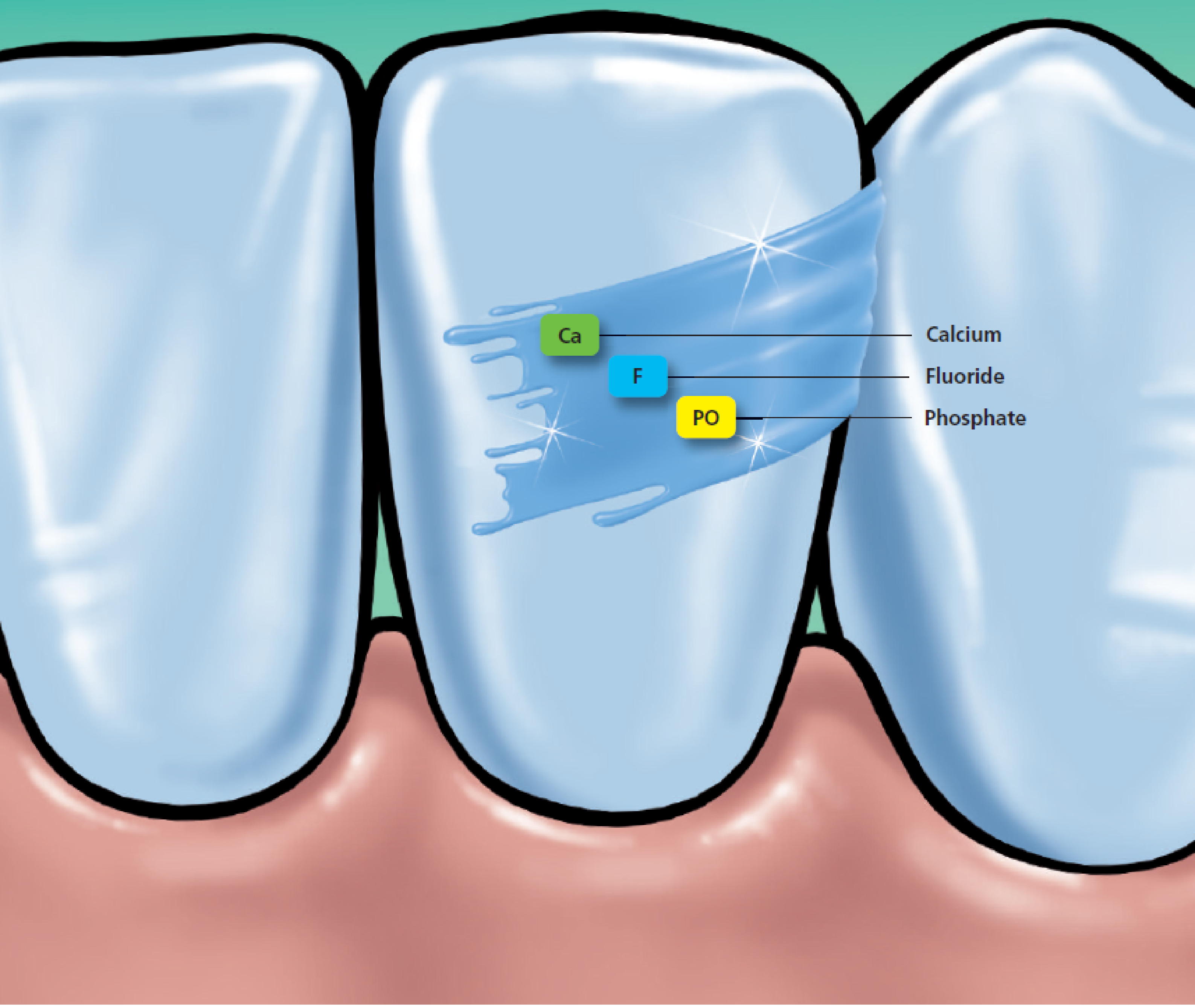
Fluor Protector Gel



Scientific Documentation

ivoclar vivadent
passion vision innovation

Table of Contents

1. Introduction

Healthy teeth are of utmost importance for the well-being and the health of people. Dental diseases may lead to pain, esthetic and functional impairments and in the worst case tooth loss. Therefore, teeth require optimum protection and care throughout the entire life of every individual.

Calcium, phosphate and fluoride play an important role in this context.

Calcium and phosphate are natural components of the dental hard tissue, which is mainly composed of hydroxy apatite, a mineral containing calcium and phosphate. Due to the acids that enter the mouth directly via food or are released from carbohydrates due to bacterial metabolism, a loss of calcium (Ca^{2+}), phosphate (PO_4^{3-}) and hydroxy ions (OH^-) occurs. Consequently, the dental hard tissue is weakened.

Saliva usually contains low amounts of natural fluoride [1; 2]. Numerous studies confirm the efficacy and importance of fluoridation as a way to maintain the health of teeth, particularly in the prevention of caries and the remineralisation of incipient carious lesions. A meta-analysis of studies, which investigated the effect of fluoride gel in children (6 to 15 years old), showed that caries incidence could be reduced by 20% compared to the control group when fluoride gel was applied [3]. Another important meta-analysis yielded similar results: The application of fluoride gel can reduce the occurrence of caries by 21% [4]. A report published by the World Health Organization [5] as well as an overview article by Rølla *et al.* [6] conclude that the use of fluoridated tooth paste has led to a significant decrease in the incidence of caries in the industrialized world during the past few decades.

The new Fluor Protector Gel is the optimum complement to professional treatment with the Fluor Protector fluoride varnish. Fluor Protector Gel can either be used by the dentist in the dental office or by the patient at home to clean and care for teeth. The gel strengthens the tooth structure due to the fluoride, calcium and phosphate it contains and provides effective protection against dental caries and tooth erosion. Xylitol, a sugar substitute, cannot be metabolized by caries-inducing streptococci. As a result, xylitol inhibits bacterial growth and supports the caries-preventive effect [7; 8]. Fluor Protector Gel has a neutral pH and does not contain any abrasive substances. Therefore, it is especially suitable for patients with sensitive teeth or teeth susceptible to erosion or with delicate restorations. D-panthenol provides protective care for the gingiva, increases its elasticity, has an anti-inflammatory effect and supports the regeneration of oral mucosal cells [9]. The use of Fluor Protector Gel is especially recommended in high caries risk patients, e.g. patients undergoing orthodontic treatment, patients with implants or partial prostheses to maintain the remaining dentition in a good state of health, or to strengthen the teeth of patients who recently have received bleaching treatment.

Fluor Protector gel can be applied in different ways, depending on the requirements:

- in the place of tooth paste to brush the teeth
- in the evening, after cleaning the teeth with customary tooth paste, Fluor Protector Gel can be additionally applied with the tooth brush
- Interdental spaces of natural dentition or of fixed dental restorations (e.g. bridges or implants) can be cleaned with Fluor Protector Gel and an interdental brush
- Fill a tray with gel, insert it once or twice daily, leaving it in place for 10 minutes each time.

1.1 Mechanism of action

The most important effects of fluoridated dental care products include strengthening of the tooth enamel due to remineralisation, protection against demineralisation, caries prevention and protection against erosion.

1.1.1 Strengthening of the enamel by protection against demineralisation and promotion of remineralisation

Tooth enamel consists of 96% hydroxy apatite [10], a mineral component which is composed of calcium, phosphate and hydroxy ions. When teeth are exposed to acids from acidic drinks such as citrus fruit juices or from the metabolism of the bacteria contained in plaque, calcium and phosphate ions are released from the hydroxy apatite of the tooth enamel (see Fig. 2a). This process is called “demineralisation”. The use of fluoridated tooth pastes leads to the formation of a calcium fluoride layer (CaF_2), which covers the natural dental enamel (see Figs. 1 and 2b). Rølla *et al.* pointed out that the amount of calcium ions present may have a limiting effect on the formation of calcium fluoride [11]. As Fluor Protector Gel contains both calcium and fluoride, the perfect conditions for the effective formation of a calcium fluoride layer and the direct incorporation of calcium ions, fluoride ions and phosphate ions into the tooth enamel are created.

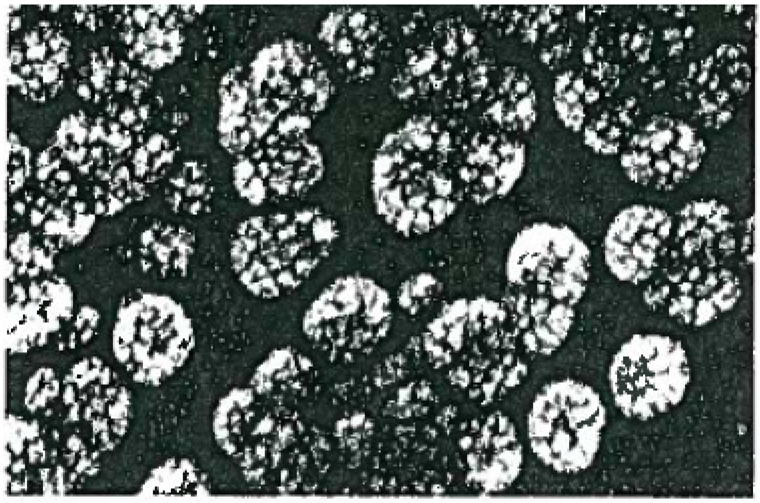


Fig. 1: The calcium fluoride layer

A scanning electron micrograph of the calcium fluoride layer which forms on human enamel after 24 hours of treatment with NaF. The particles consist of a substructure, possibly micro-crystals, and an amorphous matrix which also contains phosphate.

Modified after Rølla et al., 1990.

CaF_2 preferably deposits on demineralised surfaces. The CaF_2 layer is additionally stabilised by phosphate ions [11], which are also contained in Fluor Protector Gel. If the pH falls into the acidic range, the calcium fluoride layer releases calcium and fluoride ions (see Fig. 2c). These ions are either released into the saliva and form a depot of ions there which counteracts any further demineralisation, or they contribute to the formation of fluorapatite or fluor hydroxy apatite. This replacement of a hydroxy ion by a fluoride ion in the hydroxy apatite imparts the tooth enamel with a higher resistance to acidic attacks [12].

1.1.2 Caries prevention

The calcium fluoride layer also contributes to protecting teeth against caries in the long term. At neutral pH, CaF_2 is nearly insoluble and can remain stable for months. In an acidic environment, fluoride ions are released into the enamel and the saliva (see Fig. 2c). They protect the dental hard tissue against carious attacks by remineralising it and by inhibiting the bacterial metabolism [13].

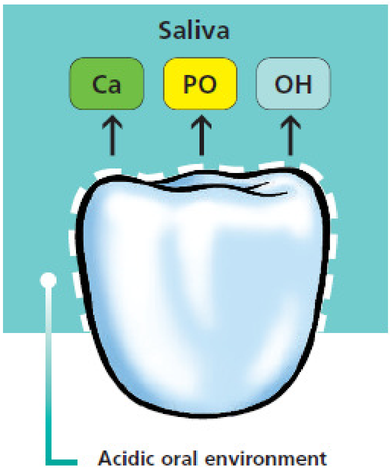


Fig. 2a: Demineralisation without fluoride protection.

At acidic pH, enamel is demineralised via the release of calcium (Ca^{2+}) and phosphate ions (HPO_4^{2-}) from the hydroxy apatite into the saliva.

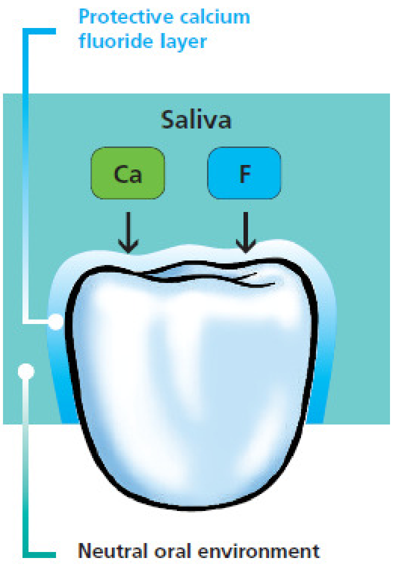


Fig. 2b: Protective calcium fluoride layer.

After the application of fluoride-containing dental care products, a calcium fluoride layer (CaF_2) forms on the tooth enamel.

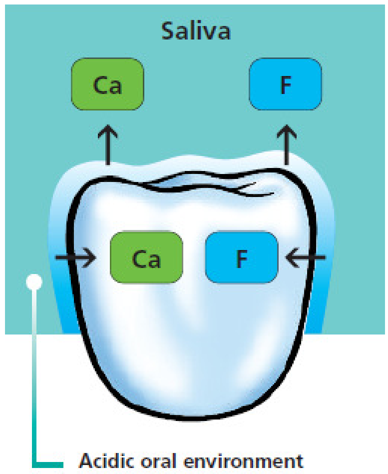


Fig. 2c: Bioavailability of fluoride.

At low pH, calcium and fluoride ions from the calcium fluoride layer are released into the enamel and the saliva. The tooth structure is no longer attacked directly.

1.1.3 Protection against erosion

The exposure of teeth to particularly acidic conditions (e.g. due to the ingestion of soft drinks, alcopops or citrus fruit) may result in a considerable loss of tooth structure (see Fig. 3). This loss of dental hard tissue is called erosion. Strengthening of the tooth enamel by the incorporation of fluoride ions, calcium ions and phosphate ions into the hydroxy apatite as well as by deposits of calcium fluoride on the tooth surface also helps to inhibit tooth erosion.

Fig. 3: Tooth erosion

Frequent ingestion of acidic food or drinks (citrus fruit, soft drinks) and special diseases associated with frequent vomiting may lead to the erosion of teeth. Exposed dentin (yellow) may lead to hypersensitivity and the discolouration of teeth.

Photo by courtesy of Prof. Dr. Lussi.

2. Composition

Percent composition by weight:

Component	wt%
Water, xylitol, thickener	97
Potassium fluoride (1450 ppm of fluoride)	0.45
Calcium glycerophosphate	< 1.0
D-panthenol	< 1.0
Additives, flavouring agents, stabilisers	< 2.0

Physical values:

pH	7.9 – 7.5
Density	1.02 g/ml

3. *In vitro* investigations

3.1 Measuring of enamel fluoridation

The remineralising, caries-preventive and anti-erosive effect of fluoride-containing dental care products is based on the fluoridation of tooth enamel. Both the formation of the calcium fluoride layer on the surface as well as the incorporation of fluoride ions into the hydroxy apatite contribute to the strengthening and protection of tooth enamel.

In the investigations described below, the effects of fluoridation following the application of different commercially available fluoride products were measured and compared.

In Table 1, the products tested are listed. In addition, their properties, e.g. fluoride content or the presence of a calcium source, are indicated.

Product name	Batch no.	Fluoride content acc. to the information of the manufacturer/ ppm	Calcium source	pH *	Manufacturer
Fluor Protector Gel	M56316	1450	Yes	7.3	Ivoclar Vivadent AG
Apa Care	1295865	1450	Yes	7.1	Cumdente GmbH
Elmex sensitive	3372M2	1400	No	4.7	GABA
Sensodyne MultiCare	6160M	1400	No	7.2	GlaxoSmithKline
Emofluor	702090	1000	No	4.9	Dr. Wild
GelKam	511113	1000	No	3.7	Colgate
Profluorid Gelee	0905365	1000	No	5.7	Voco
MI-Paste Plus	070530T	900	Yes	7.0	GC Corporation

Table 1: Overview of the fluoridated dental care products investigated.

* The pH was determined in internal investigations by R&D Ivoclar Vivadent, Schaan, Liechtenstein. The product specimens were diluted to a 10% solution with deionised water and their pH was measured with a glass electrode.

3.1.1 Determination of (alkali-soluble) fluoride deposited on the surface

Objective: Quantification of alkali-soluble fluoride formed on the enamel surface.

Investigator: R&D Ivoclar Vivadent , Schaan, Liechtenstein

Method: The test was conducted according to the Caslavaks method [14]. Test specimens were produced from bovine teeth and demineralised in diluted lactic acid (1h, pH 4.4). Subsequently, all the surfaces of the test specimens except for the enamel surface were sealed with Heliobond. The tested products were then applied to the unsealed enamel for an hour. Following this, the specimens were thoroughly rinsed with water and stored in artificial saliva (24h, 37℃). To release the alkali-soluble fluoride, the test specimens were removed from the saliva solution and placed in 1 ml 1 M KOH for 24 hours at room temperature. Prior to measuring the fluoride content with an ion selective fluoride electrode, the solution was neutralized with 1 ml 1 M HNO_3 and TISAB-II buffer was added to it. The fluoride concentration measured was put into relation to the surface treated ($\mu g/cm^2$).

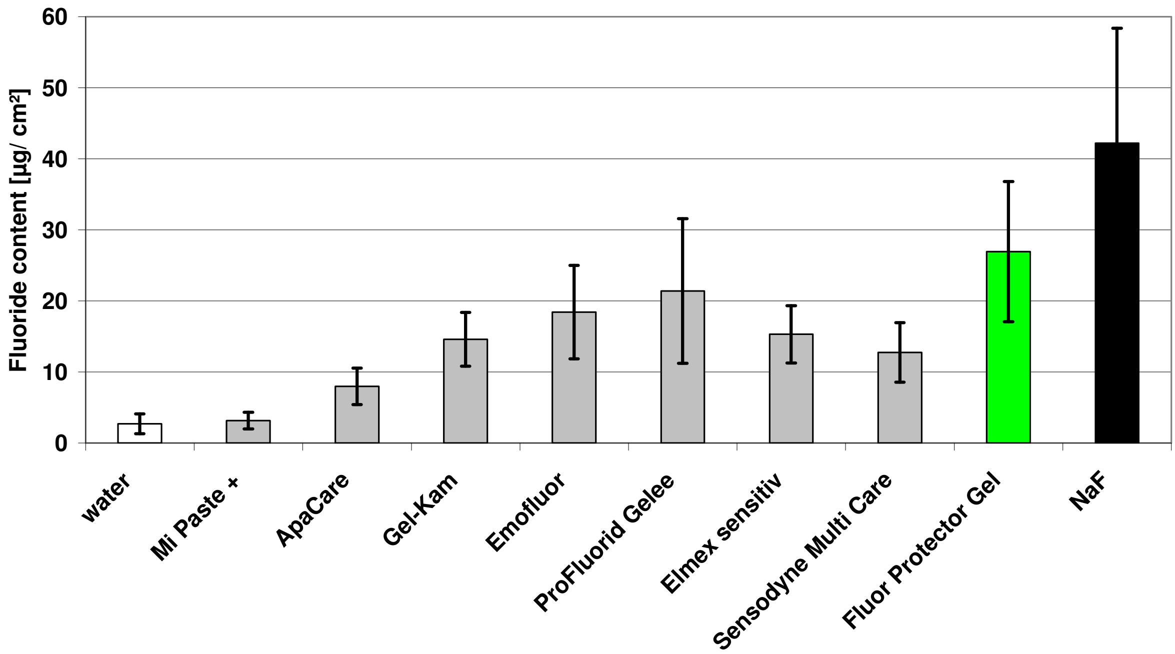


Figure 3: Alkali-soluble fluoride deposited on the surface of bovine enamel after treatment with different fluoride preparations.

After one hour of fluoridation of the demineralised enamel, different surface concentrations of alkali-soluble fluoride were achieved with the different fluoride products. Overall, the amount of fluoride deposited on the surface ranged between the results of the negative control (water) and those of the positive control (aqueous sodium fluoride solution) for all the commercially available products. Fluor Protector gel showed the highest fluoridating effect of all the products tested.

Results: The different commercially available fluoride products precipitated different concentrations of fluoride on the surface (see Figure 3). Of all the products tested, Fluor Protector gel showed the highest fluoride concentration on the surface (27 $\mu g/cm^2$). This high fluoridation achieved with the positive control NaF, which exceeds that of all other products, can be explained by the optimum availability of fluoride ions in the aqueous solution. However, from a clinical perspective, it could be advantageous if the matrix of a gel would release fluoride at a slower rate and therefore over a longer period of time.

3.1.2 Determination of structurally bound fluoride

Objective: Quantification of the structurally bound fluoride incorporated into the hydroxy apatite of the dental enamel.

Investigator: R&D Ivoclar Vivadent, Schaan, Liechtenstein

Method: The test specimens that had previously been used to determine the fluoride content on the surface were dried and resealed with Heliobond. Then they were immersed in 1 ml 0.5 M perchloric acid ($HClO_4$) for 1 hour to etch away the uppermost enamel layer (approx. 100 µm). After having added 5 ml TISAB-II buffer to the solution, the fluoride content was determined with an ion-selective fluoride electrode. The fluoride concentration measured was put into relation to the volume of the layer that had been removed by etching (µg/cm^3).

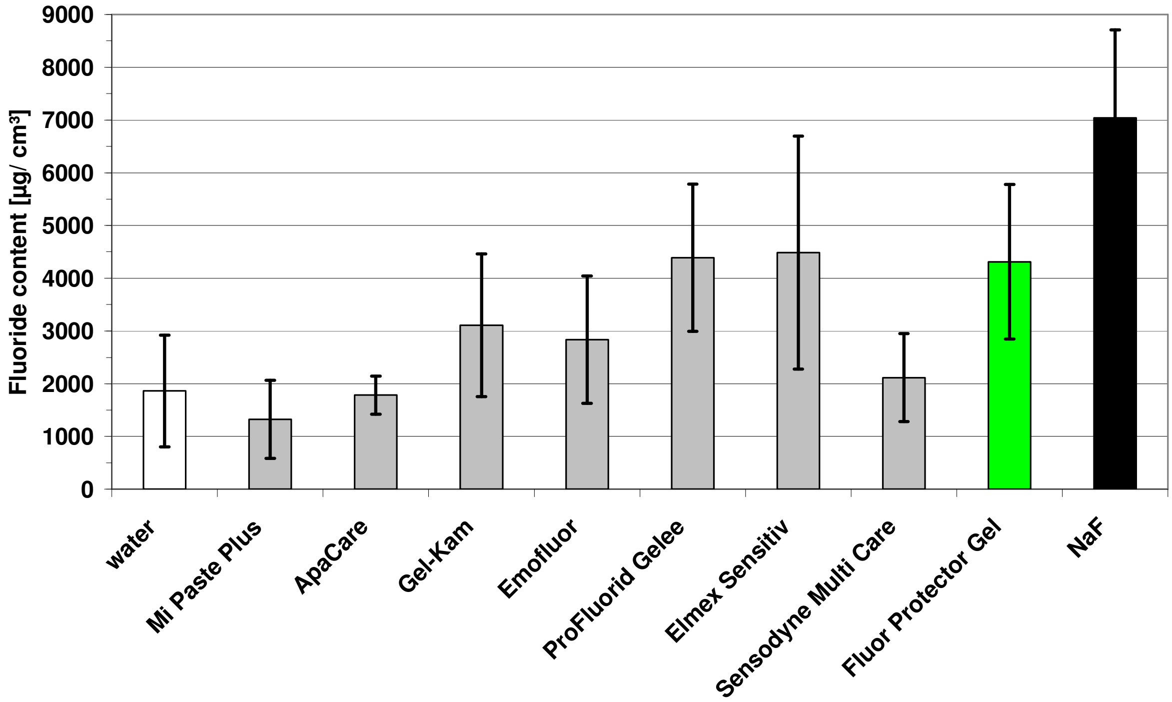


Figure 4: Structurally bound fluoride after treatment of bovine enamel with different sources of fluoride.

After fluoridating bovine enamel for one hour, different levels of structurally bound fluoride were achieved with the different fluoride products. Overall, the amount of fluoride that was structurally bound was between the results obtained for the negative control (water) and those for the positive control (aqueous sodium fluoride solution) for all the commercially available products. Fluor Protector gel was among the products that led to the highest levels of structurally bound fluoride.

Results: Different levels of structurally bound fluoride were achieved with the different commercially available fluoride products (see Figure 4). The highest levels of structurally bound fluoride (more than 4000 µg/cm^3) were achieved with Fluor Protector Gel (neutral pH) and two other products (ProFluorid Gelee, Elmex Sensitive; both with acidic pH).

3.2 Protection against demineralisation / Protection against enamel erosion

Objective: Investigation of the protective effect against demineralisation of Fluor Protector Gel conducted with human enamel test specimens under erosive conditions and compared to similar products (see Tab. 2).

Product name	Fluoride content acc. to manufacturer / ppm	Calcium source	Manufacturer
Fluor Protector Gel	1450	Yes	Ivoclar Vivadent AG
Tooth Mousse Plus	900	Yes	GC Corporation
Colgate Total	1450	No	Colgate-Palmolive Company
Elmex Gelée	12500	No	GABA

Table 2: Overview of the fluoridated dental care products investigated.

Investigator: Dr. D. Ziebolz, Medical University Göttingen, Germany

Method: Test specimens were produced from human anterior teeth, embedded in acrylic and polished. The test specimens were divided into five groups that were treated differently: control (no gel), Fluor Protector gel, Tooth Mousse Plus, Colgate Mousse Plus, Colgate Total, Elmex Gelée. All test specimens were treated with the gels/pastes according to the recommendations of the manufacturer (twice daily for 2 min or once weekly for 2 min in the case of Elmex Gelée). Then they were rinsed with water and exposed to de-/remineralisation cycles. For demineralisation, the test specimens were immersed in a citric acid solution (pH 2.3) six times per day for 5 min; remineralisation was achieved by means of immersion in artificial saliva (60 min each time). After 3, 7, 14 and 30 treatment cycles, the enamel surface was analysed by means of quantitative, light-induced fluorescence measurement, in order to measure the extent of demineralisation in the different groups.

Results: Figure 5 shows that the fluorescence of untreated test specimens decreases continuously with the course of time, which means that the enamel is increasingly demineralised. In contrast, the fluorescence of the test specimens treated with fluoride gels decreased to a lesser extent. Consequently, these preparations protect teeth against demineralisation. In the comparison between Fluor Protector Gel and Elmex Gelée, Fluor Protector Gel clearly prevents demineralisation more effectively than Elmex Gelée.

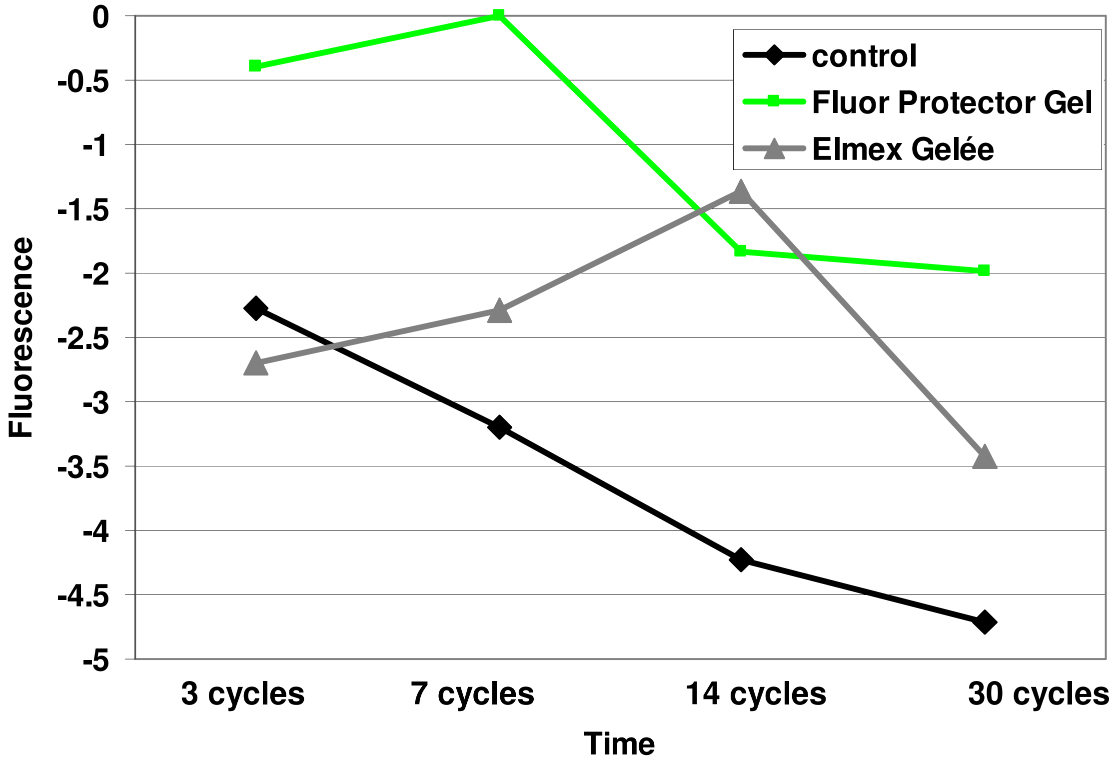


Figure 5: The protection against demineralisation provided by Fluor Protector Gel

Test specimens made of human enamel were treated with Fluor Protector Gel or Elmex Gelée or left untreated and then exposed to de-/remineralisation cycles (demineralisation: citric acid, 6 times daily for 5 min, remineralisation: artificial saliva, 60 min each time). After 3, 7, 14 and 30 cycles, the fluorescence was determined as a measure of enamel demineralisation. Untreated test specimens (control) show a continuous loss of fluorescence and thus ongoing demineralisation, while specimens treated with fluoride gels exhibit reduced demineralisation. Fluor Protector Gel provided more effective protection against demineralisation than Elmex Gelée.

3.3 Compatibility with titanium surfaces

Objective: Different laboratories have found that titanium, a material frequently used for dental implants, corrodes in the presence of fluoride, particularly at acidic pH levels [15-17]. The objective was to assess whether fluoride-containing gels such as Fluor Protector Gel, Cervitec Gel or Elmex Gelée can attack titanium surfaces. Product characteristics are given in table 3.

Product name	Fluoride content according to the manufacturer / ppm	pH	Manufacturer
Fluor Protector Gel	1450	7.3	Ivoclar Vivadent AG
Cervitec Gel	900	5.7 – 6.3	Ivoclar Vivadent AG
Elmex Gelée	12500	4.8*	GABA

Table 3: Overview of the fluoridated dental care products investigated.

*10% in water, manufacturer information

Investigator: R&D Ivoclar Vivadent, Schaan, Liechtenstein

Method: Titanium tabs were ground, polished, rinsed with demineralised water and cleaned with ethanol in the ultrasonic bath. The tested materials were applied to the titanium surface using a plastic spatula and then evenly distributed with a microbrush. The tabs were stored at 37°C for 24 hours or 168 hours (7 days).

Results: Figure 6 shows the titanium surfaces after having been treated with different fluoride-containing gels: In conjunction with Fluor Protector Gel and Cervitec Gel no changes were observed on the surface compared to the control surfaces. Elmex Gelée, however, left behind clear traces of corrosion. Corrosion was also observed in conjunction with a titanium abutment that was treated with Elmex Gelée for 24 hours.

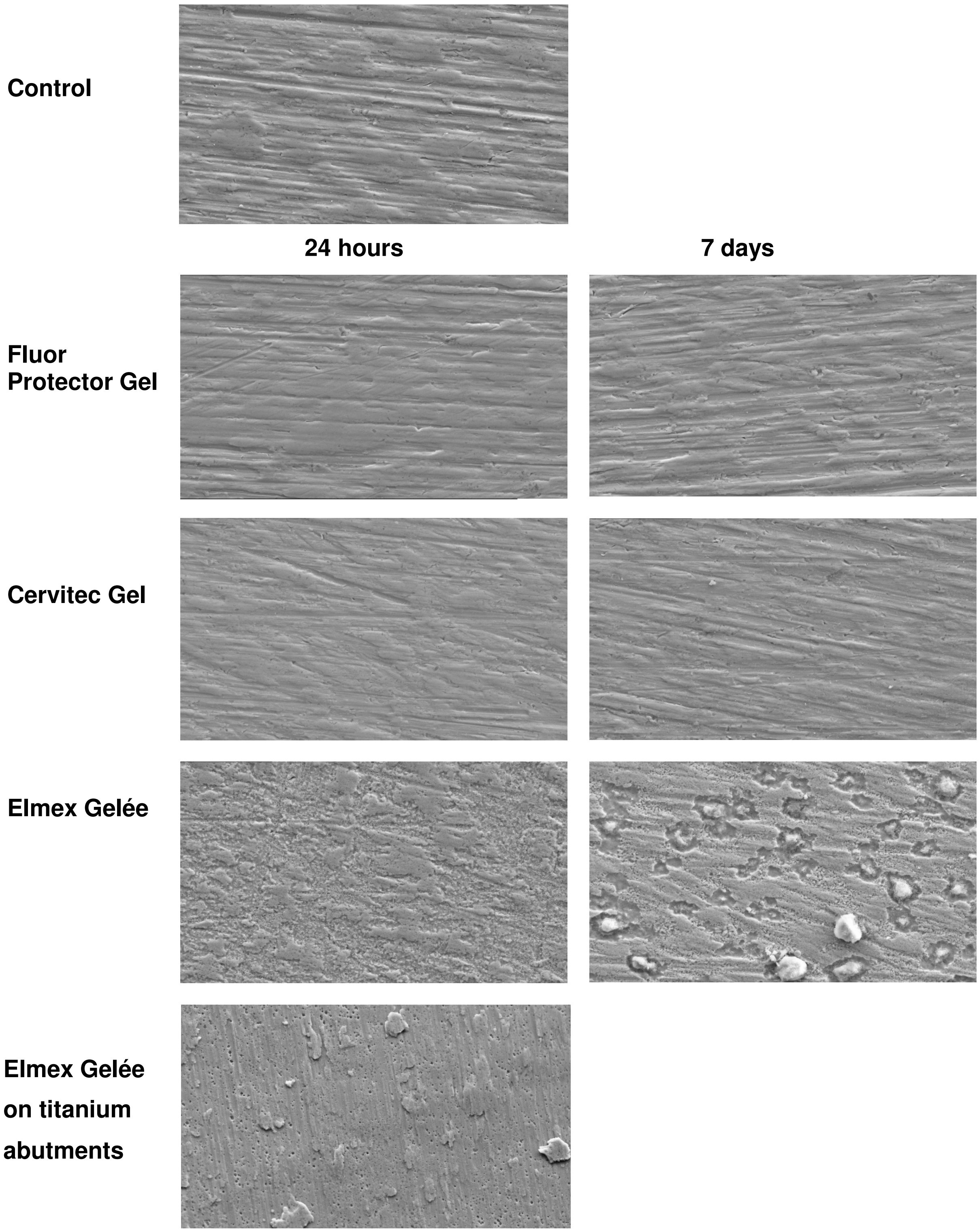


Figure 6: Corrosion of titanium surfaces in the presence of fluoride.

Titanium tabs were treated with Fluor Protector Gel, Cervitec Gel or Elmex Gelée for 24 hours or 7 days. Subsequently, their surfaces were analysed with the scanning electron microscope. In conjunction with Fluor Protector Gel and Cervitec Gel, no changes were observed on the surface. However, the titanium tabs treated with Elmex Gelée showed corrosion. One of the titanium abutments (Straumann RC) even showed pitting corrosion after it was treated with Elmex Gelée for 24 hours.

4. Biocompatibility

4.1 Carrier substances

The carrier substances hydroxyethyl cellulose and Laureth-23 are widely used in the manufacture of tooth pastes. The dose rate at which half of the laboratory animals (rats) die (LD_{50}) is 1000 mg per kg of body weight in the case of Laureth-23 (1), whereas hydroxyethyl cellulose is labelled as "low-toxic" (2). None of the two substances is known to have a sensitizing effect. The following applies to the substances in chemically pure form: hydroxyethyl cellulose causes only minor irritation which is completely reversible; Laureth-23 can be irritating to the skin and eyes. However, both substances are unproblematic when used in the concentration employed in Fluor Protector Gel.

4.2 Potassium fluoride

Potassium fluoride is toxic with an oral LD_{50} value (rat) of 245 mg/kg of body weight (3). The European Cosmetics Directive prescribes an upper limit of 1500 ppm of free fluoride for cosmetic tooth pastes. Fluor Protector Gel contains 1450 ppm of fluoride and is thus within the prescribed limits (4). For children below the age of 6, this fluoride concentration is only suitable to a limited degree. The corresponding warning is imprinted on the package.

4.3 Calcium glycerophosphate

The calcium glycerophosphate contained in Fluor Protector Gel is approved as a food additive without a threshold value for baby food (5).

4.4 Flavouring agents and xylitol

Fluor Protector Gel contains the sweeteners sodium saccharine and xylitol as well as natural peppermint oil as flavouring agent. These substances are approved as food additives in the EU. The admissible threshold value for sodium saccharine (E 954) is between 100 und 800 mg/kg for most foodstuffs (6). For the substance menthofuran contained in peppermint oil, the threshold value is between 200 and 3000 mg/kg (7). The amounts of both sodium saccharine and peppermint oil used in Fluor Protector Gel are within the prescribed limits. For xylitol (E967) no upper limit has been defined ("*quantum satis*") (6).

4.5 Summary and conclusion

Fluor Protector Gel complies with the European Cosmetics Directive. Due to the data available we can proceed on the assumption that the product does not pose any toxicological risk to the patient or user if it is used as directed.

4.6 Biocompatibility references

(1) MSDS Laureth-23

(2) MSDS hydroxyethyl cellulose

(3) Hazardous Substances Data Bank (HSDB): http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB

(4) Council Directive of 27 July 1976 on the approximation of the laws of the Member States relating to cosmetic products (76/768/EEC)

(5) Commission Directive 2006/125/EC of 5 December 2006 on processed cereal-based foods and baby foods for infants and young children

(6) European Parliament and Council Directive 94/35/EC of 30 June 1994 on sweeteners for use in foodstuffs

(7) Regulation (EC) No. 1334/2008 of the European Parliament and of the Council of 16 December 2008 on flavourings and certain food ingredients with flavouring properties for use in and on foods

5. Literature

1. Nagpal DI, Damle SG. Comparison of salivary fluoride levels following use of dentifrices containing different concentrations of fluoride. J Indian Soc Pedod Prev Dent 2007;25:20-22.

2. Twetman S, Skold-Larsson K, Modeer T. Fluoride concentration in whole saliva and separate gland secretions after topical treatment with three different fluoride varnishes. Acta Odontol Scand 1999;57:263-266.

3. van Rijkom HM, Truin GJ, van 't Hof MA. A meta-analysis of clinical studies on the caries-inhibiting effect of fluoride gel treatment. Caries Res 1998;32:83-92.

4. Marinho VC, Higgins JP, Logan S, Sheiham A. Fluoride gels for preventing dental caries in children and adolescents. Cochrane Database Syst Rev 2002:CD002280.

5. WHO. Fluorides and oral health. Report of a WHO Expert Committee on Oral Health Status and Fluoride Use. World Health Organ Tech Rep Ser 1994;846:1-37.

6. Rølla G, Øgaard B, Cruz Rde A. Clinical effect and mechanism of cariostatic action of fluoride-containing toothpastes: a review. Int Dent J 1991;41:171-174.

7. Bar A. Caries prevention with xylitol. A review of the scientific evidence. World Rev Nutr Diet 1988;55:183-209.

8. Knuuttila ML, Makinen K. Effect of xylitol on the growth and metabolism of Streptococcus mutans. Caries Res 1975;9:177-189.

9. Ebner F, Heller A, Rippke F, Tausch I. Topical use of dexpanthenol in skin disorders. Am J Clin Dermatol 2002;3:427-433.

10. Eisenmann D. Enamel structure. Mosby; St. Louis 1998.

11. Rolla G, Saxegaard E. Critical evaluation of the composition and use of topical fluorides, with emphasis on the role of calcium fluoride in caries inhibition. J Dent Res 1990;69 Spec No:780-785.

12. Fischer C, Lussi A, Hotz P. Kariostatische Wirkungsmechnismen der Fluoride. Schweizer Monatsschrift für Zahnmedizin 1995;105:311-317.

13. Dijkman TG, Arends J. The role of 'CaF2-like' material in topical fluoridation of enamel in situ. Acta Odontol Scand 1988;46:391-397.

14. Caslavska V, Moreno EC, Brudevold F. Determination of the calcium fluoride formed from in vitro exposure of human enamel to fluoride solutions. Arch Oral Biol 1975;20:333-339.

15. Lindholm-Sethson B, Ardlin BI. Effects of pH and fluoride concentration on the corrosion of titanium. J Biomed Mater Res A 2008;86:149-159.

16. Nakagawa M, Matsuya S, Udoh K. Corrosion behavior of pure titanium and titanium alloys in fluoride-containing solutions. Dental Materials Journal 2001;20:305-314.

17. Strietzel R, Hosch A, Kalbfleisch H, Buch D. In vitro corrosion of titanium. Biomaterials 1998;19:1495-1499.

Ivoclar Vivadent AG
Research and Development
Scientific Services
Bendererstrasse 2
FL - 9494 Schaan
Liechtenstein

Contents: Dr. Kathrin Fischer
Issue: August 2010