Topical fluoride applications have the aim of increasing the fluoride uptake in enamel and consequently reducing caries. In the early 1960s fluoride varnishes were introduced because they had a long contact period with the enamel which resulted in a higher fluoride uptake than from other topical applications. Recently the importance of small amounts of fluoride in caries prevention and remineralization has been stressed and the importance of large amounts of fluoride acquired in the teeth is being seriously questioned.

The aim of this thesis (Chapter 1), was to investigate the effect of fluoride varnishes with a relatively low fluoride content on fluoride uptake, on protection against mineral loss and on remineralization of enamel. The fluoride varnishes were polyurethane based (Fluor Protector, Vivadent, Schaan Liechtenstein; abbreviated FP) and contained 0.7%, 0.1%, 0.05% and 0% fluoride by weight.

Chapter 2 gives a survey of the literature on the cariostatic action of fluoride. The effect of fluoride on enamel solubility, de- and remineralization and plaque metabolism is discussed.

For many years it was believed that fluoride incorporated in the enamel was the main reason for caries reduction. Incorporation of fluoride in the hydroxyapatite mineral leads to less soluble enamel in laboratory investigations. There is, however, in vivo no clear relationship between the fluoride content in enamel and the prevalence of caries. Small amounts of fluoride in the "liquid phase" (between the crystallites) are more important in decreasing the kinetic enamel dissolution than fluoride incorporated in the solid crystallites and they enhance remineralization. This liquid fluoride is supplied continuously by fluoride in saliva, plaque and topically applied agents. Topical fluoride applications, furthermore, provide a "CaF$_2$-like" coating on the outer enamel surface, which provides a fluoride releasing depot. In laboratory investigations the effect of fluoride on plaque metabolism has been shown. No indisputable evidence has been presented showing that fluoride directly influences plaque at normal in vivo levels.

An extensive review on fluoride varnishes is presented in Chapter 3. It is clear from the literature that varnishes supply fluoride more effectively than other topical agents. In laboratory investigations and in animal studies, fluoride varnishes have proved to have good demineralization inhibiting properties. Many clinical trials have been carried out especially on Duraphat (Wola Pharma, Eschwege, FRG) and Fluor Protector. Caries reductions of 18-56% have been reported for Duraphat when applied to permanent teeth. Inconclusive results have been reported concerning the primary dentition. Fluor Protector, on the other hand, has been investigated to a lesser extent and of the papers which have been published it is difficult to draw overall conclusions due to problems of study design. As well as possessing caries preventive properties the fluoride varnishes are known to be toxicologically safe, convenient and easy to use.
In Chapter 4 the fluoride acquisition on and in enamel after a single application of polyurethane varnishes is discussed. The fluoride uptake was measured immediately after the removal of the varnishes in vitro and after one week in vivo. Eleven participants wore a newly developed intra-oral device based on a frame prosthesis in which 5 enamel specimens were held. This method is flexible and allows for experimentation as close as possible to the in vivo situation.

Alkali-soluble fluoride on the enamel surface (F [on]) was measured after KOH extraction; fluoride in enamel (F [in]) was determined by acid etching 5 thin enamel layers.

The results show that the amounts on fluoride present after application and after one week are strongly dependent on the fluoride content in the varnish. The fluoride uptake ranks after 24 hours for F [on] and F [in]:

**In vivo** the fluoride uptake ranking was:

\[
FP_{0.7\%} > FP_{0.1\%} > FP_{0.05\%} = FP_0 = \text{control.}
\]

In Chapter 5 the results of demineralization at pH 5 are presented. It is shown that the fluoride varnishes applied for 24 hours on the enamel can inhibit demineralization completely. No demineralization inhibition with the 0% varnish was observed. It was calculated that the inhibiting effect was not due to fluoride leakage into the demineralization solution.

In Chapter 6 the effect of the fluoride varnishes on demineralization at pH 4.5 was investigated under the same experimental conditions. Additionally, a single-section microradiography technique was used to follow lesion formation at the same area during demineralization. It was concluded that with increasing fluoride content in the varnishes, the enamel surface was better protected against severe acid attack. The ranking in demineralization protection was:

\[
FP_{0.7\%} > FP_{0.1\%} > FP_{0.05\%} > FP_0.
\]

It could be seen from the single-section microradiographic tracings that subsurface lesion formation was preceded by a surface softening mineral distribution. A significant correlation was confirmed by the single-section microradiography technique.

The caries preventive effect was studied by lesion formation on the enamel. An unfluoridated control period was 4 months, followed by a fluoride varnish application period in vivo. The enamel slab was sectioned and subjected to the same experimental conditions as the unfluoridated control. The lesion depth and mineral loss were measured by microradiography at the end of each experimental run.

The results of lesion formation in the fluoride varnish application period are shown in Figure 4.1. It is apparent that the fluoride varnishes applied for 24 hours on the enamel can inhibit demineralization completely. No demineralization inhibition with the 0% varnish was observed. It was calculated that the inhibiting effect was not due to fluoride leakage into the demineralization solution.

In Chapter 7 the effects of fluoride varnishes on demineralization at pH 4.5 were investigated under the same experimental conditions. Additionally, a single-section microradiography technique was used to follow lesion formation at the same area during demineralization. It was concluded that with increasing fluoride content in the varnishes, the enamel surface was better protected against severe acid attack. The ranking in demineralization protection was:

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Fluoride uptake was measured after red by acid etching content in the varnishes. Unfluoridated enamel was etched substantially in interprismatic regions.

The caries preventive effects of the polyurethane based varnishes and Duraphat were studied in a clinical caries model (Chapter 7). The plaque accumulation on the enamel promoted a substantial cariogenic challenge. An unfluoridated varnish was chosen as a control. The varnish application period was 24 hours, after which the varnishes were removed. Fifteen participants, divided into two experimental groups, wore varnished human enamel slabs in a frame appliance for 2, 4 and 6 months. At the end of that period microradiography was carried out on all samples and mineral loss, lesion depth and mineral distribution of the demineralized enamel was measured.

The results of this study showed that in vivo there were no difference in protective effect between FP 0.7%, FP 0.1% or FP 0.05% after 4 or 6 months. After 4 months all 3 polyurethane varnishes showed better protective properties than Duraphat. No difference was found between Duraphat and the unfluoridated control. The effect of all the fluoride varnishes was comparable after 6 months and although trends could be indicated a preventive effect was no longer statistically observable.

In Chapter 8 the mechanism of the fluoride varnish interaction with enamel is discussed. The formation of CaF$_2$-like material on the outer enamel surface after fluoride varnish application is most likely the main parameter in the inhibition of demineralization. CaF$_2$-like material has a low acid solubility and can resist a moderate acid attack. At lower pH (e.g. 4.5) demineralization is substantially retarded and the enamel dissolution rate is influenced directly by the amount of CaF$_2$ formed on the surface. CaF$_2$ has also has a "depot" function and the slow fluoride release affects further fluoride uptake in enamel and as a consequence influences de- and remineralization processes.

The effect of fluoride varnishes with ranging fluoride contents on remineralization of initial caries lesions was studied in a pilot study. The fluoride varnishes do not enhance or retard remineralization, as there was no difference between fluoridated and control enamel. An important conclusion is that CaF$_2$ formation in the lesion body does not influence de- or remineralization because the fluoride is lost. This is confirmed by the SEM-micrographs of in vivo demineralized enamel.

Once CaF$_2$ is formed in the lesion, fluoride is obviously inactivated and is not dissolved easily. This conclusion is in agreement with the results of clinical trials. Fluoride is retained permanently in enamel after fluoride varnish application but no long lasting caries preventive effect is seen unless application is repeated.

The major effect of fluoride varnishes is on sound enamel in preventing a caries attack.