Xilitol and dental caries.
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Dental caries is a widespread multifactorial disease. The main symptoms are mineral loss from tooth enamel and dentine, eventually leading to total destruction of the teeth, pain, impairment of mastication and problems with facial esthetics.

The total mineral loss from enamel and dentin is the net result of demineralization (mineral loss) and remineralization (mineral gain). Both demineralization and remineralization are primarily determined by the concentrations of ions, such as calcium, phosphate, fluoride and the pH near the tooth surface. Several external factors directly or indirectly influence the concentrations of these ions, and thereby dental caries.

**Fig. 7.1.** De- and remineralization (demin and remin) of enamel are directly or indirectly influenced by several factors, such as plaque, saliva, oral hygiene, diet and socio-cultural variables.
The relationship between external factors - such as plaque ecology, saliva, oral hygiene, dietary habits, social and cultural circumstances - on the one hand and enamel de- and remineralization on the other is schematically given in figure 7.1.

The results of a large scale epidemiological experiment published in 1975, showed that substitution of sugar in the daily diet by other sweeteners, such as xylitol lead to 100% caries reduction. This finding can be explained by the effect of xylitol either

(i) on plaque,
(ii) on saliva,
(iii) directly on the de- and remineralization process,

or by combinations of i, ii and iii.

The aim of the investigations described in this thesis is to determine the influence of xylitol on de- and remineralization of human enamel in vivo.

Chapter 2 gives a review of the literature on the effects of xylitol in epidemiological studies, and studies on plaque, saliva and enamel demineralization. Most epidemiological studies showed that xylitol had substantial caries reducing properties. The studies on plaque showed that xylitol reduces growth and acid production of some, but not all, micro-organisms. Xylitol also seems to reduce the thickness of the plaque layer on the teeth and appears to affect the calcium content in plaque covering the teeth. The studies on saliva show a reduction in the number of acid producing micro-organisms under the influence of xylitol. Several studies on enamel de- and remineralization, using an in vivo model, have shown mineral gain after daily application of a xylitol solution on enamel. Comparable results were found in laboratory studies.

Chapters 3 and 4 of this thesis describe the effect of xylitol containing toothpastes on human enamel in a condition favouring
remineralization in vivo. In an experimental set-up, demineralized enamel blocks were mounted in the prosthesis of 20 participants, who brushed the blocks twice a day with a toothpaste. In a random mode experiment in four periods of 28 days each participant used four different toothpastes, based on either glycerine or xylitol and containing either 0 or 500 ppm fluoride.

The effects of the toothpastes on the enamel surface microhardness are described and discussed in chapter 3. It was found that the enamel defects rehardened substantially in vivo, but that these changes in enamel hardness were not measurably affected by the presence of xylitol or 500 ppm fluoride in the toothpastes. Brushing with a toothpaste containing 1,500 ppm fluoride (Gerhard, 1982) has a comparable effect on enamel microhardness as the toothpastes used in this study.

Chapter 4 describes the fluoride analysis of the enamel specimens after the use of these toothpastes in vivo. Fluoride profiles were determined in 48 of the rehardened enamel blocks using an abrasive technique to remove thin enamel layers. Twelve of these 48 blocks were also analysed using the Secondary Ion Mass Spectrometry (SIMS) technique.

The average fluoride content in the outer enamel layer with a thickness of approximately 7 μm was about 200 ppm, as determined with the abrasive technique. SIMS analysis showed a higher fluoride content of approximately 500 ppm within 7 μm from the enamel surface.

No statistically significant differences were found between the fluoride uptake from the four toothpastes. There was, however, a trend that the two xylitol based toothpastes induced a slightly higher fluoride content in the enamel compared with the two glycerine based toothpastes.

Chapter 5 describes the demineralization of human enamel in standardized artificial U-shaped grooves in vitro. The artific-
Summary

A Groovc model was developed to examine in vivo de- and remineralization in plaque-covered enamel in the grooves, as well as in plaque free enamel near these grooves at the surface of the enamel blocks. These grooves or model fissures have a depth of approximately 0.5 mm and a width of 0.2 mm. In vitro demineralization of 48 enamel blocks, each with two artificial grooves, resulted in the formation of subsurface enamel lesions at the enamel surface and in the formation of surface softened enamel (no surface layer) in the walls and bottom of the artificial grooves. Enamel demineralization was investigated using both polarized light microscopy and microradiography.

The main conclusions of this in vitro experiment are:

- A linear relation was found between the length of the demineralization period and the lesion depth along the walls and bottom of the grooves. This shows that the ions present at the surface of the mineral crystallites in the enamel determine lesion progress.

- Lesion depth in the bottom of a groove was approximately 2 \times the lesion depth at the wall of a groove. No relation was found between lesion depth and demineralization period in the lesions in the surface enamel.

- Enamel demineralization in the grooves took place without the formation of a surface layer. In contrast, demineralization of surface enamel always resulted in the formation of subsurface lesions with a surface layer.

Chapter 6 describes an in vivo experiment, using the artificial groove model described in chapter 5, to determine the effect of xylitol on enamel in conditions favouring demineralization. Human enamel blocks, with two grooves each, were demineralized in vitro and mounted in the prostheses of 11 participants. They used a 2.5% xylitol, a 2.5% sucrose or a water solution in a randomized cross-over study for three periods of 16 days. The prostheses were submerged twice a day in the test solution for 5 minutes. Mineral loss and lesion depth in enamel were measured before and
after the in vivo part of the experiment using quantitative microcraniography and polarized light microscopy. It was found that enamel demineralization occurred during the test periods. No differences were found in the lesions in the grooves between the xylitol, the sucrose and the water treatments. At the enamel surface, however, a significant reduction in enamel demineralization was found after the xylitol treatment with respect to sucrose and water. In this case the mineral loss after sucrose or water treatment were both approximately 3 X the mineral loss after the xylitol treatment.

Chapter 7 is a general discussion on the role of xylitol in dental caries. Apart from the influence of xylitol on caries via changes in saliva and plaque, the results presented in this thesis indicate a direct interaction of xylitol on de- and remineralization. This interaction is most probably based on physico-chemical interactions between xylitol and calcium. The strength of this interaction and the severity of the cariogenic attack might act as major parameters for the xylitol effects on dental caries.

It can be concluded that the caries reduction obtained after the use of xylitol is caused by effects on (i) plaque, (ii) saliva, (iii) enamel de- and remineralization directly, or by combinations of these factors. Clinical effects of xylitol on the de- and remineralization process seem to occur primarily in mild de-mineralizing conditions.