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XYLITOL AND DENTAL CARIES

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INTRODUCTION

All forms of dental caries are due to microorganisms (1). Numerous studies have thus been conducted in order to identify and define these organisms (2). Such studies have also considered the influence of dietary carbohydrates (sugars in general and sucrose in particular) as substrates on which microbes could form the entire range of noxious metabolites that play a key role in dental hard tissue destruction and the formation of dental caries.

Recently, however, a parallel line of research suggested that the cariogenicity of various carbohydrate sweeteners may vary within extreme limits, implying that several of these substances were low- or noncariogenic.

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In the case of xylitol, a pentahydric sugar alcohol, anticariogenic properties were suggested (3).

The chemical properties of xylitol have been reviewed (4). Its most important properties in relation to dental caries are: (*a*) open-chain structure; (*b*) absence of reducing carbonyl groups, a fact that renders xylitol (and sugar alcohols in general) chemically less reactive than the corresponding aldoses and ketoses; (*c*) the shorter "length" of the xylitol molecule when compared with that of hexitols; (*d*) the similarities in the configuration at various C-atoms with common sugars; and (*e*) The ability of xylitol (and several other sugar alcohols) to form complexes with certain metal cations (Ca^{2+}, for example) or compounds containing these metal atoms. These properties of xylitol affect the metabolisms of both microbial and mammalian species. The fitness
its ubiquity in nature (4–6), its established safety in moderate, peroral human use (7–10) and its participation as a normal intermediate in human metabolism—e.g. in the glucuronate-xylulose cycle (4).

In this review we survey xylitol's anticariogenic aspect, with particular regard to xylitol-induced effects in the animal model and as observed in clinical caries trials. Furthermore, we view the background of these mechanisms in terms of microbiological observations, physico-chemical effects in plaque and saliva, influence on enzymatic activities, and biochemical effects.

THE ANIMAL MODEL

With one exception (11), experimental studies in rats demonstrated an extremely low caries rate in relation to a xylitol-containing diet (12–21). Total substitution of xylitol for sucrose in the diets of rats resulted in caries scores comparable to (22) or lower than (20) those of sugar-free controls.

Partial substitution of xylitol for dietary sucrose is considered a more realistic approach than total substitution. The results from such experimental studies are contradictory; sucrose supplemented with xylitol did not result in a caries reduction (12, 23), although the severity scores were significantly
alternate feeding of sucrose and xylitol was associated with low increment scores (19, 24). Of particular interest was the experiment of Gey & Kinkel (25), in which rinsing with a xylitol solution after sucrose-containing meals decreased the cariogenicity of the diet. Similarly, dentinal caries in rats, produced by exposure to sucrose, was significantly
supplemented diet (26, 27). Not merely a bland noncariogenic agent, xylitol was found to exert a genuinely therapeutic action against caries (27).

The animal model has permitted experimentation that for various ethical, logistic, and economic reasons is not possible in human subjects (28, 21).

Such studies suggest extreme differences between the cariogenicity of sucrose and xylitol. Despite certain limitations preventing direct translation to human caries, ingenious animal models are expected to contribute to the understanding of cariostatic mechanisms.

CLINICAL CARIES TRIALS: TURKU SUGAR STUDIES

So far, experimental information on xylitol's effect on human caries derives from two clinical trials. Four other studies are in progress; the results from these WHO clinical-trial/field-studies
studies), and Hungary are expected in 1982–1984.

Two-Year Clinical Trial

The first
fructose (F) or xylitol (X) during a period of 2 years. In addition to the clinical and radiographic registrations of dental caries, biochemical and microbiological investigations were carried out in order to monitor oral and general health and to identify eventual side effects.

The initial population consisted of 125 subjects, mean age 27.6 years. The subjects were divided partly on individual preference basis into three groups. The S-group comprised 35, the F-group 33, and the X-group 52 subjects, the latter group rendered oversize in case some of its members quit the experiment. During the study 10 subjects discontinued or were otherwise excluded. Only in one case was this due to osmotic diarrhea in relation to xylitol consumption; the other cases were due to difficulties in adhering to the strict dietary regimen, to other personal reasons, and in three cases —two in the S-group and one in the F-group—to excessive caries incidence. The final results were thus based on 115 individuals.

Initially no significant differences were observed with regard to age, sex, number of primary and secondary carious surfaces, filled
extracted teeth, or the DMFS-index. During the trial, dental conditions were registered on eight occasions, the frequent inspections being due to the potential need for early diagnosis, treatment, and termination of participation in cases of adverse reaction. The clinical and radiographic registrations were utilized for calculating the reversals in diagnosis between the examinations, and the resulting net change. The positive reversals involved a change in diagnosis from an intact to a carious or filled surface, or, when considering an increment in size, from a white spot lesion to a defect. A negative reversal indicated a corresponding change in the opposite direction. Consequently net increment was expressed as new carious surfaces—i.e. positive minus negative reversals, according to the recommendations of the FDI

Commission on Classification and Statistics for Oral Conditions (30).

According to the clinical and radiographic registrations, carried out without knowledge of the experimental group, a highly significant reduction (exceeding 85%) was found in the X-group when compared to the S-group after one year of the dietary regimen. After two years the increment in the number of decayed, missing, and filled tooth surfaces was 7.2 in the S-group, 3.8 in the F-group, and 0.0 in the X-group. The caries incidence was also expressed in combined quantitative and qualitative terms, by considering in addition to the increment in terms of the conventional DMFS-index also the changes in lesion size and the incidence of secondary caries. Irrespective of the way of expressing the caries increment rate in qualitative, quantitative, or combined terms, the reduction in the caries incidence in the X-group exceeded 85%, (30% in the F-group) in comparison to the S-group.

One-Year Intake of Chewing Gum

In the second study (31) the initial population comprised 102 subjects, mean age 22.2 years. The registration of dental conditions was carried out clinically and radiographically (29). Before the study, dietary habits were analyzed (32). The population was divided randomly into the future S- and X-groups.

The subjects were instructed to maintain their regular dietary habits and oral hygiene procedures. Instructions were further given to consume between three and seven sticks of chewing gum per day (sucrose- or xylitol-sweetened for S- and X-groups, respectively, and to keep a complete record of the consumption during the projected study year.

The final results were based on 100 subjects. Initially there were no significant differences between the groups with regard to the experimental variables, except that the number of missing teeth was slightly but significantly higher among the females in the X-group than in the S-group. This feature was considered to have no influence on the results obtained. The consumption of chewing gum, calculated as average number of sticks per day, was 4.0 in the S-group and 4.5 in the X-group, the difference between the groups being insignificant.

culated before and during the study as the sum of the S-containing products ingested in liquid and solid form, at and between meals, was 4.24 times per subject per day in the S-group and 4.94 in the X-group.

The caries incidence rate was calculated in terms of the conventional DMFS-index, as well as in combined quantitative and qualitative terms corresponding to those used in the two-year clinical trial discussed above (29). Regardless of measurement mode, the reduction of the caries incre-

ment rate in the X-group (chewers of xylitol gum) was 82% greater than that of the S-group.

DISCUSSION OF THE TRIALS AND FURTHER FINDINGS

Some of the inherent weaknesses of the first trial (29)
second study. In the latter, for example, a total substitution of sucrose through fructose or xylitol was not attempted, and subjects were assigned to their groups on a random basis. Other weaknesses in the experimental design—e.g. a young, homogeneous age group would have been advantageous—remain common to both studies. However, the solidity of the above long-term trials may rest on the general arrangement, the independently assessed clinical and radiographic findings
of biochemical and microbiological assays of plaque and saliva, and follow-up studies monitoring the health of the subjects.

The assessment of caries in terms of quantitative and qualitative reversals, and particularly the evaluation of changes in size of buccally located carious lesions through stereomicroscopic registration (33) has been criticized, mainly because this use of unconventional methods renders comparison with other studies difficult.

In fact, the values originating from the microscopic registrations were not included in the results so far published (29, 30). These findings
utilized in conjunction with a planimetric evaluation of incipient caries (34). We emphasize, however, that the caries increment rate in these trials was presented in regular terms, the increment of the DMFS-index being based solely on clinical and radiographic registrations of caries. The changes in number and size of lesion, as evaluated clinically and radiographically for primary and secondary caries, were presented separately. An attempt was thus made to depict the total quantitative and qualitative development, in order to add dimensions that otherwise escape attention. The conventional DMFS-index does not provide a complete description of the total quantitative development, as the incidence of secondary caries remains obscured by such tooth surfaces already being considered as filled.
the microscopic evaluation of the buccal lesions were not included in the results so far presented (29, 31) but will be published separately in conjunction with a planimetric analysis of the findings

Other trials on sugar substitutes invariably indicate significant caries reductions in comparison to sucrose. Most such studies concern the replacement of sucrose with polyols and mixtures of these—i.e. sorbitol (35–39) and Lycasin (40). Caries activity also decreased when sucrose was replaced

by an equimolecular mixture of fructose and glucose (41). The reduction thus achieved, especially during the second year of the trial, resulted in an overall development markedly similar to that observed with fructose substitution (29).

The results from the above trials were reviewed in terms of duration, age and number of subjects, compound and vehicle used, frequency of intake, and caries reduction in relation to groups exposed to known or *ad libitum* intake of sucrose (42). A detailed comparison seems unjustified, and we emphasize the need for further controlled clinical trials of sufficient duration, preferably through large-scale field
prevalence populations.

The fundamental reasoning for sugar substitution is based on the concept of replacing sucrose, particularly in foodstuffs proven to be highly cariogenic. In addition to the many studies containing circumstantial evidence for the cariogenicity of sucrose, the strong covariation between sucrose consumption and caries scores, this property is further inferred from studies where definite
(43, 44). Recently, dietary restriction of sugar was found not only to enhance other methods but to be the most effective single method of caries prevention, an essential part of a regimen to achieve a caries-free state (45). Thus the very low incidence of dental caries in relation to xylitol consumption requires special consideration. It may be argued that the effect in the 2-year feeding study was achieved through virtually complete omission of dietary sucrose. However, partial substitution of sucrose by xylitol achieved the same low caries incidence rate as that recorded in connection with total substitution, indicating that xylitol may possess a therapeutic, caries-inhibitory effect (3). It seems unlikely, however, that such mechanisms could be demonstrated beyond doubt by negative reversals in clinical caries trials. Nevertheless, the results from three recent studies indicate that xylitol may enhance natural defence mechanisms. Xylitol influenced lesion formation and remineralization by means of physicochemical effects (46). Regression of fissure
Remineralization/rehardening due to xylitol-supplemented diets was reported in bovine enamel in subjects with rampant caries. Such development occurred particularly in predemineralized enamel (47).

EFFECT OF XYLITOL ON QUANTITY OF PLAQUE

Dental plaque forms as a gelatinous organized structure on the teeth, which consists mostly of microorganisms imbedded in an extracellular matrix of salivary, microbial and dietary origin (48–51). The amount and growth rate of dental plaque in the human depend on factors determined by the oral

hygiene, dietary habits, and genetic properties of the individual. Dental plaque is involved in both the initiation and propagation of dental caries. Sucrose and other common, soluble carbohydrates consisting of C_6-units usually enhance plaque growth (48, 49). Partial substitution of dietary sucrose with xylitol for a period of 4 or 5 days on reduced oral hygiene decreased the plaque fresh weight by 50% (52, 53). A similar reduction in plaque fresh weight was obtained after 2- or 3-day consumption of chewing gum containing about 50% xylitol (54–56). The visible plaque index decreased in children given a xylitol-sorbitol mixture (1 : 0.67) in the form of gum arabic pastils and chewing gums for a period of two weeks (57) and after the use of chewable xylitol pastils for a period of two months (58).

In another partial-substitution study 1-month use of xylitol-sweetened chewing gums significantly
results were obtained by determining the plaque fresh weight and clinical plaque indexes by conventional methods. Application of planimetric, computerized methods supported these findings
ing gum trial (31), the consumption of xylitol-sweetened (49%) chewing gum significantly
responding consumption of sucrose-sweetened gums (61). Thus daily doses of xylitol amounting to 3–15 g may significantly
plaque provided that the consumption of sucrose is not simultaneously increased.

Plaque registrations were also performed in the 2-year Turku sugar studies. The results (62) were identical to those obtained both in the short-term and partial-substitution studies mentioned above. The human clinical trials so far carried out thus suggest that (*a*) it is possible to reduce plaque growth by up to 50% and (*b*) even partial substitution for sucrose may be sufficient. We emphasize, however, that mixtures of sucrose and xylitol should be avoided; substitution here means replacement of sucrose candies and chewing gums with those containing xylitol as the only sweetener (with possible small additions of sorbitol, mannitol, or Lycasin).

EFFECT OF XYLITOL ON THE GROWTH OF ORAL MICROORGANISMS

The Turku sugar studies provided information about the effects of dietary xylitol on human plaque flora
with xylitol did not affect the proportions of major microbial categories in saliva and dental plaque. The acidogenic and aciduric oral flora were, however, reduced (63). The consumption of a xylitol diet significantly
ered the incidence of *Streptococcus mutans,* a potent cariogenic organism (64). Similar results were obtained in the 1-year chewing gum trial; the use

of xylitol-sweetened chewing gums was associated with decreased colony-forming unit values on Rogosa S. L. agar (61).

Several short-term in vivo and in vitro experiments have supported the microbiological findings of
and coworkers demonstrated both the poor fermentability of xylitol by rat and hamster oral microorganisms (65) and the absence of *Str. mutans* in the dental plaque of rats fed xylitol (66). Plaque grown during sucrose feeding, however, harbored these organisms. Other authors have confirmed (*a*) the unfermentability or very low fermentability of xylitol by *Str. mutans* and other oral microorganisms and (*b*) the reduced incidence of *Str. mutans* in combination with plaque inhibition during xylitol consumption (67–78).

Some additional studies on the effect of xylitol on isolated cultures deserve consideration. The metabolism of several simple carbohydrates was studied with five different xylitol-metabolizing streptococcal strains from the rat oral cavity (75). The amounts of carbohydrates metabolized were smallest with xylitol and sorbitol, and considerably larger with mannitol and fructose. By far the highest levels of CO_2 were measured in the presence of glucose, while for some reason sucrose was not metabolized by these isolated strains at all. The results confirmed
of these microorganisms to use xylitol (75). The oral cavity of rats and hamsters may harbor microorganisms capable of breaking down xylitol at a low rate (65). In rats these are enterococcoid germs and *Proteus* sp., in hamsters short gram-negative rods. The metabolism of polyols by these organisms is, however, slow and forms little acid. Metabolism of xylitol was the poorest (65). Another strain of *Str. mutans,* as well as *Actinomyces viscosus,* neither fermented nor utilized xylitol (74). The little acid formed by a further strain of *Str. mutans* may have stemmed partly from the fermentation of proteinaceous ingredients of the medium used (79).

Although the above-mentioned studies have demonstrated the poor or nil fermentability of xylitol by human oral microorganisms, the existence of a transport mechanism of xylitol into some bacterial cells suggests that xylitol-utilizing microorganisms do occur (4, 80). In some cases xylitol may be transported through a system primarily serving other functions. In *Aerobacter aerogenes* (a non-oral strain) there is an active transport system for D-arabitol, which also acts on xylitol (81). Other related cases have been previously discussed (4, 82).

In view of these findings it is anticipated that occasional low fermentability of xylitol will be displayed in human dental plaque. A few such cases were revealed in the Turku sugar studies (61, 64) and in one in vitro experiment (82). However, the slow fermentation rate demonstrated in vitro does not indicate that similar decomposition will occur to any sizable extent in the oral cavity. In oral biology, it may be desirable to consider the *relative*

fermentability of dietary carbohydrates by plaque microorganisms. The available literature indicates that the relative fermentability of xylitol in the human oral cavity is very low indeed. It can be regarded microbiologically as an almost inert compound in the human dental plaque.

METABOLIC PROPERTIES OF DENTAL PLAQUE AS AFFECTED BY XYLITOL

Dental plaque does not contain specific
significant
into plaque microoganisms is nil or very slow (Figure 1) (69, 71, 83, 84).

The metabolic inertness of xylitol in the human dental plaque leads, however, to indirect consequential phenomena, especially if the daily consumption levels of xylitol equal the normal consumption levels of six-carbon sugars. For example, during the consumption of large amounts of xylitol in place of sucrose, the plaque microorganisms become deprived of a preferred substrate and start to synthesize extracellular proteolytic enzymes for

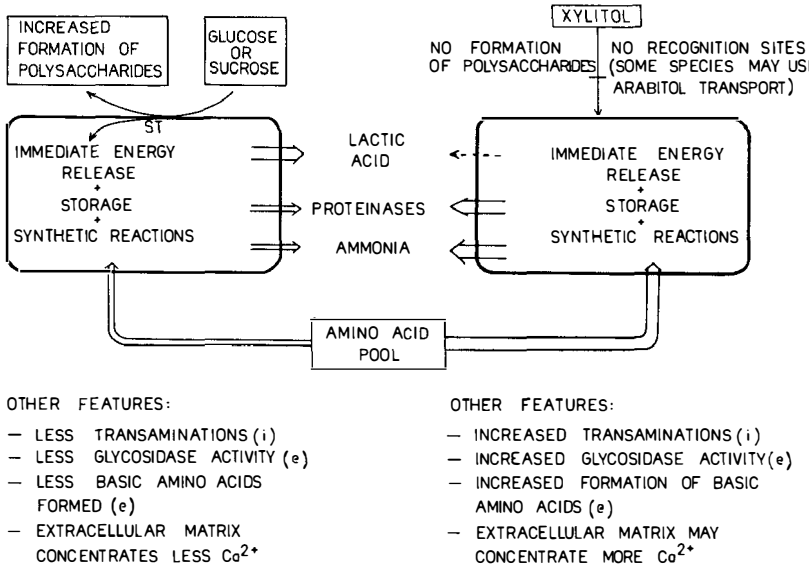

Figure 1 Summarizing, schematic presentation of some biochemical reactions occurring in dental plaque during the consumption of a predominantly hexose-based diet or a xylitol diet. The bacterial cells (shown by the heavy lines) typically represent those of a cariogenic strain of *Str. mutans* in the logarithmic phase of growth. The biochemical phenomena indicated occur during habitual consumption of the diets indicated, with daily consumption levels of xylitol exceeding 10–20 g. The thickness of the arrows indicate the relative activities or concentrations of enzymes and metabolites, respectively; e = extracellular; i = intracellular; ST = sugar transport.

the hydrolysis of the proteins and peptides of the medium. The cells of *Streptococcus mutans* that were maintained in a medium containing xylitol instead of glucose showed no uptake of ^{14}[C(U)]-xylitol, but exhibited strong increase in the extracellular proteinase activity (84). Xylitol behaved as an inert carbohydrate with respect to the increases in the extracellular proteinase activities. This finding
general increase in protein metabolism upon starvation of a fermentable carbohydrate (glucose). Similar increases in the proteinase activities occurred in whole saliva and dental plaque when high quantities of xylitol were habitually consumed (62). Because of the nonspecificity
nases discovered (62, 83), they may attack salivary proteins and peptides in vivo. In fact, increased proteinase activity against denatured hemoglobin was found in whole saliva of human subjects consuming high amounts of xylitol (62). Since saliva is rich in glycoproteins, it is understandable that the activity levels of certain plaque glycosidases also increased during habitual xylitol consumption (62). The above reactions of dental plaque were found to be associated with increased transamination rates (62) and sorbitol dehydrogenase levels (85). The increase of sorbitol dehydrogenase activity in plaque may be due to the simultaneous presence of xylitol and sorbitol in the chewing gums used (85). In no case has any significant xylitol
drogenase activity been detected in the whole saliva or plaque of subjects habitually consuming xylitol. The activity of this enzyme was nil in most samples (62, 70, 85).

Striking differences between the sucrose- and xylitol-consuming subjects were found in the activity levels of invertase-like enzymes obtained from whole saliva and dental plaque; the consumption of xylitol reduced this enzyme activity significantly
metabolic consequence is the decreased production of lactic acid in plaque in the presence of xylitol (62, 85). All these metabolic events may be related to the fact that, during sucrose consumption, gluconeogenetic enzymes are no longer necessary. The nitrogen and protein metabolism is thereby reduced. When sucrose is replaced with xylitol, there is an increased search for metabolizable proteinaceous nutrients of the medium (saliva and plaque extracellular phase), with a concomitant increase in the general nitrogen metabolism. There is no evidence that these metabolic changes of plaque would be detrimental to the oral tissues. Some of these phenomena, like the increase in the size of the amino acid pool (87) and the decrease in the production of lactic acid in plaque, are factors that should be included in the explanation of the effect of xylitol on dental caries. The increase of the amino acid pool renders higher deamination rates possible, thereby increasing the concentration of ammonia (58, 62, 87). The presence of glucose in

the medium of *Str. mutans* reduced the free amino acid pool (88). Addition of protein hydrolysates to the medium enlarged the pool. The above biochemical features are summarized in Figure 1.

In contrast with xylitol, the hexitols, sorbitol and mannitol, are readily metabolized by plaque streptococci, almost exclusively by glycolysis (Embden-Meyerhof pathway) (4, 89, 90).

The suitability of a dietary carbohydrate as a sucrose substitute can also be demonstrated by intraoral wire-telemetry. This method revealed that neither xylitol chewing gum nor xylitol mouthwash produced a pH drop of plaque (79, 91–93), whereas with readily fermentable carbohydrates rapid reduction in pH values occurred. pH-Telemetry has thus demonstrated the nonacidogenic nature of xylitol in human use.

EFFECT OF XYLITOL ON SALIVARY PARAMETERS

The consumption of a xylitol diet increased lactoperoxidase (LPO) activity in human (94) and monkey (95) parotid or submandibular saliva. A similar finding was made with the α-amylase of monkey parotid saliva (96). Detailed studies with human parotid saliva in the authors' laboratories suggested that peroral xylitol slightly increased the secretion of sialic acid or sialoproteins (86, 95–97) and sulphate (85, 95) in saliva. The elevated sulphate levels may be due to raised secretion of sulphated polysaccharides.

The possibility that dietary carbohydrates may influence the concentration of salivary enzymes was shown by Walker more than 55 years ago (98). That xylitol consumption may increase the activity levels of salivary LPO is interesting in view of the participation of the LPO-system in defense mechanisms (99–101). The action of this system also requires the presence of SCN^-. A few studies have indicated that the consumption of large amounts of xylitol was associated with increased levels of salivary SCN^- (62, 86). Therefore, in order to elucidate the effects of dietary sugars on the activity of the LPO-system one may have to determine not only the enzyme activity or concentrations but also the levels of the auxiliary compounds (SCN^- and H_2O_2) and reaction products ($OSCN^-$). Use of xylitol in the form of mouthwash or chewing gum caused a quick increase in the pH value of whole saliva (93). Since this pH response occurs within 120 sec following stimulation of saliva, it is possible that basic equivalents rapidly appear in saliva not only from plaque but from the oral mucosa as well (97). These findings thus suggest that dietary xylitol exerts selective effects on the consumption of saliva.

MICROBIAL ADAPTATION

The microbial ecosystem of the oral cavity has been largely affected by carbohydrates that are based on common six-carbon structures and are easily soluble in water. During evolution, such carbohydrates became ecological chemodeterminants just as the common amino acids became determinants in the nitrogen and protein metabolism of oral microorganisms. The easily soluble, common dietary sugars (e.g. glucose, fructose and sucrose), starches and related common six-carbon compounds (including sorbitol and mannitol) and their multiples are effectively metabolized by cariogenic species. These facts must therefore be considered when discussing possible microbial adaptations enabling clinically meaningful acidogenic breakdown of xylitol in plaque. The Turku sugar studies (63, 64) revealed no such adaptation nor was any significant adaptation detected after 4.5 years of continous consumption of xylitol (70).

Earlier studies had indicated that adaptation enabled dental plaque microorganisms to utilize xylitol as a carbon source (67, 84). It was discovered later that the plaque microorganisms started instead to exploit extracellular, chiefly salivary and dietary proteins, peptides, and amino acids as sources of energy, as discussed above. Thus no sizable adaptation to use xylitol has been found. Microbial adaptation to use xylitol may be an uneconomic way to gain energy. This situation may be particularly true for oral microorganisms.

The slow decomposition of xylitol by oral bacteria may also be based on the use of other, preexisting transport systems rather than on the appearance of specific new xylitol transport mechanisms. In yeasts that actively ferment pentose sugars (4), the situation may be different. Therefore, it is advisable in future long-term trials to arrange microbiological follow-up studies to check this matter. The Turku feeding studies indicated that the consumption of a xylitol diet reduced the incidence of oral *Candida* (63). The current literature suggests that the almost complete lack of xylitol fermentation in human dental plaque is genetically fixed, for reasons of evolutionary expediency.

COMPLEXING OF POLYOLS WITH METAL IONS

Complexing of multivalent cations with polyoxygen systems has been exploited in technology and biology, but has received virtually no attention in oral biology. Cyclic polyhydroxy compounds (e.g. the cyclitols and sugars) complex rather strongly with various multivalent cations (102–104). The site of specificity of complexation of the various alditols shows that the strength of complex formation is strongly dependent on the configuration

of the ligand. Using Pr^{III}, the following order of preferential configuration with respect to complex formation in aqueous solution has been given: xylo > threo > arabino (lyxo) > glycerol > erythro, ribo (102–104). Although these results were obtained with Pr^{III}, they are probably applicable to isosteric cations such as Na^{I} and Ca^{II}.

Sugar alcohols like xylitol, sorbitol, and mannitol form complexes with calcium salts, and the precipitation of calcium proteinates in saliva strongly depends on the type of the polyol used (105). Application of these chemical aspects to oral biology has only recently been considered, and it is not possible at this stage to indicate to what extent such phenomena contribute to the non- and anticariogenicity of xylitol in humans. The plaque of subjects consuming polyol-containing chewing gums contained more calcium than plaque collected from the same subjects before the use of chewing gums (85). Whether this calcium was present in plaque owing to its complexation with xylitol or sorbitol remains to be elucidated. Such calcium, however, would be available for remineralization of Ca-deficient
the interphase of dental plaque.

The proposed therapeutic effect of xylitol (29, 31) in the dental caries of humans should be viewed against the following facts: (*a*) Xylitol causes nil or minimal decrease in plaque pH; (*b*) xylitol increases the formation and/or secretion of basic equivalents in the oral cavity; and (*c*) xylitol affects the precipitation of Ca-proteinates in saliva and itself forms complexes with Ca^{2+}. Other factors may also participate in the rehardening of carious lesions. One such factor, still incompletely understood, is the redox state of plaque extracellular fluid
tion. Further findings
of xylitol in a 6% sucrose-containing medium strongly decreases the ratio of insoluble polysaccharides to water-soluble polysaccharides in plaque. Consideration of these effects may facilitate understanding of the long-term human clinical trials (29, 31).

CONCLUSIONS AND CONSIDERATIONS

A massive reduction of the increment rate of dental caries was observed with total and partial substitution of dietary sucrose by xylitol. Similar results were obtained in experimental studies, as reviewed in the initial sections of this paper.

These findings
logical and biochemical properties of xylitol. These include the stimulation of salivary secretion; elevation of certain electrolyte concentrations of oral fluid; increase of buffering of saliva, and increase or maintenance of high pH levels in oral fluid and plaque; lack of suitability for microbial metabo-

lism; influence on enzymatic activities; and also the increase of certain amino acids of oral fluid. Peroral xylitol stimulates a number of existing defense mechanisms against caries.

Strict sugar restriction over an extended time undoubtedly leads to a massive caries reduction. In view of biologic and behavioral preferences for sweets, however, restriction of sucrose intake without suggestion of alternatives is a recommendation that lies somewhere between hypocrisy and malpractice. In cases of rampant caries, extremely caries-susceptible tooth structure, sucromania, and reduced salivary secretion rate, the strategy of substitution should thus be considered and applied.

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