth of subjects in the Turku study were analysed blind in greater detail. The buccal surfaces were photographed seven months after the beginning and at the end of the two-year trial. While the area of white spots increased over the seventeen months in the sucrose group, the area decreased in the xylitol group: the author concluded that xylitol consumption caused remineralisation of incipient white spot lesions on buccal surfaces. A quantitative measure of the mean size of lesions seen on bitewing radiographs was made using a digitised planimetric technique. The mean lesion size increased in the sucrose group but there was no increase in the mean size of lesion in the xylitol group.

• Partial substitution studies and confectionery supplementation studies

Since the Turku sugar substitution study, a number of clinical field trials have been conducted on daily use of xylitol products as part of the usual sugar-containing diet – either partial substitution or supplementation.[1,7,15-35] Field trials differ from clinical trials in that they may have no particular control group; the study may not be blind or there may be no special selection or supervision of participants. Even with these intrinsic weaknesses, field trials are important as they allow the effectiveness and acceptability of preventive agents or methods previously shown in a clinical trial to be effective, to be evaluated in a particular setting. In two of these field trials, xylitol was given as several items of confectionery[17,21] while in other studies, xylitol was given in chewing gum only[20, 23,27] and these studies will be considered later.

Both of the confectionery studies lasted three years. The 6–11-year-old Hungarian children consuming xylitol confectionery developed 45% less caries than control children who consumed usual sugar confectionery. Partial substitution of xylitol for dietary sugars had been intended in this trial but analysis revealed that the pattern of consumption of xylitol was largely additive; the frequency of sucrose consumption had not decreased.[16] The study therefore demonstrated the cariostatic effect of xyli-

tol through its use as a supplement. The field trial of Kandelman[21] recorded 37% less caries in 6–12-year-old Polynesian children who consumed up to 20 g xylitol confectionery per day compared with a control group who ate sugar confectionery. Both field studies were plagued by significant numbers of drop-outs among subjects; approximately 30% in the Hungary study and 37% in the Polynesian study and the studies were not blind. However, comparisons of the caries prevalence of participants and drop-outs in this latter study demonstrated that, within each age group, there were only small differences in baseline mean caries values and that the participants appeared to be a representative sample of the entire population.

• Chewing gum supplementation studies

There has been considerable growth in the use of sugarless chewing gums – about 85% of gum sold in the UK is now sugar-free. The benefits of sugarless gum have been investigated in a number of clinical trials. In some of these, the control group had chewed sugared gum, thus testing the substitution of polyols for sugar. In other trials, the control group did not chew any gum, testing the beneficial effect of chewing sugarless gum – its non- or anti-cariogenic properties.[36,37] Follow-on studies from these clinical trials of chewing gum have also been important in establishing the mechanism for the efficacy of sugarless gums.

The one year Turku chewing gum study assessed the effect on caries development of low doses of xylitol compared with the use of sugared gum, and showed a cumulative caries increment of +2.92 tooth surfaces in the group chewing sugared gum compared with a negative caries increment of –1.04 tooth surfaces in the group chewing a mean of 4.5 xylitol gums (each containing 1.5 g xylitol) per day.[38]

A further two-year study was designed to determine whether the daily use of xylitol gum increased the efficacy of routine caries preventive measures in 11–15-year-old school children in Finland – a country with low baseline caries levels. After two years, this blind study showed a mean reduction in caries in the children chewing xylitol gum of 44% compared with the control group who did not chew any gum.[18] The caries preventive effectiveness was observed three[22] and five years[26] after discontinuation of the use of xylitol – the greatest long-term preventive effect being seen on second permanent molars which erupted during the xylitol gum trial.[39] Scheie and Fejerskov,[12] in their review of this trial, point out that an important factor to be considered in the interpretation of the results was the impact that chewing xylitol gum had on decreasing the intake of conventional solid sweets during the trial and they also suggest that participation in the trial may have raised oral health awareness during the subsequent five years. However, Isokangas[18] stated that 'the frequency of consumption of sweets was not, however, significantly affected by the use of xylitol gums.'

The results of a similarly-designed (although not blind) field study in Montreal showed that children who chewed xylitol gum had significantly lower net progression of caries than the control group children after 24 months, and a significant number of reversals of carious lesions were seen in the test group suggesting that remineralisation had occurred.[19]

A series of double blind clinical studies carried out in Belize approximately 10 years ago were the first to provide direct comparisons between xylitol and sorbitol gums.[27,28,30,31] Before this study, trials of xylitol-containing gum had given superior results to trials of sorbitol-containing gums, but they had not been compared in the same trial. The trials investigated caries-preventive effects in primary teeth of younger children and permanent teeth of older children. The study on older children included nine groups; testing, among other things, the effectiveness of chewing xylitol gum compared with chewing no gum and chewing a sugared gum. Compared with the no gum control group, the relative risk of caries development for each of the groups was: sugared gum 1.20 (ie an increase in risk); xylitol pellet five times per day 0.27 (ie a decreased risk of caries); xylitol pellet three times a day 0.41; xylitol stick five times a day 0.44; xylitol stick three times a day 0.48. The findings that the pellet gums with a harder texture were more effective than sticks and that chewing five times per day was better than three times a day, appear to confirm a dose response and/or suggest that factors related to stimulating salivary secretion are important in the sugar-free chewing gum effect. However, the more rapid release of xylitol from the coating of a pellet form may be a significant factor. In the youngest children with primary teeth the use of all polyol gums resulted in a significant decrease of the caries onset rate ($p<0.05$) with no significant difference in the caries onset risk between xylitol stick gum and sorbitol stick gum.[30] The largest caries risk reduction compared with no gum was found in the group receiving xylitol pellet gum (relative risk 0.35) and the sorbitol pellet gum (relative risk 0.44).

The long-term effects of chewing sugar-free gum were demonstrated by Hujoel *et al*,[34] five years after the two year Belize chewing gum programme ended. In this blind follow-up study, xylitol gum had reduced the caries risk by 59% and sorbitol gum by 35%, compared with a no gum group. In view of the long-term caries risk reduction of 93% found after 1–2 years of gum chewing compared with no-gum, the authors concluded that the optimum time for introducing gum for caries prevention should be at least one year before permanent teeth start to erupt.

• Xylitol candies versus chewing gum study

A recent clinical study in Estonia tested the effect of dietary supplementation of two types of xylitol candies and xylitol gum on dental caries occurrence compared with a control group who received no supplements.[7] The subjects of the study were children aged ten years who were given two pieces of gum or two candies three times a day on school days. A double blind design was possible between the use of the two candies, but not between candy and gum use. The gum was chewed for ten minutes and then collected for disposal while the candies were consumed in the usual way, the authors reporting that 'it took approximately the same time for the candies to disappear from the mouth.' The results showed that, for each cluster of schools, the caries increment was 35%–60% higher in the control group who received no supplements than in the xylitol groups. Furthermore, there was no difference between the two groups consuming xylitol candies and xylitol chewing gum.

• Mother and child study

This innovative clinical study initially investigated the effect of a mother's habitual xylitol consumption on transmission of mutans streptococci to her child.[2] The 106 mothers randomly allocated to the first study group chewed xylitol gum at least two to three times a day, starting three months after the birth of their child. There were two other study groups: in one, thirty mothers received chlorhexidine varnish six, twelve and eighteen months after delivery; in the other, fluoride varnish was used at the same intervals. The children received no intervention. Follow-up studies have looked at the occurrence of dental decay in children as well as their plaque and salivary colonisation with mutans streptococci at three and six years of age.[3,4] There was a 74% reduction in dmft seen in the 5-year-olds whose mothers had used the xylitol around the period described as 'the discrete window of infectivity'[40] compared with children whose mothers had used chlorhexidine. There was a 71% reduction in dmft seen in the 5-year-olds whose mothers had used the xylitol compared with children whose mothers had used fluoride varnish. In all three groups,

children in whom *Streptococcus mutans* had not been detected at two years of age showed lower caries experience at all annual examinations than children who had been colonised with mutans streptococci.

SPECIFIC CARIES-PREVENTIVE ACTIONS OF XYLITOL

The caries-preventive effect of total substitution of dietary sugars by xylitol could be explained by the exclusion of fermentable sugars from the diet. But the impressive caries-preventive effect of partial substitution or supplementation by xylitol requires other explanations: the caries-preventive effect seems to be greater than could be expected from simple substitution, and the result was intense research into the properties of xylitol. Proposed mechanisms are listed in Table 2.

Xylitol is not fermented by dental plaque.[41-43] There is ample evidence that the oral flora does not adapt to metabolise xylitol when tested over prolonged periods in humans.[44,45] Any ability of a few organisms to ferment xylitol is negated by the inaction of other more numerous plaque organisms so that no fall in plaque pH occurs on exposure to this polyol.[46,47]

The use of xylitol has been shown to lead to a reduction in the proportion of mutans streptococci in plaque.[46,48] This is most probably due in part to both non-specific and specific effects of xylitol (Table 3). The non-specific effect is a result of non-fermentability not encouraging bacterial growth.[48,49] In addition, there appears to be a number of effects specific to xylitol. First, a selective effect on mutans streptococci resulting in the development of mutant xylitol-resistant strains which may be less virulent in the oral environment.[45,50,51] Second, the concentrations of ammonia and basic amino acids increase when plaque is exposed to xylitol, resulting in neutralisation of plaque acids.[52-54] Third, *in-vitro* studies have shown some strains of oral streptococci take up xylitol and convert it to xylitol-5-phosphate resulting in the development of intra-cellular vacuoles and degraded cell membranes in mutans and sobrinus streptococci, and through this mechanism xylitol is acting in a bacteriostatic way.[55-59] Lastly, some streptococcal strains take up xylitol which participates in what is termed 'the futile metabolic cycle'.[59-62] In this cycle, xylitol is taken into the cell, phosphorylated to xylitol-5-phosphate, and is then split by sugar-phosphate phosphatases and the resulting xylitol is expelled from the cell. The clinical relevance of this process has not yet been established, but it is more likely to benefit oral health than damage it.

Table 3 Xylitol reduces proportions of mutans streptococci in plaque through non-specific and specific effects.

Non-specific	Because xylitol is non-fermentable it does not encourage bacterial growth.[48,49]
Specific	When mutans streptococci are exposed to xylitol they can develop mutant xylitol-resistant strains which may be less virulant in the oral environment.[45,50,51]
	Exposure of plaque to xylitol leads to an increase in the concentrations of amino acids and ammonia, neutralising plaque acids.[52-54]
	Xylitol can act in a bacteriostatic way: some strains of oral streptococci take up xylitol and convert it to xylitol-5-phosphate, resulting in the formation of intra-cellular vacuoles and degraded cell membranes.[55-59]
	Xylitol can cause a 'futile metabolic cycle'. Streptococcus strains take up xylitol and phosphorylate it to xylitol -5-phosphate. This is then split by sugar-phosphate phosphatases and the xylitol is then expelled from the cell.[59-62]

Much evidence from well controlled clinical studies indicates that xylitol decreases the growth of plaque compared with sugars and other polyols.[1,15,25,46,49,63,64] These studies include the Turku sugar studies and trials of partial substitution and supplementation. There is also good evidence that the ability of plaque to produce acids by metabolism of sugars is reduced by xylitol.[46,47] This seems to be adequately explained by a selective decrease in mutans streptococci in plaque exposed to xylitol and possibly by a decrease in plaque quantity.

Of the above intra-plaque mechanisms of xylitol in caries prevention, only the conversion of xylitol to xylitol-5-phosphate, with its subsequent accumulation, as well as the induction of less virulent strains of cariogenic bacteria, can be considered to be truly bacteriostatic. These mechanisms have been emphasised but further research is needed to assess their clinical importance. Although not truly bacteriostatic, other mechanisms listed earlier (Table 2) will assist caries prevention.

As well as these specific effects, xylitol consumption by the mother at the critical period of mother-child transmission of oral flora can reduce the transmission and colonisation of mutans streptococci to her child on a long-term basis, as described previously.[2,4] Other evidence has shown that xylitol leads to a reduction in the quantity of plaque, possibly by interfering with mechanisms of adhesion between plaque organisms and the tooth's surface.[65-68] This is the most likely explanation for the reduced colonisation of mutans streptococci in the mouths of these children.

As far as the evidence regarding salivary flow is concerned, flow rate increases during and immediately after chewing, and a sweet taste increases flow rate even further.[69,70] There is no evidence, though, that xylitol is better than any other sweetener in this respect. While chewing results in substantial immediate increases in salivary flow, there have been several investigations into whether chewing gum results in increased capacity for salivary flow long term. The majority of these latter studies have found no increase in the capacity to produce saliva after chewing sweetened gum over varying lengths of time, in people with normal salivary flow; certainly, there was no indication that xylitol had any specific effect.[46,47,69-71]

Pre-cavitation (white spot) carious lesions were observed to remineralise (heal) during clinical studies of xylitol, as mentioned above. This led to speculation that xylitol had a specific action on enamel, and a number of studies have investigated the effect of xylitol and other sweeteners on tooth structure and the potential for remineralisation; laboratory-based studies have included *in vitro* experiments and rat

Table 2 Proposed actions of xylitol

Plaque	Non-fermentability by plaque organisms
	Reduction in plaque quantity
	Selective reduction of mutans streptococci
	Induction of mutans streptococcus strains with reduced virulence
	Increased concentration of ammonia in plaque
	Accumulation of xylitol-5-phosphate in some plaque streptococci
	Participation in a futile metabolic cycle in some plaque organisms
	Reduced adhesion of plaque flora
	Reduced transmission of mutans streptococci
Saliva	Changes in quantity and quality of saliva
Enamel	Aids remineralisation

caries studies. Remineralisation occurred in nearly all experiments where non-sugar sweeteners were used during the 'healing' phase but there was no clear indication that xylitol had any greater effect than other non-sugar sweeteners when evaluated in short-term studies.[72-76]

Remineralisation is likely to be adequately explained by the increased flow of saliva, rich in calcium and phosphate, and by the shorter time that plaque pH is low and has the potential to cause demineralisation. Any specific anti-caries action of xylitol is therefore likely to be due to its effect on plaque and plaque organisms.

XYLITOL COMPARED WITH OTHER NON-SUGAR BULK SWEETENERS

All the bulk sweeteners listed in Table 1 have been investigated and shown to be non-cariogenic or to have very low cariogenic potential. The amount and type of evidence varies greatly between sweeteners, with xylitol and sorbitol being the most thoroughly investigated.

Studying the fermentability of sweeteners by plaque and plaque organisms is the simplest type of investigation: these can be carried out entirely *in vitro* or in the mouth where they are known as plaque pH experiments. One study reported xylitol fermentation by plaque bacteria:[77] however, these bacteria represent only a small proportion of plaque organisms and, in mixed cultures, they were outgrown or their acid production masked by the activities of other micro-organisms. In contrast, sorbitol, manitol, lactitol, maltitol, hydrogenated glucose syrup and isomalt are all fermented slowly by plaque organisms but the rates are very much slower than that for sucrose or fructose.[41,42,78,79]

Reduction in plaque quantity on using xylitol appears to be a reflection not only of the non-fermentability of xylitol, ensuring its non-availability metabolically as an energy source for oral bacteria, but also its ability to change the adhesive and cohesive properties of plaque leading to decreased plaque quantity. A number of chewing gum studies, in particular, have investigated changes in plaque quantity after use of xylitol, sorbitol or xylitol-sorbitol mixtures. Most of these studies show that while plaque quantity reduces with xylitol, there is little change in the plaque quantity after the use of sorbitol; with the xylitol-sorbitol mixtures reducing the plaque quantity compared with sorbitol but not as much as with xylitol only.[25,32,46,80-82] The clinical significance of these changes, however, has been questioned. If one accepts that reduced adhesion of plaque organisms was the major explanation for the fairly large dental effect of xylitol in the mother and child study, inclusion of a sorbitol group into any further study would be helpful. Xylitol would appear to have a unique effect in reducing adhesion and it could be expected that other polyols might not show this clinical effect.

Reports of the first clinical trials of sorbitol chewing gums appeared thirty-five years ago.[36] Caries increments were much less with their use compared with sugared gums. Since then, many clinical trials and field studies have indicated the dental benefit of chewing gum and other confectionery made with sorbitol,[84] hydrogenated glucose syrup,[85] as well as xylitol.[36] The majority of studies tested xylitol and results indicate that dental effects seemed to be greater with xylitol, but it was not until the Belize study[27,30] that sorbitol and xylitol were compared 'head to head'. The results showed clearly that xylitol in gum was superior to sorbitol, and that mixtures of xylitol and sorbitol were not as good as xylitol but were better than sorbitol alone. The results of the study in older children[27] (Table 4) recorded that, compared with the no gum control group, the relative risk for xylitol pellet gum used five times daily was 0.27 (ie a decreased risk of caries) and for sorbitol pellet gum used five times daily 0.74. These equate to 73% and 26% reduction in caries development respectively. Two different ratios of xylitol to sorbitol were also investigated: the 3:2 xylitol:sorbitol gum gave an odds ratio of 0.56, while the 1:3 xylitol:sorbitol gum gave an odds ratio of 0.49. The xylitol:sorbitol mixtures were more effective in reducing caries risk than sorbitol alone, but were less effective than xylitol alone. In the study of younger children with primary teeth[30] all polyol gums resulted in a significant decrease of the caries onset rate ($p<0.05$); the difference in the caries onset risk between xylitol stick gum and sorbitol stick gum was not statistically significant. The largest caries risk reduction compared with no gum was found in those children receiving xylitol pellet gum and the sorbitol pellet gum (relative risks 0.35 and 0.44 respectively).

In summary, xylitol exhibits dental health benefits which are superior to other polyols in all areas where polyols are shown to have an effect. In addition, xylitol's specific effects on oral flora and especially on certain strains of mutans streptococci add to its caries-preventive profile and give it a potentially unique role in caries prevention.

OTHER ISSUES RELATED TO XYLITOL USE

While some of the intense sweeteners are cheaper than sugar, for any given level of sweetness, all the bulk sweeteners are more expensive than sugar. This means that while sugar-free soft drinks should be no more expensive than sugared drinks, sugar-free confectionery could be more expensive than its sugar-containing counterparts. While sorbitol is about twice as expensive as sucrose, xylitol is about six times the price of sucrose.[86,87]

The flavour profile of bulk sweeteners is generally considered to be good and combinations of sweeteners are often used to produce the best sweet taste. In addition, a cool sensation is experienced when eating polyols due to the unusual property of a negative heat of dissolution.

Perhaps the biggest potential disadvantage of polyols is their liability to cause osmotic diarrhoea if eaten in large amounts. For xylitol, little discomfort is experienced with intakes of about 20 g per day, although threshold levels will be lower for children. It should be remembered that adults in the Turku sugar studies consumed about 50 g of xylitol per day for two years: only one of the 52 subjects withdrew from the study because of intestinal discomfort.[1] In Switzerland and Finland, countries with high levels of consumption of polyols by children, intestinal discomfort does not appear to be a problem.

IS XYLITOL A UNIQUE MAGIC BULLET?

In one of the earliest reviews, Bär[88] concluded that 'xylitol may be regarded as the best of all nutritive sugar substitutes with respect to caries prevention.' He drew attention to human studies which showed 'massive reductions in caries following consumption of relatively small amounts of xylitol' but stated that consensus on anti-cariogenic status of xylitol had not been reached. Soderling and Scheinin[89] also commented that 'partial substitution of dietary sucrose by low doses of xylitol was associated with pronounced caries reduction' and that the favourable action of xylitol was likely to be multi-factorial, but did not conclude that xylitol was anti-cariogenic. Makinen[90] reviewed the large amount of evidence on this topic and concluded 'all adequately supervised clinical caries studies have yielded essentially identical results providing evidence of the

Table 4 Relative risk of dental caries following use of polyol-containing or sugared chewing gum compared with a control group with no gum (Based on carious lesion onsets per 1,000 permanent tooth surfaces per year)[27]

Gum	Relative risk
Xylitol pellet gum used 5 times per day	0.27
1:3 xylitol:sorbitol gum used 5 times per day	0.49
3:2 xylitol:sorbitol gum used 5 times per day	0.56
Sorbitol pellet gum used 5 times per day	0.74
Sugared stick gum used 5 times per day	1.20

cariostatic and even anti-cariogenic effect of xylitol.'

Imfeld[91] reviewed the clinical caries studies of polyalcohols and concluded that sorbitol, mannitol, xylitol, maltitol, lactitol, hydrogenated glucose syrup and isomalt have all been proven to be non-cariogenic or of extremely low cariogenicity in rat caries experiments and/or human clinical studies. He stated that claims of possible active effects of xylitol due to its bacteriostatic and/or cariostatic properties 'have not yet been substantiated in clinical trials.' Following publication of further studies, Trahan[92] concluded that the reduction in dental caries associated with xylitol consumption could be attributed mainly to xylitol not being significantly metabolised by the oral microflora, and other mechanisms, mostly saliva and plaque related. More recently, Levine,[93] in a briefing paper on xylitol, described xylitol as exhibiting both passive and active anti-caries properties.

Scheie and Fejerskov[12] agreed that all clinical studies concerning the effect of xylitol on caries development consented to its non-cariogenicity. However, they felt that claims that xylitol possessed anti-caries or therapeutic effects and was superior to other polyols were still to be confirmed 'by well designed and conducted studies from independent research groups.' Recognition of the need for independent research is an important recurring issue in the xylitol debate. This appears to have arisen since much of the research into xylitol has been carried out by one group of researchers led by Dr K. K. Makinen. In contrast to the conclusions of Scheie and Fejerskov mentioned above, Makinen, in an editorial published concurrently in the same journal[10] stated that 'there is enough scientific evidence to argue that there indeed exists a pentitol-specific or a xylitol-specific caries-preventive effect that is different from that exerted by hexitols such as sorbitol.'

Very recently in the United States, Hayes[94] reviewed the evidence for the effect of non cariogenic sweeteners on the prevention of dental caries, particularly in relation to criteria for causality – consistency, strength, association, biologic plausibility, temporal sequence and dose response relationship. She concluded that 'Given that several of the criteria for causality are met, it is concluded that xylitol can significantly decrease the incidence of dental caries.'

The dramatic effects of consuming small amounts of xylitol referred to by Bär[88] above, were observed in chewing gum studies, and one of the difficulties has been to distinguish between the caries-preventive effects of salivary stimulation due to chewing gum, and xylitol. One pointer is that xylitol gum was more effective than sorbitol gum in the Belize trial.[27-31] Another approach has been to compare the effect of chewing xylitol gum with chewing an unsweetened gum base. Two such studies have been undertaken – one short-term plaque study in habitual xylitol consumers showed a xylitol-specific effect[51] and the other study – a 3 year community intervention trial[35] – did not, although this study did have some problems in its design which may have been reflected in the results. Of some relevance is the Estonian xylitol trial,[7] which compared the dental effects of xylitol in candy and chewing gum form. Although sucking the candy stimulated salivary flow, the results suggested that the xylitol was active in caries prevention, as well as the form of the vehicle used (ie chewing gum or sucking candy). The favourable properties of xylitol within plaque (Table 2) are likely to explain xylitol's superior caries-preventive effectiveness. Those most likely to be of clinical relevance are: xylitol's non-fermentability by plaque micro-organisms, selective reduction of mutans streptococci in plaque and selection within plaque of xylitol-resistant mutans streptococci which appear to have reduced adherence and therefore reduced transference. The remarkable result of the mother and child study has been explained by the reduced transmission of plaque micro-organisms from mother to child. Only one chewing gum group (using xylitol gum) was included in this trial: it is hoped that this mother and child trial will be replicated and, if so, a clearer idea of the clinical importance of reduced transference would emerge if a sorbitol gum group were to be included in this trial.

In summary, from the available evidence it can be concluded that:

- xylitol is non-cariogenic;
- xylitol in chewing gum is anti-cariogenic as are other polyols in chewing gum;
- the inhibition of mother/child transmission of cariogenic oral flora leading to reduced caries development in young children is caries preventive; and
- the dental properties of xylitol are superior to other polyols so far investigated – this is likely to be due to a combination of several specific effects of xylitol as well as the general effects of polyols in sucrose substitution and saliva stimulation.

Xylitol exhibits dental health benefits which are superior to other polyols in all areas where polyols have been shown to have an effect. In addition, xylitol's specific effects on oral flora and especially on certain strains of mutans streptococci add to its caries-preventive profile and give it a unique role in preventive strategies for dental health.

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Table 5 Xylitol: Sources of evidence for its effects

Reduced dental caries in humans:
Long-term clinical studies
• Total substitution studies
• Partial substitution studies and confectionery supplementation studies
• Chewing gum supplementation studies
• Toothpaste studies
• Xylitol candies versus chewing gum study
• Mother and child study
Non-fermentability:
Long-term clinical studies
Incubation experiments
Plaque pH studies
Ecology and composition of dental plaque:
Long-term clinical studies
Plaque pH studies and enamel slab experiments
In vitro laboratory experiments
Animal studies
Natural defence mechanisms:
Long-term clinical studies
Enamel slab experiments
In vitro laboratory experiments
Animal studies

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