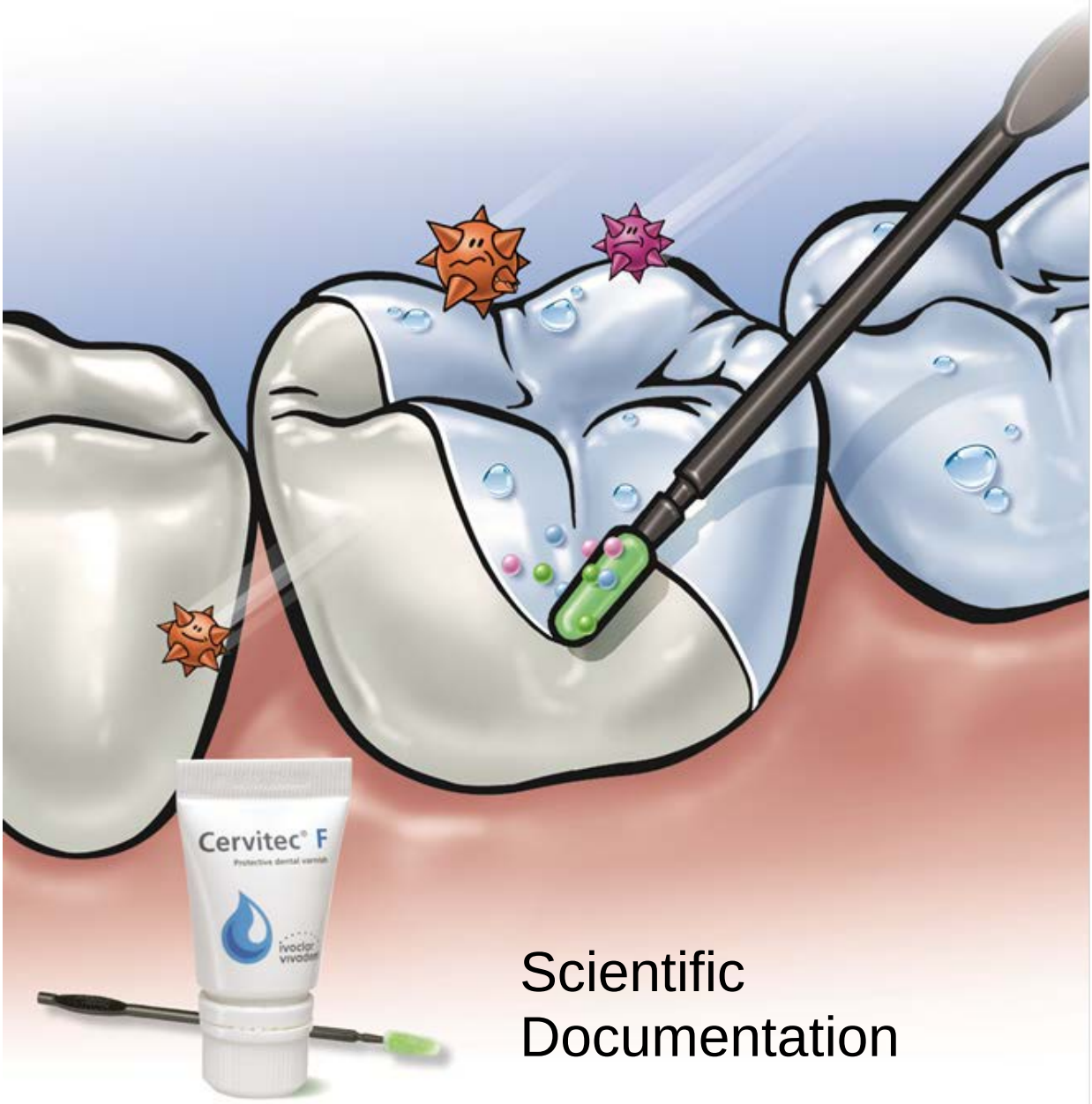
Cervitec® F



Scientific Documentation

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Contents

1. Introduction

1.1 Good health begins in the mouth

It is quite true to say that good health begins in the mouth. Oral health is an important prerequisite for well-being, freedom of pain and social recognition. An epidemiological study conducted in Germany among 2050 volunteers aged between 16 and 79 years, revealed a clear connection between oral health and quality of life [1]. Moreover, it has been found that dental pain has an adverse effect on social behaviour [2] and children with a high caries prevalence perceive themselves and are perceived by others more negatively than children with healthy teeth [3; 4].

Caries is one of the most common diseases of the oral environment, affecting 20% of children between 2 and 4 years and over three quarters of the human population over 18 years of age [5]. In the aged population, exposed root surfaces in particular are often affected by caries. In the 1990s, a survey conducted in Sussex in Great Britain found that roughly one third of the patients aged over 55 were affected by root caries [6]. A Canadian study carried out in 2014 found that 19.7% of the patients aged over 65 had untreated root caries [7]. As people live longer lives, root caries is becoming an increasingly significant problem. Fluoride and effective bacterial control are among the most important weapons in the fight against caries and its undesirable effects.

Fluoride is an ingredient of many dental care products - frequently found in toothpastes and gels, but also in mouth rinses and varnishes.

Fluoride varnishes were first developed around the 1960s and early 70s. The idea was that by lengthening the time the fluoride is in contact with the teeth the fluoride uptake should be increased and improved [8; 9]. In support of this argument, Zero *et al.* state that the primary anti-caries activity of fluoride occurs topically [10]. Moreover, Zimmer *et al.* note that fluoride uptake, reaction and release in enamel are strongly dependent on the duration of contact [11]. Since the 1980s, fluoride varnishes have been widely used throughout Europe.

The WHO note that fluoride varnishes have a significant caries reducing potential [12]. A Cochrane review of randomised/quasi-randomised controlled trials, comparing fluoride varnishes with placebo or no treatment, concluded that fluoride varnishes exhibited a significant caries-inhibiting effect in both permanent and deciduous dentitions [13].

In-vitro- and *in-vivo* studies have also shown that varnishes supply fluoride more efficiently than other topical agents, e.g. gels and foams, with reductions in caries ranging from 50 to 70% [14; 15]. Furthermore, from a toxicological safety point of view, varnishes are preferable, because the bioavailability of fluoride in varnish is relatively low. In contrast, gels may have a bioavailability of almost 100%. Depending on the initial concentration of the formulation examined, plasma peaks of around 1500 ng/ml have been measured. Cousins and Mazze suggested that a plasma level of 850 ng/ml is nephrotoxic [16].

Thus, the wide acceptance of fluoride varnishes results from their easy, safe and convenient application procedure [17]. According to the American Dental Association, the application of fluoride varnishes is particularly beneficial in individuals with a moderate or high caries risk; for children below the age of 6 years, fluoride varnish is the only recommended fluoridation product due to the low risk of ingestion and undesirable side effects [18].

Furthermore, poor oral health is often associated with microorganisms living in the oral cavity: bacteria such as mutans streptococci, lactobacilli or yeast fungi, e.g. *candida albicans*. Dental hard tissues infected by bacteria tend to be susceptible to caries, endodontic problems or loss of restorations due to secondary caries. Infected soft tissues may lead to periodontitis, periimplantitis, inflammatory gingival diseases such as mucositis or gingivitis or halitosis.

Chlorhexidine (CHX) and cetylpyridinium chloride (CPC) are important substances that have a beneficial effect on the bacterial environment in the oral cavity. These cationic substances

adhere to surfaces with a negative charge (e.g. cell walls of bacteria) and thereby inhibit plaque formation and bacterial metabolism.

1.2 Cervitec F

Cervitec F contains 1400 ppm fluoride from ammonium fluoride in a varnish base with ethanol and water as solvents. In addition, the varnish contains nearly 0.3% chlorhexidine and 0.5% cetylpyridinium chloride.

A substantial advantage of the special formulation of Cervitec F is the ease of application. In contrast to high-viscosity varnishes in natural resin, the low viscosity of Cervitec F ensures that the entire tooth surface is reliably wetted (Fig. 1). Due to its low viscosity, Cervitec F even gains access to proximal surfaces or dentin, e.g. in the case of crown margins, without difficulty. Finally, the varnish hardens to a clear transparent film on the tooth surface, providing a highly esthetic result.

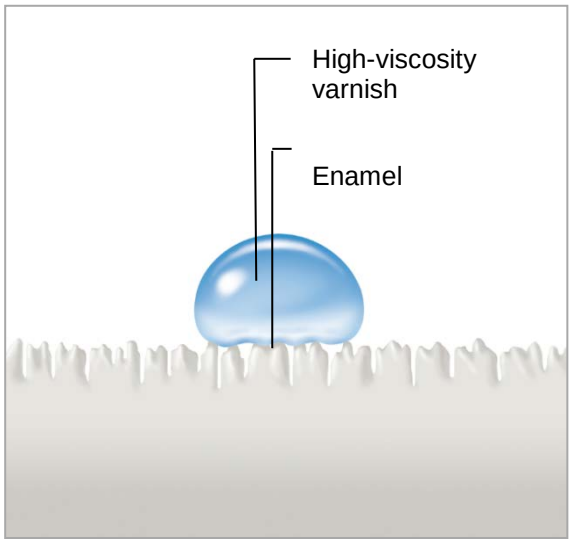


Fig. 1a: Flow properties of high-viscosity varnishes High-viscosity varnishes sit on the enamel surface and wet the tooth only to a limited degree.

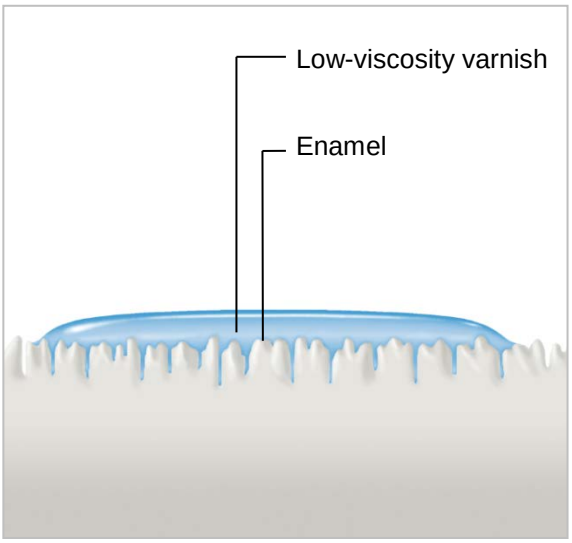


Fig. 1b: Flow properties of low-viscosity varnishes Low-viscosity varnishes such as Cervitec F feature ideal flow and wetting properties and spread easily on the tooth surface.

Cervitec F is a varnish designed for mechanical protection of the tooth structure, fluoridation and antimicrobial action. The varnish is suitable for

- caries prevention in risk groups
- fluoridation of dental enamel
- remineralization of incipient caries
- protection of hypersensitive teeth
- antimicrobial action

1.3 Working principle

1.3.1 Formation of fluorapatite and a calcium fluoride layer

The benefits of fluoride in preventing enamel demineralization, promoting remineralization, reducing plaque growth and helping to prevent dental caries are well documented [19].

In the past, the inhibition of caries by fluorides was ascribed to the reduced solubility of enamel due to the incorporation of fluoride ions into the crystal lattice of enamel, or the formation of fluorapatite (Fig. 3).

Hydroxyapatite		Fluorapatite
$[Ca_3(PO_4)_2]_3 \cdot Ca(OH)_2$	$\leftrightarrow$	$[Ca_3(PO_4)_2]_3 \cdot Ca(F)_2$

Fig. 3: Conversion of hydroxyapatite to fluorapatite. In the presence of fluoride ions, the hydroxyl ion (OH^-) of the hydroxyapatite can be exchanged by fluoride (F^-), yielding fluorapatite.

Though important, this is now known to have a more limited effect, with general acceptance that the primary anti-caries activity of fluoride occurs via a different mechanism, i.e. the formation of a calcium fluoride layer over the teeth [10; 20].

Depicted in Fig. 4a, demineralization refers to the loss of calcium and phosphate ions from the tooth structure that occurs during an acid attack by cariogenic bacteria. Fluoride can help prevent this mineral loss.

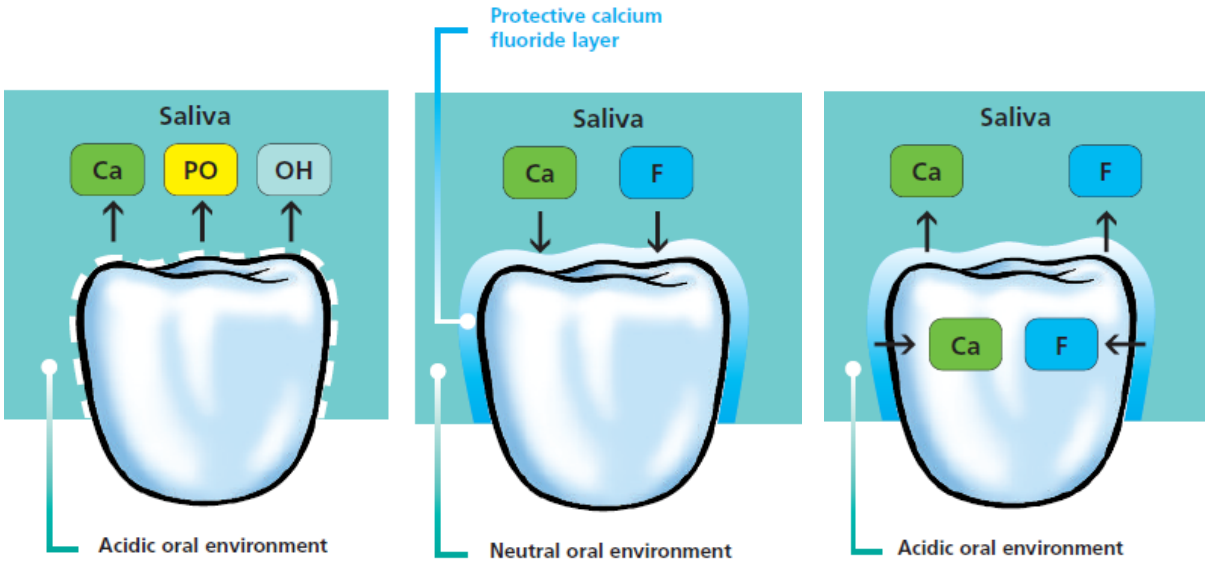


Fig. 4a: Demineralization without fluoride protection

At low pH, enamel is demineralized via the release of calcium (Ca^{2+}) and phosphate (HPO_4^{2-}) ions into the saliva.

Fig. 4b: Protective calcium fluoride layer

After application of fluoride, a protective calcium fluoride layer (CaF_2) forms.

Fig. 4c: Bioavailability of fluoride

At low pH, calcium (Ca^{2+}) and fluoride (F^-) ions are released. The tooth structure is no longer attacked directly.
The calcium fluoride layer forms a depot releasing fluoride over time to the saliva.

Human saliva is usually saturated with calcium, such that following a topical application of fluoride, hardly soluble calcium fluoride (CaF_2) is formed and a calcium fluoride-like layer precipitates over the treated tooth surface (Figs 4b and 5).

$$Ca^{2+} + 2\ F^- \longrightarrow CaF_2$$

Fig. 5: Formation of calcium fluoride. After the application of fluoride varnish, fluoride ions and calcium ions (Ca^{2+}) contained in the saliva precipitate to form calcium fluoride (CaF_2).

It has been shown that CaF_2 particles adhere especially well to porous surfaces such as fissures and demineralized areas [21]. The adsorption of hydrogen phosphate ions additionally stabilizes the CaF_2 layer [20; 22]. At neutral pH, the CaF_2 layer is practically insoluble and may remain on the teeth for months [23].

Under acidic conditions, e.g. after carbohydrate intake and bacterial metabolism, the CaF_2 layer releases fluoride and calcium ions (Fig. 4c). The fluoride ions may remain in the saliva or settle in free spaces on the crystal lattice of the tooth structure, producing fluorapatite or fluor hydroxyapatite, which is more stable against acid than hydroxyapatite. Fluoride ions dissolved in saliva prevent fluoride attached to the enamel from being dissolved by acids [24]. The CaF_2 layer functions therefore as a pH-controlled fluoride reservoir and is the most important supplier of free fluoride ions during the cariogenic attack [20].

Studies show that the fluoride uptake, reaction and release in the enamel are strongly dependent on the duration of contact with the fluoride agent [25]. There is no distinct difference in the caries preventive effects of concentrate fluoride solutions, gels or varnishes

[17]. However, as fluoride varnishes adhere to tooth surfaces preventing immediate loss after application, they may be optimal in this respect.

In conclusion, fluoride provides protective action through the control of the demineralization and remineralization processes. Via the deposition of a calcium fluoride layer on the tooth surface, fluoride hampers acidic demineralization of the tooth structure and promotes remineralization.

1.3.2 Anti-plaque activity

Bacterial biofilms and dental plaque are a prerequisite for the development of caries and periodontal disease. In addition to strengthening the enamel, fluoride can help reduce plaque growth and activity. The formation of a CaF_2 layer has been suggested to impair plaque development [26]. Moreover, fluoride also reduces the cariogenic lactic acid formation in plaque bacteria, such as *Streptococcus mutans* and impairs bacterial glucose uptake and glycolysis [27; 28]. However, chlorhexidine exerts a considerably higher anti-microbial effect than fluoride [29].

Over the last few decades, chlorhexidine has evolved into the gold standard among the antimicrobial substances used in dentistry. It has been demonstrated to be effective against a wide spectrum of pathogenic organisms. In high concentrations (100 ppm), chlorhexidine is capable of destroying the cell membranes of bacteria and thus has a bactericidal effect. A bacteriostatic effect is achieved at a concentration of only 0.11 ppm. The cariogenic *S. mutans* is particularly sensitive to chlorhexidine. The particular effectiveness of chlorhexidine compared to other substances is certainly related to its high substantivity. As a result, chlorhexidine deposits on oral surfaces, creating slow-release reservoirs. The substantivity of chlorhexidine is attributable to interactions between chlorhexidine, which carries a positive charge, and structures which carry a negative charge, such as proteins, glycoproteins of the saliva and plaque and the enamel hydroxyapatite. The use of a varnish system decisively promotes the depot formation effect. Long-term therapy with chlorhexidine mouth rinses and gels can lead to discolouration of teeth, the mucosa, tongue and composite restorations. These undesirable side effects can be avoided by using a chlorhexidine-containing varnish such as Cervitec F or Cervitec Plus.

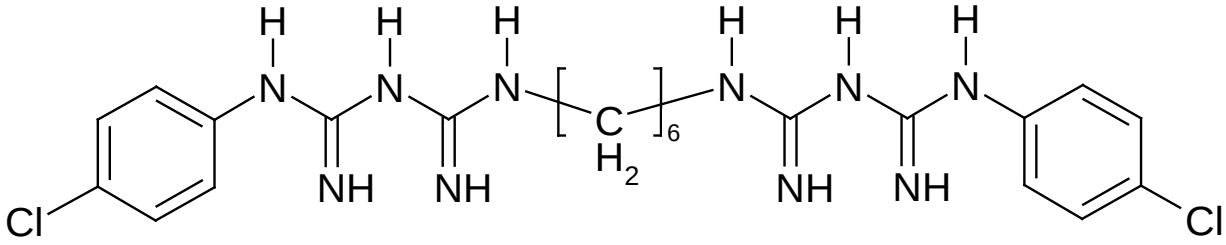


Fig. 6: Chlorhexidine. The structural formula shows, among others, the numerous NH groups responsible for the positive charge of the molecule.

Cetylpyridinium chloride is used in dental care products to prevent plaque formation and inflammatory diseases of the gingiva. It adds to the effect of chlorhexidine.

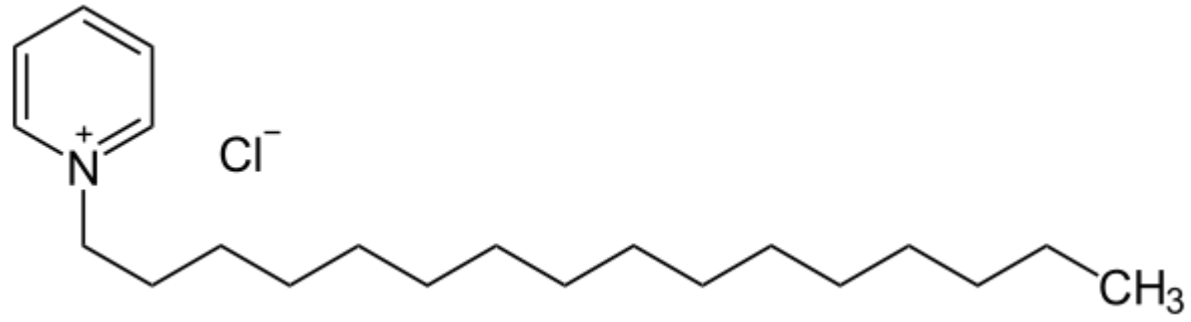


Fig. 7: Cetylpyridinium chloride. The molecule is a cationic, organic, quaternary ammonium compound.

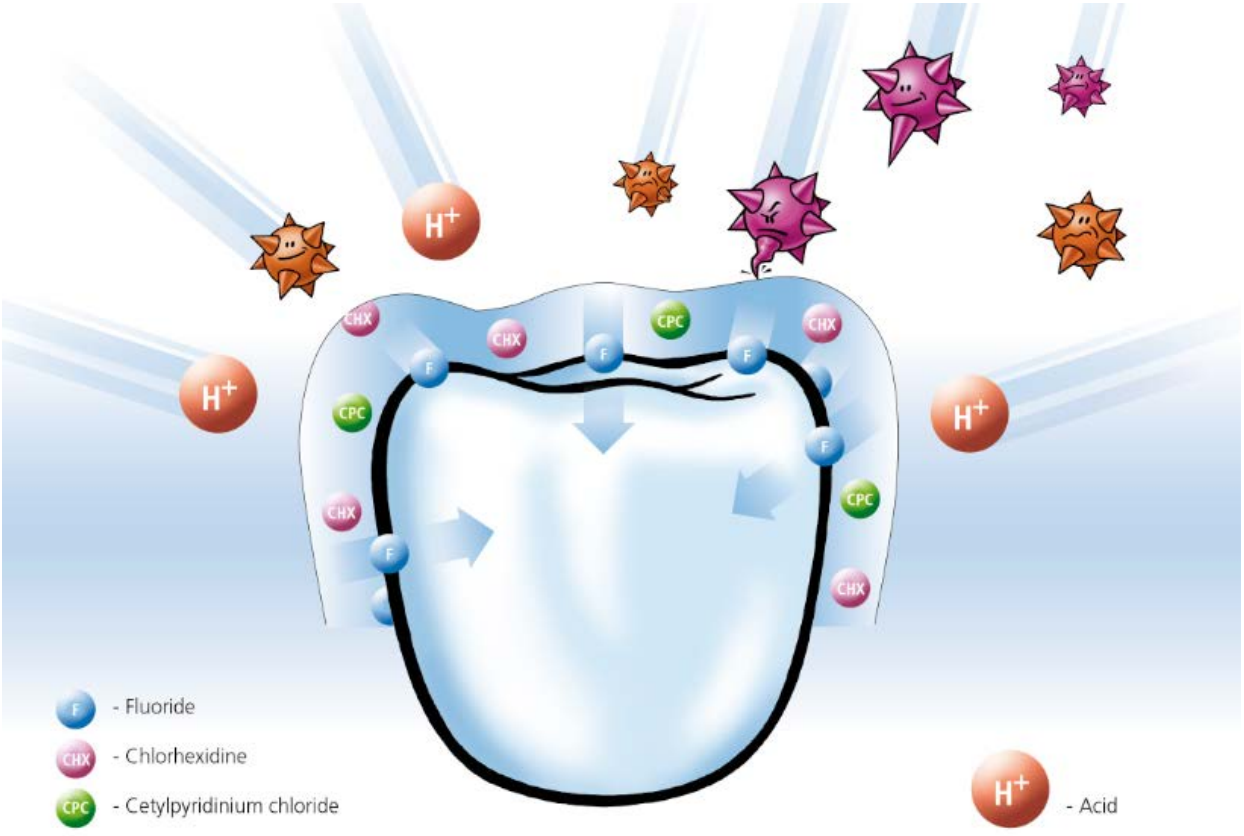


Fig. 8: Effect of Cervitec F. Cervitec F protects the teeth from acids and the effects of bacterial activity in three ways: with fluoride (F, blue spheres), chlorhexidine (CHX, pink spheres) and cetylpyridinium chloride (CPC, green spheres).

2. Composition

Cervitec F

Protective dental varnish

Standard composition (in wt%)

Function	Component (INCI)	Weight%
Solvent	Alcohol, Aqua	80-90
Polymer/ Varnish base	VA/Crotonates Copolymer	8-12
Preservative	Chlorhexidine diacetate (CHX), Cetylpyridinium chloride (CPC)	<1
Antiplaque	Ammonium fluoride	<1
Aroma	Aroma (Peppermint), Saccharin	<1

Properties

Feature	
pH	>4.0

3. *In-vitro* investigations

3.1 Enamel fluoridation

The remineralizing caries-preventive and anti-erosive effect of fluoride-containing dental care products is based on the fluoridation of enamel. Both calcium fluoride formation at the tooth surface and incorporation of fluoride ions into the hydroxyapatite lattice help strengthen and protect the enamel.

The studies below measured the degree of fluoridation after the application of Cervitec F.

3.1.1 Measurement of superficial (alkali-soluble) fluoride

Objective: To quantify the superficial alkali-soluble fluoride (i.e. calcium fluoride layer) formed on the enamel surface.

Investigator: Ivoclar Vivadent R&D, Schaan, Liechtenstein

Method: The study was performed according to the method described by Caslavska [30]. Samples were produced from bovine teeth and demineralized in diluted lactic acid (1h, pH 4.4). Subsequently, the samples were sealed using Heliobond, excluding the enamel surface. The unsealed enamel surface was coated with varnish. After one hour, 1 ml of artificial saliva was added and then the samples were stored at 37°C. One hour later, the varnish was removed from the enamel with ethanol. After that, the samples were thoroughly rinsed with water and inspected for varnish residues. Subsequently, they were immersed in 1 ml of 1 M KOH at room temperature for 24 h to allow the release of alkali-soluble fluoride. Before measurement of the fluoride content with an ion selective fluoride electrode, the solution was neutralized with 1 ml of 1 M HNO_3 and TISAB II buffer solution was added. At least 6 samples were examined for each material. Enamel treated with water was used as the negative control. The fluoride concentrations measured were expressed as ratios according to the size of the sample surface-areas treated (µg/cm^2).

Results: Enamel fluoridation was significantly higher after the treatment with Cervitec F compared to the treatment with water (Fig. 9).

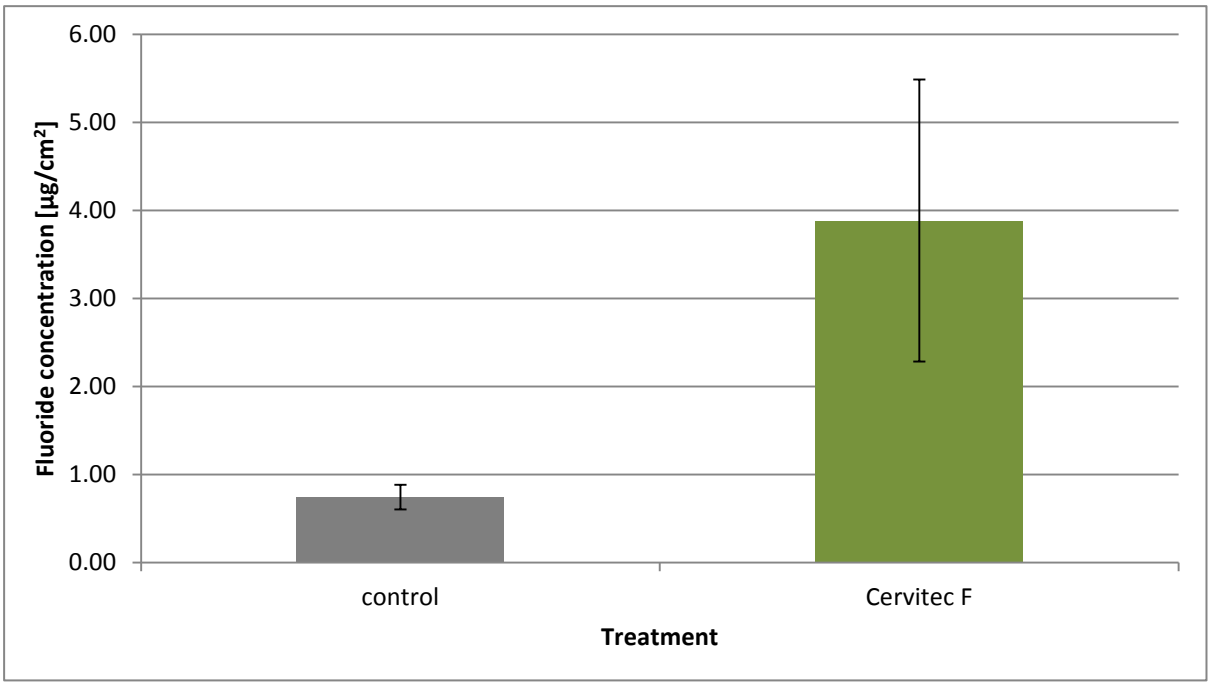


Fig. 9: Superficial alkali-soluble fluoride after treatment with Cervitec F for one hour. Cervitec F resulted in a significantly higher enamel fluoridation than the negative control (water).

Conclusion: Cervitec F results in the formation of a calcium fluoride layer on the enamel as quickly as after the treatment for one hour.

3.1.2 Measurement of structurally bound fluoride

Objective: To quantify the amount of structurally bound fluoride incorporated into the hydroxyapatite crystals of dental enamel.

Investigator: Ivoclar Vivadent R&D, Schaan, Liechtenstein

Method: The samples that were previously used to determine the superficial fluoride content were dried and re-sealed with Heliobond. Subsequently, 1 ml of 0.1 M perchloric acid ($HClO_4$) was added and the uppermost enamel layer (approx. 100 µm) was removed by etching for 15 minutes. Then, 5 ml of TISAB II buffer solution was added and the fluoride content of the solution was measured with an ion selective fluoride electrode.

Results: Fluoridation of the enamel is complete as soon as one hour after the application of Cervitec F and one hour after storage in artificial saliva. Additional storage in artificial saliva for up to 48 hours did not result in an increase in structurally bound fluoride in the enamel.

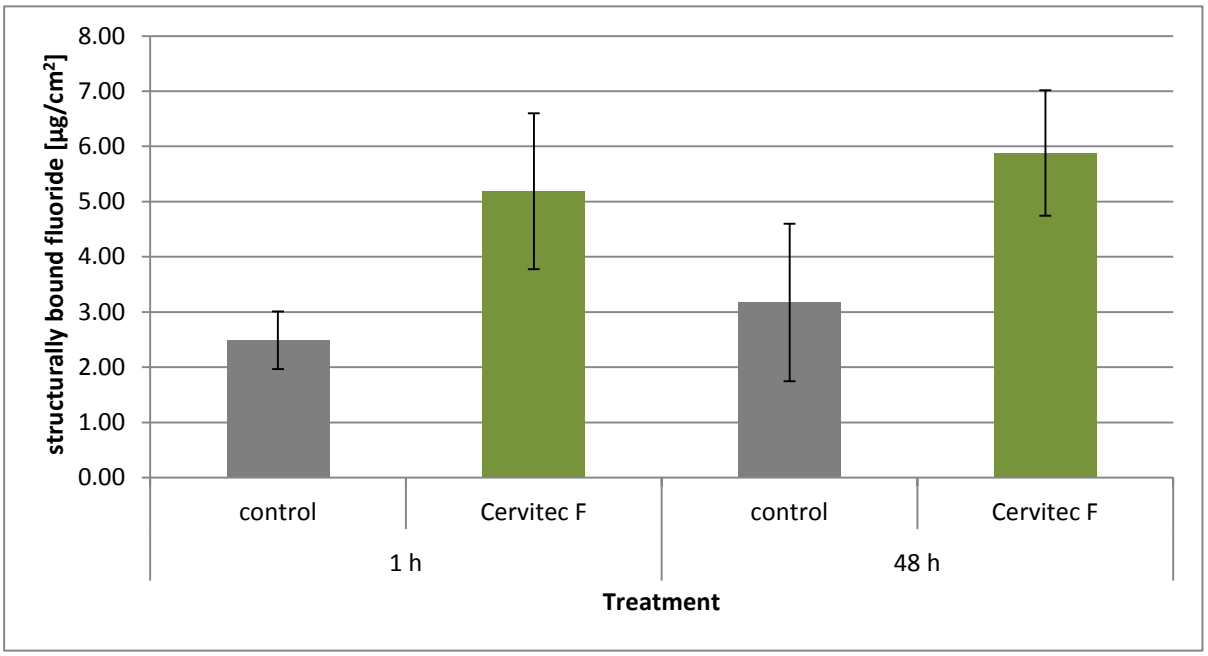


Fig. 10: Structurally bound fluoride after treatment with Cervitec F. Fluoridation one hour after the treatment with Cervitec F and after one hour / 48 hours of immersion in artificial saliva, is significantly higher than in the samples that have not been treated.

Conclusion: Cervitec F results in rapid fluoridation of the enamel.

3.2 Inhibition zone assay

Objective: To investigate the antimicrobial effect of Cervitec F and Cervitec Plus on key oral microorganisms.

Investigator: Nicolle Reinhöfer, University Hospital Jena, Germany

Method: Bamelli agar was inoculated with 24-hour cultures of the relevant strains and poured into petri dishes. After the agar had solidified, reservoirs were punched (d = 10 mm) and filled with 0.3 ml of the varnishes in a standardized fashion. The petri dishes were stored in a fridge for one hour to allow the ingredients to diffuse and, subsequently, the samples were placed in an anaerobic chamber and incubated at 35 ± 2 °C for 24 hours. The resulting inhibition zones in the bacterial and/or fungal lawn were measured metrically.

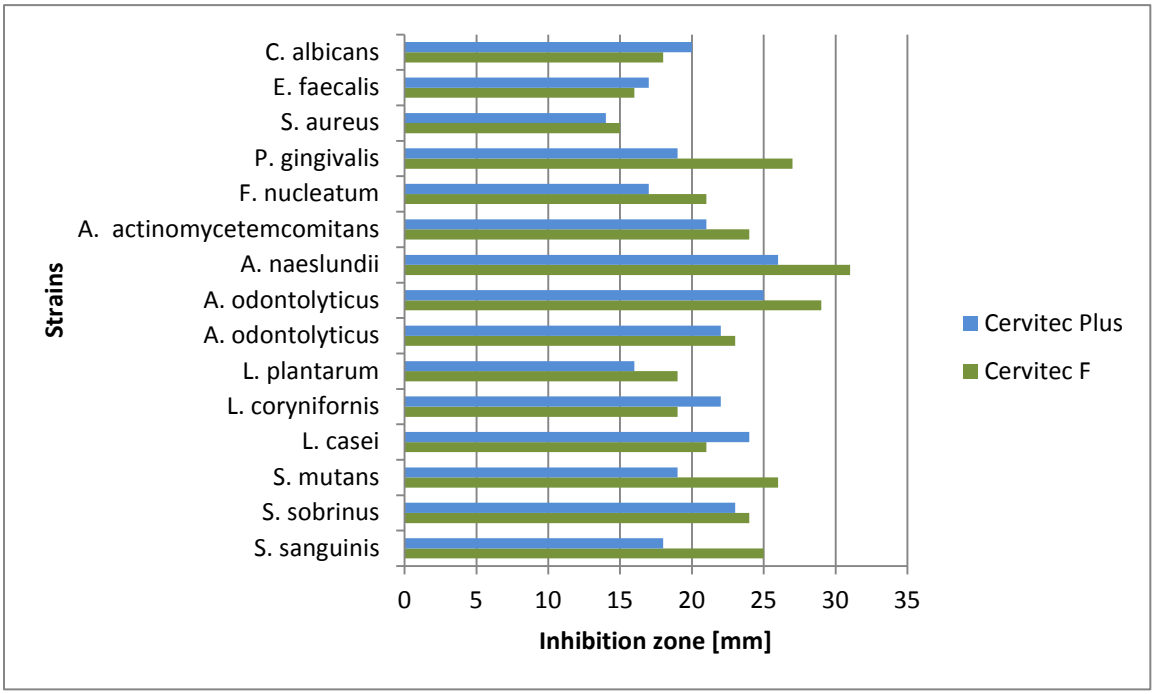


Fig. 11: Inhibition zones of various oral microorganisms in conjunction with Cervitec F and Cervitec Plus. Both varnishes hampered the growth of all micoorganisms tested.

Results: Both Cervitec F and the proven antibacterial varnish Cervitec Plus inhibited the growth of all the strains examined (Fig. 11). The inhibition zones measured up to 31 mm in diameter. Cervitec F is effective not only against the cariogenic bacteria *S. mutans* and *L. casei* but also against the yeast fungus *C. albicans*.

3.3 Treatment of hypersensitive cervicals /reduction of dentin permeability

Hypersensitive cervicals are a common occurrence. Not just painful, hypersensitive teeth may lead to the neglect of oral hygiene. Hypersensitivity can usually be traced back to exposed dentin tubules. The circumstances leading to exposed dentin are manifold and include gingival recession, periodontitis, bruxism, erosion, professional tooth cleaning, scaling and root planing and even bleaching treatments, which may lead to a temporary loss of the smear layer.

The hydrodynamic theory of tooth sensitivity as described by Brännström is widely accepted as the explanation [31]. The theory concludes that certain stimuli such as temperature changes, sweet foods or osmotic activity elicit pressure changes in the dentin. This causes bidirectional fluid flow within the dentin tubules, which activates the dental nerves. *In-vivo* studies have revealed that the response of the pulp is related to the pressure exerted and thus to the rate of fluid movement [32].

Consequently, there are two main approaches to treating hypersensitive teeth: blocking the dentin tubules to prevent fluid movement or inhibiting the neuronal transmission of the stimuli. The first mechanism – blocking of the dentin tubules – is employed by the large majority of products currently available.

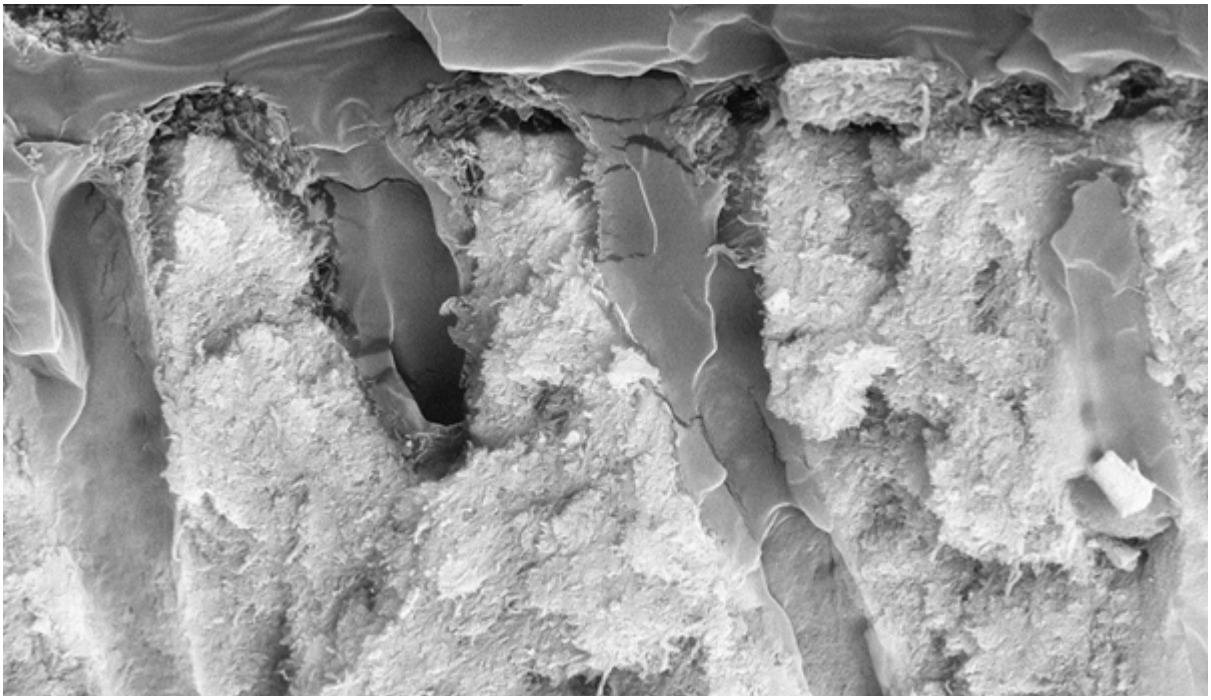


Fig. 12: Blocking of dentin tubules with Cervitec F: The low-viscosity varnish can easily diffuse into the dentin tubules. Scanning electron micrograph; magnification: 1000x. R&D Ivoclar Vivadent, Schaan. The cross-section of broken dentin discs was examined. To prepare the samples, bovine teeth were ground down to the dentin. Subsequently, the smear layer was removed using phosphoric acid etching. The samples were dry blotted for a short while and the varnish was applied to the entire dentin disc and then allowed to dry for 18 h at 40°C and 200 mbar.

Cervitec F also operates via sealing open dentin tubules. The low viscosity varnish is able to penetrate well into the tubules and block the entrances mechanically (Fig. 12).

Objective: To investigate the efficacy of desensitizing varnishes in the treatment of hypersensitive teeth

Investigator: Gianna Nardi, Università degli Studi di Roma Sapienza, Italy

Method: Ninety patients suffering from hypersensitive teeth were allocated to three groups and treated with either Fluor Protector S (7700 ppm fluoride), Cervitec F (1400 ppm fluoride, CHX and CPC) or a placebo varnish. Hypersensitivity was recorded at baseline as well as after 30 and 90 days using the Schiff's scale.

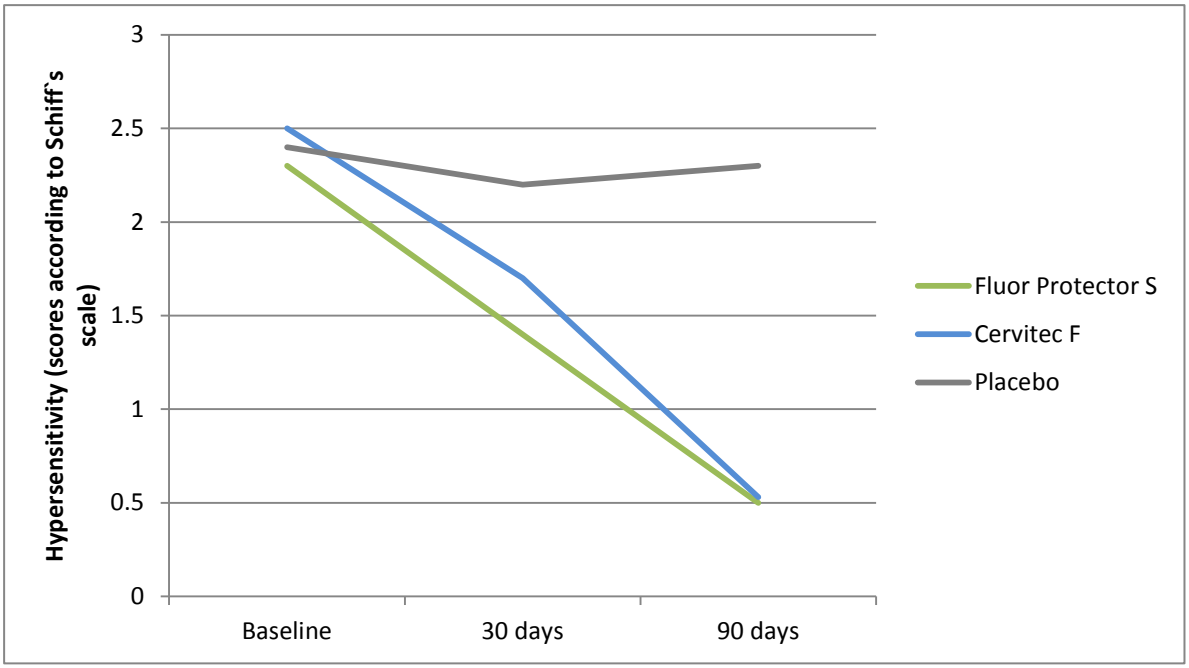


Fig. 13: Dentin hypersensitivity in 90 patients. Application of the protective varnishes Fluor Protector S and Cervitec F resulted in a significant reduction of the hypersensitivity initially present in all the groups (baseline). The reduction in hypersensitivity lasted for at least 90 days.

Results: No improvement was reported for the placebo group. By contrast, a statistically significant reduction in hypersensitivity was reported for those patients who had been treated with either one of the two varnishes (Fig. 13).

Conclusion: Cervitec F has proven its effectiveness in the desensitization of hypersensitive teeth.

3.4 Resistance to discolouration on contact with food

Investigator: Ivoclar Vivadent AG, Schaan, Liechtenstein

Method: Embedded bovine teeth with exposed polished enamel were used for this test. A coating of Cervitec F was applied to the right half of the enamel. After drying in the air for one minute, the enamel was immersed in artificial saliva for 15 minutes at 37°C and then in water, black tea, coffee and red wine again at 37°C. The samples were visually assessed after one and five minutes.

Results: After 5 minutes of immersion, the varnish layer showed only light staining on contact with black tea and coffee (Fig. 14).

Fig. 14: Discoloration test with Cervitec F: After 5 minutes of immersion in water – black tea – coffee – red wine (clockwise from top left), the varnish layer showed only light staining on contact with black tea and coffee.

Conclusion: Cervitec F not only provides an esthetic result immediately after application, it is also largely resistant to discolouration due to food consumption.

3.5 Compatibility with restorative materials

Dental varnishes play a particularly salient role in caries prevention in patients with a high caries risk. However, these patients often already have one or more restorations. If a varnish is applied, it is desirable that the esthetic qualities of the existing direct composite or indirect ceramic restorations are not altered or impaired.

Investigator: Ivoclar Vivadent R&D, Schaan, Liechtenstein

Method: The composite Tetric EvoCeram (TEC) and the ceramic IPS e.max CAD were selected as restorative materials for this test. Cervitec F was applied to the entire test samples or to half of the samples (ceramic specimens), allowed to dry for 24 hours and then immersed in water at

37°C. After removing the varnish with ethanol, the appearance (shade, gloss) was compared with an untreated sample.

Results: Changes in shade or lustre were not visible to the naked eye in either of the two restorative materials (Figs 15 and 16).

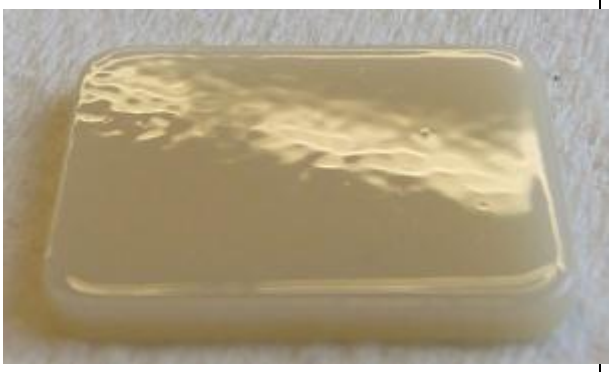
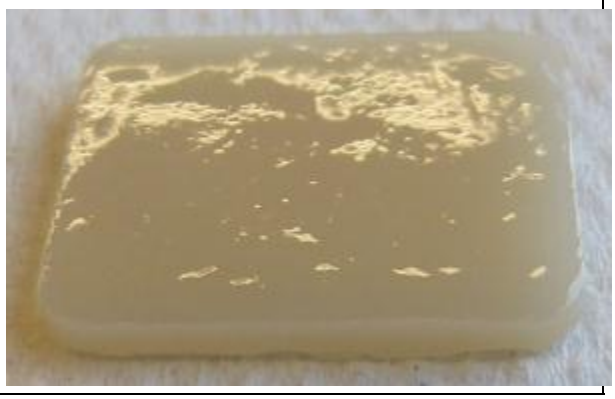
IPS e.max CAD (self glaze)	IPS e.max CAD (polished)
	
IPS e.max CAD + Crystall/Glaze	**IPS e.max CAD + Ceram Glaze Paste**
	

Fig. 15: Compatibility with restorative materials: IPS e.max CAD was tested in four different configurations. The surfaces were treated either with water (left half of the samples) or with Cervitec F (right half of the samples). No visible differences between the two treatment methods were detected on the samples.

	Water	Cervitec F
Tetric EvoCeram **Colour A3**		

Fig. 16: Compatibility with restorative materials: No visible differences were detected between the samples treated with Cervitec F (on the right) and the samples treated with water (on the left).

Conclusion: Cervitec F maintains the esthetic appearance of tooth-coloured restorations.

3.6 Adhesion to enamel

Given its innovative formulation and low-viscosity consistency, Cervitec F is not only easy to apply but it also adheres well to tooth surfaces, providing ample time for its protective substances to reach the enamel before the varnish rubs off via eating, drinking or tooth cleaning. This is illustrated by a test in which the colourless clear varnish was dyed bright blue, using cosmetic colour pigments and then applied to individual teeth in a volunteer.

Investigator: Ivoclar Vivadent R&D, Schaan, Liechtenstein

Method: Cervitec F was dyed with Cosmenyl blue and applied to the incisors of a volunteer using a Vivabrush G. Subsequently, the teeth were photographed. After the varnish had dried for one to two minutes, the volunteer was allowed to close the mouth. Additional pictures were taken after 5, 60 and 120 minutes. The volunteer ate lunch in the time between 60 and 120 minutes.

Results: Immediately after application, the varnish had a shiny, wet appearance. After drying and contact with saliva, it looked rather matt. The entire facial tooth surface was covered with a thin, even varnish layer. When examined at 60 minutes, the varnish was still completely present. After lunch, residues of Cervitec F were still present on the tooth surfaces.

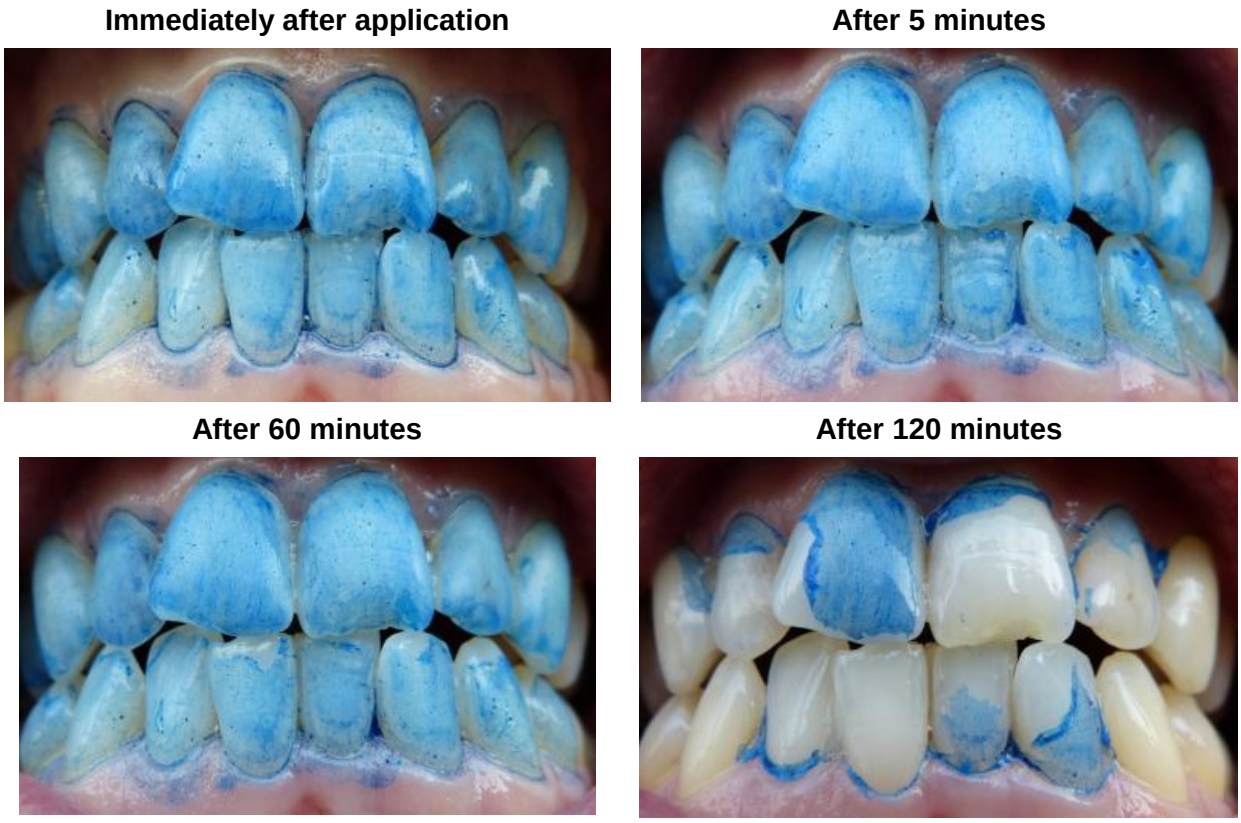


Fig. 17: Adhesion of Cervitec F to enamel: Blue dyed varnish was applied to individual teeth and photographed at various intervals. Between "60 minutes" and "120 minutes", the volunteer ate lunch. Cervitec F adhered firmly to the teeth for at least 1 hour.

Conclusion: Cervitec F adheres well to teeth and, consequently, provides effective protection. As the varnish quickly releases its effective substances to the enamel and, in the process, creates a depot of active compounds, the teeth are protected beyond the duration during which the varnish adheres to the teeth.

4. Clinical investigations

4.1 Caries prevention

Objective: To investigate the application of Cervitec F in the fissures of young permanent molars.

Investigator: Lídia Lipták, Nóra Bársony, Svante Twetman, Melinda Madléna; Semmelweis University, Budapest, Hungary, University of Copenhagen, Denmark and Halland Hospital, Halmstad, Sweden

Study design: Fifty-seven school children aged between 7 and 14 years participated in this study. In a split mouth design, 87 pairs of non-cavitated permanent teeth were treated randomly either with Cervitec F or Cervitec Plus. The varnishes were applied to the fissures at baseline and then at 6-week intervals over a period of 24 weeks. As endpoints, the mutans streptococci count was determined with a CRT bacteria test and the laser fluorescence of the occlusal surfaces measured with a Diagnodent device at the recalls. The fluorescence detects bacteria and changes, e.g. carious lesions, in the tooth structure.

Results: At the beginning of the study, more than half of the fissures showed high mutans streptococci counts ($\geq 10^5$ CFU). The fluorescence values were similar in all the samples.

Treatment with the varnishes resulted in an immediate significant reduction of the bacteria counts. After 24 weeks, only 5% of the fissures still showed high mutans streptococci colonizations (Fig. 18). The two varnishes did not differ significantly from each other during the entire trial. The fluorescence values also decreased in both groups and were significantly lower after 24 weeks than at the baseline, particularly in the Cervitec Plus group. No negative incidents were reported.

Conclusion: Both varnishes were similarly effective in reducing bacterial counts. Cervitec F is consequently suitable for caries prevention.

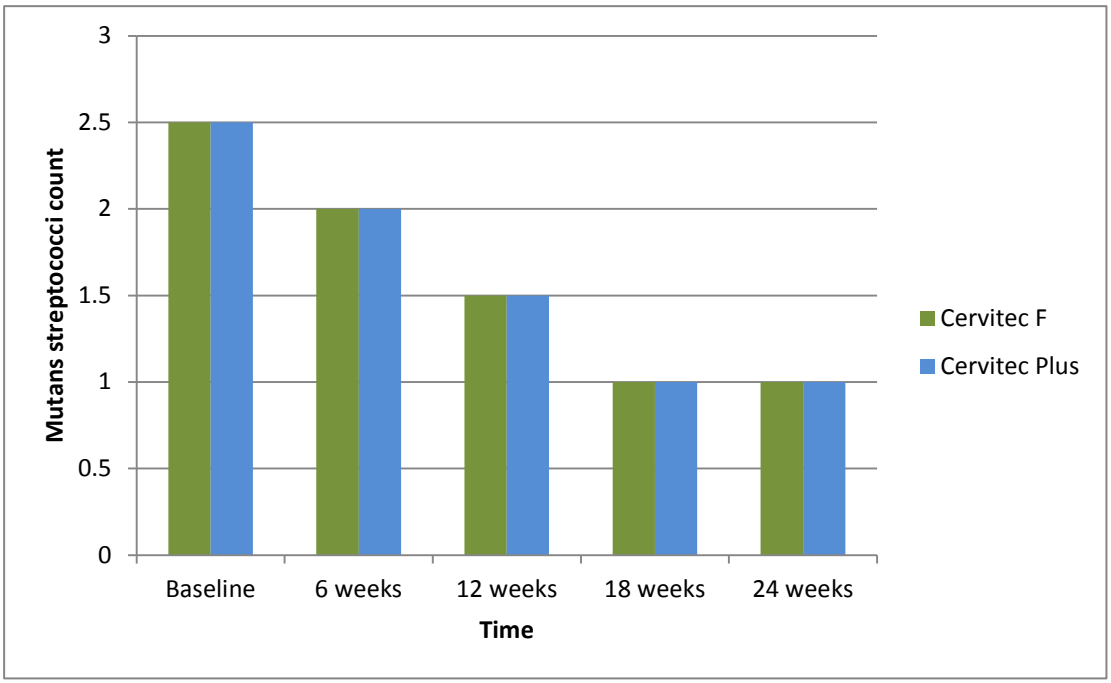


Fig. 18: Mutans streptococci count in occlusal fissures at baseline and after treatment with Cervitec F or Cervitec Plus. The varnishes were applied to the molar fissures at 6-week intervals. The mutans streptococci counts were measured at the baseline of the study and after 6, 12, 18 and 24 weeks. Both varnishes resulted in a significant reduction in the bacterial counts.

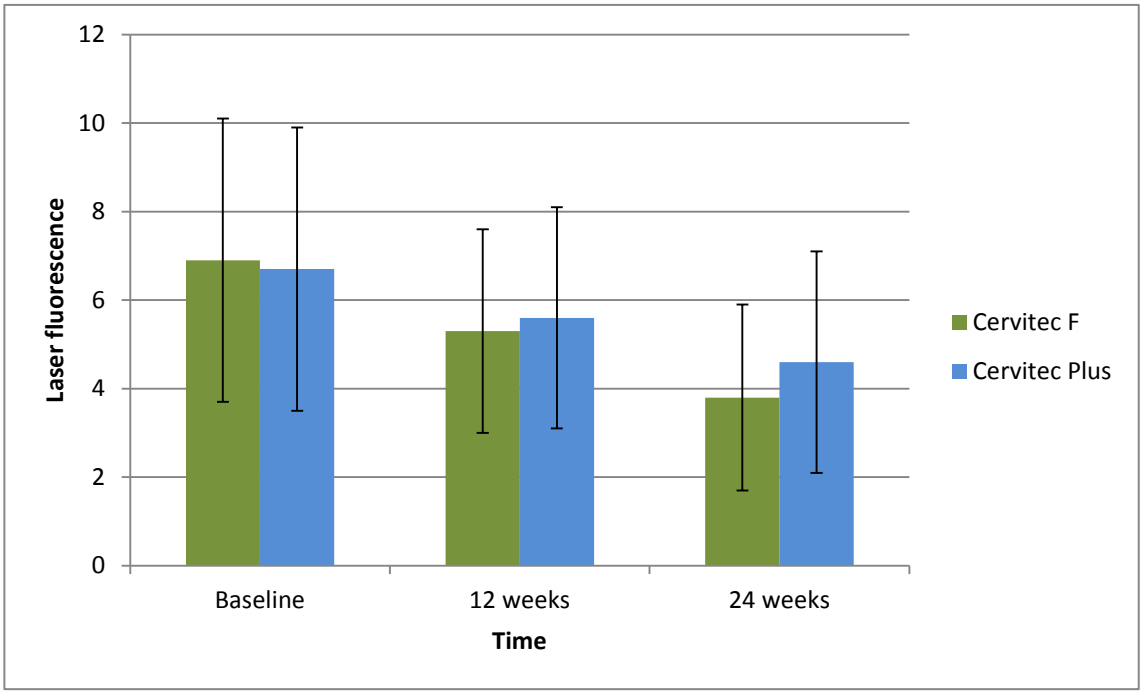


Fig. 19: Laser fluorescence measured in the occlusal fissures at baseline and after 12 and 24 weeks of treatment with Cervitec F or Cervitec Plus. The varnishes were applied to the molar fissures every 6 weeks. Laser fluorescence was measured at the baseline of the study and after 12 and 24 weeks. Both varnishes resulted in a reduction in the fluorescence value.

5. Biocompatibility

5.1 Acute toxicity

Apart from ammonium fluoride and cetylpyridinium chloride, which together account for less than 1 per cent by weight of the varnish, all the components are of low acute oral toxicity (LD_{50} oral > 2000 mg/kg body weight). The toxic level of fluoride is between 32 and 64 mg/kg for adults and 5 mg/kg for children. The fluoride content of Cervitec F is 1400 ppm. This means that Cervitec F would have a toxic effect on a child that weighs 10 kg if it were applied in a quantity of 50 g. When applied correctly, approximately 0.25 g of material is used – posing no danger of poisoning.

5.2 Sensitization and irritation

Some components of Cervitec F may potentially have a sensitizing effect: peppermint oil, chlorhexidine, cetylpyridinium chloride and alcohol. However, these substances are used in many dental products and are tolerated well by most patients. In addition, all ingredients are listed on the packaging so that it can be easily established if the product is safe to use for allergy sufferers and/or the dental professional.

Cervitec F may cause slight reversible irritation on contact with mucous membranes. A note to this effect is included in the Instructions for Use.

5.3 Conclusion

When administered as recommended, Cervitec F is toxicologically safe for patients and users.

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