ORIGINAL RESEARCH

Remineralization of Enamel Using Topical Agents among Patients with Orthodontic Brackets: *In Vivo* and *In Vitro* Randomized Control Trial

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Abstract

Aim and background: To evaluate the *in vivo* and *in vitro* effects of three topical agents in reducing enamel demineralization around orthodontic brackets. Postorthodontic enamel demineralization persists to be undesirable and common complication.

Materials and methods: Twenty patients, who consented, were included into three experimental and a control group, following screening for inclusion, exclusion, and randomization. The experimental group was intervened with either GC Tooth Mousse Plus®, Clinpro® Tooth Cream, or Amflor® toothpaste. The baseline values were recorded using DIAGNOdent® following oral prophylaxis and brackets were bonded. The intervention group received the respective topical application of agents. Posttreatment values were recorded after 90 seconds of intervention and 20th day postintervention. Extraction of respective tooth was done on the 21st day to evaluate the microhardness using the Vickers hardness test.

Results: The results show the effectiveness of GC Tooth Mousse Plus® over Amflor® toothpaste followed by Clinpro® Tooth Cream for remineralization among patients undergoing orthodontic treatment and microhardness was highest for GC Tooth Mousse Plus®.

Conclusion: Topical agents can be used effectively as remineralizing agents in patients undergoing orthodontic treatment.

Clinical significance: Advanced diagnostic tools like the DIAGNOdent Pen® and remineralizing agents contribute to a comprehensive and proactive approach to dental care, particularly in populations with specific risk factors like children with high sucrose consumption.

Keywords: Demineralization, Microhardness, Randomized clinical trial, Remineralizing agents, Topical agents.

International Journal of Clinical Pediatric Dentistry (2024): 10.5005/jp-journals-10005-2975

Introduction

Enamel decalcification around orthodontic bands and brackets is a significant concern, primarily because these orthodontic appliances such as brackets, bands, elastics, power chains, sleeves, and springs make the maintenance of oral hygiene challenging and lead to increased plaque accumulation. The prevalence of enamel demineralization among orthodontic patients varies widely, reported between 2 and 96%.[1] A combination of fluoride application, oral hygiene education, and dietary control has generally been recognized as effective in reducing the risk of demineralization during orthodontic treatment. However, the success of these preventive measures often relies heavily on the patient's adherence.[1] Research has demonstrated a direct relationship between plaque buildup and the onset of carious lesions in orthodontic patients.[2] Unfortunately, the full extent of demineralization damage often becomes apparent only after orthodontic appliances are removed, with the characteristic white spots forming around where brackets were placed. This leaves patients with well-aligned but visually compromised teeth, somewhat negating the benefits of treatment. The balance between demineralization and remineralization processes is crucial—no net mineral loss occurs if they are in equilibrium, whereas an imbalance can lead to either progressive demineralization or remineralization of white spot lesions that are previously formed.

Casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) compound is the biologically active constituent in GC Tooth Mousse Plus®. Reynolds et al. developed CPP-ACP nanotechnology at Melbourne University; this involves phosphoproteins derived from bovine milk that form nanoparticles by complexing with calcium and phosphorus. When the water-based cream is applied in the mouth, the CPP attaches to the oral tissues, allowing calcium and phosphate ions to dissolve and penetrate the enamel, where they form apatite crystals.[3–5] CPP-ACP functions effectively as a remineralizing agent in acidic environments (as low as pH 4.0), as well as in neutral and alkaline conditions.[3,4] GC Tooth Mousse Plus® also contains CPP clusters that can bind fluoride, in addition to calcium and phosphate, which helps stabilize these elements as soluble complexes known as casein phosphopeptide-amorphous calcium fluoride phosphate.[5,6]

Clinpro® Tooth Cream, a white paste, contains 950 ppm sodium fluoride and 500 ppm functionalized tricalcium phosphate (TCP). TCP is milled with sodium lauryl sulfate and releases calcium, phosphate, and fluoride upon contact with saliva during brushing.

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How to cite this article: Sain S, Hegde SK, Bhat SS, *et al.* Remineralization of Enamel Using Topical Agents among Patients with Orthodontic Brackets: *In Vivo* and *In Vitro* Randomized Control Trial. Int J Clin Pediatr Dent 2024;17(10):1093–1098.

Source of support: Nil

Conflict of interest: None

The tooth enamel naturally absorbs these components, preventing demineralization and promoting remineralization. Clinpro® contains the same ions found in saliva, and TCP helps increase calcium levels in both plaque and saliva.[3]

Amflor® toothpaste contains 1000 ppm amine fluoride, which supports the remineralization of calcium and phosphate. Amine fluorides were initially studied for their cariostatic potential in Zurich, Switzerland.[7] They were designed to improve fluoride's affinity to enamel by using an organic cationic molecule, making the enamel more resistant to acidic conditions. In 1967, Muhleman demonstrated that organic fluoride was more effective than inorganic fluoride in preventing caries.[7] Amine fluoride raises fluoride concentration in the enamel, exhibits antienzyme effects on microbial activity, and reduces plaque formation due to its surfactant properties.[8,9]

DIAGNOdent® is a portable diode laser fluorescence device, based on research by Hibst and Gall, that utilizes laser autofluorescence at a wavelength of 655 nm (output <1 mW). The device projects light *via* an angled tip to the tooth's occlusal surface. Surrounding the central fiber, additional fibers collect the emitted fluorescence. This reflected light is filtered, and a photodiode measures fluorescence intensity, displaying the result as a score ranging from 0 to 99 with an audible beep. Scores include: 0–12 for healthy tooth structure, 13–24 for decalcification, and >25 for dentinal caries.[10–12]

Hardness is a measure of a material's resistance to localized deformation, such as a dent or scratch. Hardness testing involves applying a small, sharp object to the material and measuring the indentation's size or depth, which correlates to a hardness value. Softer materials have larger and deeper indentations, resulting in lower hardness numbers. The microhardness of materials is typically assessed using Vickers or Knoop hardness tests with loads <2*N*.[13,14]

Aim of the Study

The primary goal of this research was to assess the effectiveness of GC Tooth Mousse Plus®, Clinpro® Tooth Cream, and Amflor® toothpaste in both *in vivo* and *in vitro* settings for reducing enamel demineralization around orthodontic brackets. Additionally, the study aimed to compare the performance of these products against a control group that did not receive any of the topical treatments.

Study Objectives

The specific objectives of this study were:

To evaluate remineralization effects: Determine how GC Tooth Mousse Plus®, Clinpro® Tooth Cream, and Amflor® toothpaste influence the remineralization process of enamel surrounding orthodontic brackets in both *in vivo* and *in vitro* environments.

To detect the *in vivo* changes in fluorescence of enamel surface subjected to remineralization by GC Tooth Mousse Plus®, Clinpro® Tooth Cream, and Amflor® toothpaste using laser fluorescent device, that is, the DIAGNOdent® at three different points of time (1) before starting the treatment, (2) immediately after placing the bracket, and (3) after 20 days.

To evaluate the microhardness of enamel following the remineralization using a microhardness tester.

Materials and Methods

Study Setting and Ethical Considerations

This investigation was conducted at the Department of Pedodontics, Yenepoya Dental College in Mangalore. Participants were selected from the Department of Orthodontics to ensure they met the study criteria. Before initiating the study, ethical approval was obtained from Yenepoya University to ensure that all research protocols adhered to ethical standards and protected the rights and well-being of the participants.

Source of Data

The study involved 20 participants aged between 11 and 17 years who were scheduled to undergo premolar extractions for orthodontic purposes.

The parents of those patients, who are willing to participate in the study had been supplied with printed information sheets both in English and Kannada, detailing the study procedure except for the name of the material being used, that is, the patient will be blinded. All cases will be performed by a single operator.

The materials evaluated in this research included:

GC Tooth Mousse Plus®: Contains Casein Phosphopeptide-Amorphous Calcium Fluoride Phosphate (CPP-ACFP, Recaldent, GC Corporation) LOT111205S.

Clinpro® Tooth Cream: Features functionalized tricalcium phosphate (fTCP) and sodium fluoride (NaF) from 3M ESPE, LOT10011.

Amflor® Toothpaste: Comprises amine fluoride from Group Pharmaceuticals, B.AM109 (Fig. 1).

For fluorescence measurements, the DIAGNOdent Pen® (KaVo, Germany) was utilized (Fig. 2), and the Vickers hardness tester

Fig. 1: Topical agents used for the study

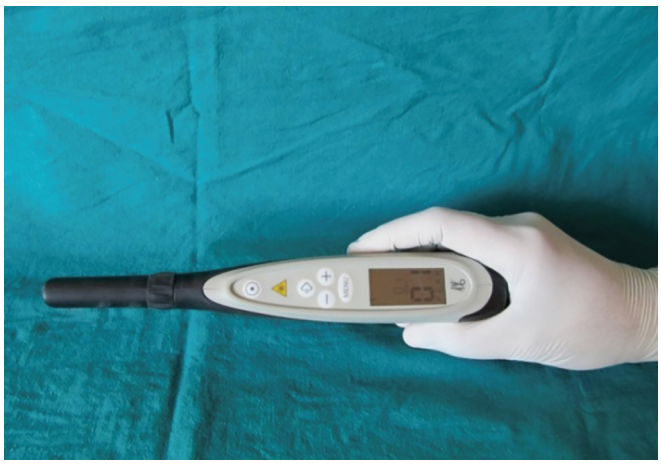

Fig. 2: DIAGNOdent

(Clemex, National Institute of Technology, Suratkal) was employed for assessing microhardness (Fig. 3).

Data Collection Methodology

Twenty patients within the age range of 11–17 years, all scheduled for premolar extractions for orthodontic reasons, were enrolled in the study after obtaining written consent from their parents. The study was designed as a parallel group trial, with three experimental groups and one control group. Initial assessments included clinical and radiographic evaluations to determine baseline caries risk. All participants received oral prophylaxis before treatment, and their salivary flow rate, pH, and buffering capacity were measured. Baseline values for selected teeth were recorded using the DIAGNOdent® device before bracket placement.

Inclusion Criteria

There should not be any active caries lesions. Baseline values were selected as follows: salivary flow rate in the normal range of >1.0 mL/minute, pH between 6.8 and 7.8, and buffering capacity ranging from 6.0 to 9.0.

Exclusion Criteria

There should not be visible signs of caries, fluorosis, developmental defects, or fractures. Patients with periodontally compromised teeth were also excluded.

Saliva-Check Buffer

An *in vitro* test was done to evaluate saliva quality, pH, and buffering capacity.

Saliva quantity: Unstimulated saliva was collected in a measuring cup; quantities exceeding 1.0 mL/minute were deemed normal.

pH measurement: Patients expectorated saliva into a collection cup, and a pH test strip was immersed for 10 seconds. The resulting color was compared against a standardized chart.

Buffering capacity: A buffering strip was placed on absorbent tissue. Saliva was applied using a pipette, and the strip was observed for color changes after 2 minutes. Points were assigned based on color, categorizing buffering capacity as very low (0–5 points), normal (6–9 points), or high (10–12 points).

Methods

All participants were examined for eligibility based on the inclusion and exclusion criteria. Salivary flow rate and buffering capacity were documented. Baseline fluorescence values of the selected teeth were measured using the DIAGNOdent® Pen before bracket placement, with readings taken from four sites around each bracket: mesial, distal, occlusal, and cervical.

Participants were randomly assigned to one of four groups using a lottery method, ensuring blinding for both the principal investigator and the patients. A total of 76 Begg brackets were bonded to the premolars designated for extraction. The bonding process involved surface preparation with gel of 37% phosphoric acid, application of the bonding agent Transbond Plus® (3M Unitek, United States), and placement of stainless steel premolar orthodontic brackets using flowable composite Transbond XT® (3M Unitek, United States). Excess resin was removed, and the resin was polymerized using a curing light for 20 seconds. Postbracket placement, DIAGNOdent® readings were taken to assess demineralization.

Group allocation:

- Group I: GC Tooth Mousse Plus®.
- Group II: Clinpro® Tooth Cream.
- Group III: Amflor® Toothpaste.
- Group IV: Control group (no topical agents).

Topical agents were applied around the orthodontic brackets in the intervention groups and left undisturbed for 5 minutes to standardize application. Throughout the study period, all participants used nonfluoridated dentifrice, maintained their normal brushing habits without additional oral hygiene instructions, and were instructed to avoid antibacterial substances like mouth rinses. Remineralization was evaluated using DIAGNOdent® at the four specified sites. After 20 days, the brackets were removed, and the teeth were extracted, stored in gauze with 2% formalin to maintain pH, and analyzed for demineralization using a microhardness tester.

Microhardness Assessments

A single, blinded operator conducted the microhardness assessments. The roots were sectioned at the cementoenamel junction using a diamond disk, and the crowns were embedded in dental stone, exposing a 1 mm area around the brackets (Fig. 4). The crown sections were polished with abrasive paper (600, 800, and 1200 grit) and a polishing cloth. Microhardness was measured with a Vickers hardness tester under load of 100 kg for 30 seconds. Three indentations were made per tooth, and digital readings were recorded.

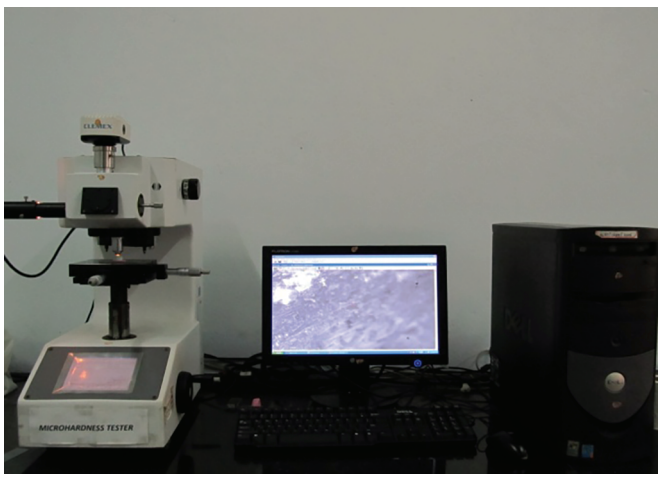

Fig. 3: Microhardness tester (digital)

Fig. 4: Sectioned teeth mounted in dental stone

Statistical Analysis

Statistical analysis data were nonparametric, not assuming a specific population distribution. Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) version 17.0. Teeth were grouped for each subject during *in vivo* evaluations. The Kruskal–Wallis test and Mann–Whitney *U* test were utilized to compare average DIAGNOdent® readings across different materials and stages (Fig. 5). Microhardness was compared using Scheffe multiple comparisons (Fig. 6).

Results

Descriptive statistics and results of laser fluorescence are shown in Table 1. Multiple comparisons of intergroup show remineralization potential was more with GC Tooth Mousse Plus® when compared with Clinpro®, and Amflor® ($p < 0.01$). Clinpro® was better than Amflor® when both of the agents were compared using laser fluorescence ($p < 0.01$). It signifies that remineralization potential of GC Tooth Mousse Plus® > Clinpro® Tooth Cream > Amflor® toothpaste using laser fluorescence.

Descriptive statistics and results of microhardness are done by Scheffe multiple comparisons (Table 2). It shows high statistical

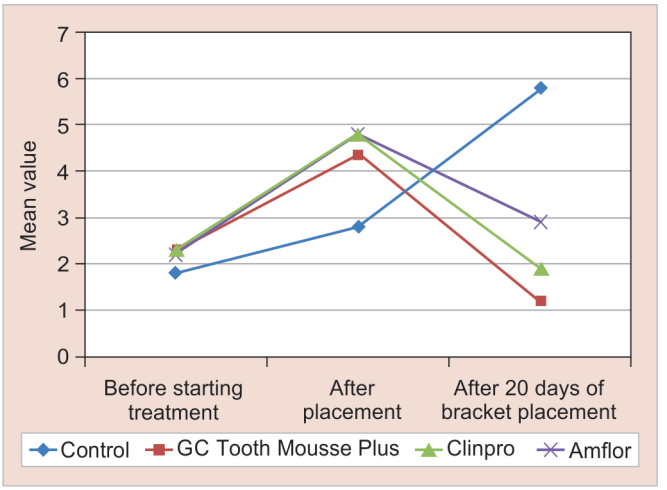

Fig. 5: The line diagram depicts the mineralization rates (of various topical agents at prebracket placement, 90 seconds after bracket placement, and 20 days postbracket placement

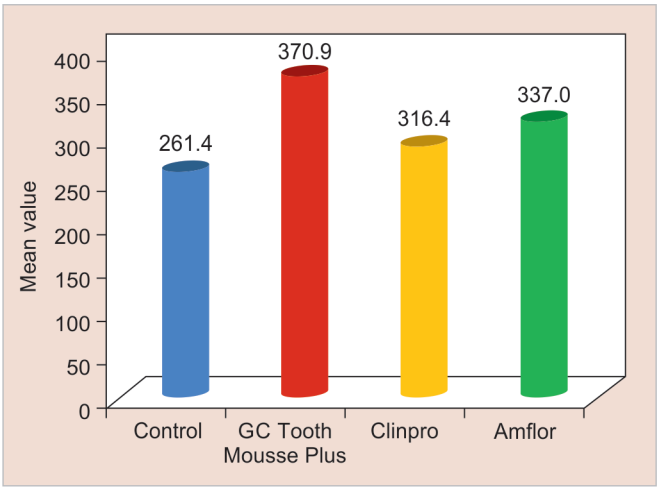

Fig. 6: The bar diagram depicts the remineralization potential of various topical agents and controls

Table 1: Comparison of average DIAGNOdent readings for different material at different stages

Distal	*Group*	*Mean ± SD*	*Median*	*$X^{2\#}$*	*p*	*Pair*	*$p^{\$}$*
Pretreatment	Control (IV)	1.8 ± 0.9	1.8	5.42	0.143		
	GC Tooth Mousse Plus (I)	2.3 ± 0.8	2.1				
	Clinpro (II)	2.3 ± 0.7	2.1				
	Amflor (III)	2.2 ± 0.8	2.0				
90 seconds after placement	Control (IV)	2.8 ± 1.1	2.6	27.43**	0.000		
	GC Tooth Mousse Plus (I)	4.4 ± 1.3	4.3			B vs C	0.163
	Clinpro (II)	4.8 ± 0.9	4.9			B vs D	0.168
	Amflor (III)	4.8 ± 1.3	4.9			C vs D	0.799
After 20 days of bracket placement	Control (IV)	5.8 ± 1.8	5.6	67.62**	0.000		
	GC Tooth Mousse Plus (I)	1.2 ± 0.2	1.0			B vs C	0.000
	Clinpro (II)	1.9 ± 0.3	2.0			B vs D	0.000
	Amflor (III)	2.9 ± 0.4	3.0			C vs D	0.000

$^{\#}$Kruskal–Wallis Test; $^{\$}$Mann–Whitney *U* test; **Significant at 0.01 level

Table 2: Comparison of microhardness among topical agents on the 21st day following the intervention using Vickers hardness tester

						Scheffe multiple comparisons		
Group	*Mean*	*SD*	*N*	*f*	*Sig.*	*Pair*	*f*	*p*
Control (IV)	261.4	28.0	20	142.78**	0.000	A and B	136.09**	0.000
GC Tooth Mousse Plus (I)	370.9	16.4	20			A and C	32.57**	0.000
Clinpro (II)	316.4	6.5	18			A and D	61.38**	0.000
Amflor (III)	337.0	4.8	18			B and C	31.9**	0.000
						B and D	12.39**	0.000
						C and D	4.3	0.008

**Significant at 0.001 level

significant differences among all four groups in this study ($p < 0.01$). It can be concluded that GC Tooth Mousse Plus® shows better microhardness than Clinpro® and Amflor®.

Overall, the study concluded that applying GC Tooth Mousse Plus®, Amflor®, and other agents to tooth surfaces around orthodontic brackets effectively prevented demineralization. The null hypothesis was supported, indicating that CPP-ACFP, TCP-NaF, and amine fluoride are viable remineralizing agents.

Discussion

Enamel consists of hydroxyapatite crystals enveloped by a layer of tightly bound water, creating an electrically charged hydration shell that attracts remineralizing ions. The porous nature of enamel allows acids to penetrate deeper layers, but it also facilitates the return of beneficial ions for remineralization, enabling enamel to repair noncavitated lesions with minimal intervention.[15]

Mineral-rich agents supplying calcium and phosphate ions can diffuse through porous enamel to promote remineralization.[16–19]

Studies conducted by Uysal et al. and Bailey et al. had shown a high positive correlation in their studies when GC Tooth Mousse Plus® was used for remineralization. There are only limited studies done with GC Tooth Mousse Plus®.[20–22] Krithikadatta conducted a randomized study to assess the efficacy of GC Tooth Mousse Plus®, Tooth Mousse®, and the results were highly promising when compared to fluoride alone. This was in agreement with the present research.[23] However, some studies, such as those by Sitthisettapong et al. and Beerens et al., reported mixed or insignificant results, possibly due to differing study parameters.[24,25]

Research on Clinpro® supported the present study, with Jo et al. finding that toothpaste containing fTCP and CPP-ACP were more effective than those with 1000 ppm fluoride.[26] Robert et al. concluded that Clinpro® provided superior surface and subsurface remineralization and that combining 5000 ppm fluoride with the tricalcium phosphate system offered substantial anticaries benefits.[27]

Studies on Amflor® were consistent with the current study's results. Priyadarshini et al. reported that amine fluoride compounds significantly increased enamel microhardness, and Shetty et al. found that organic fluoride (amine fluoride) was more effective in restoring enamel hardness than inorganic fluoride.[28,29]

In this study, when laser fluorescence was considered four sites in each premolar were taken into account and the average value was taken. Then readings of premolars were averaged for intercomparison of groups. So, the case of only two premolar extractions included in the study does not make a difference when average value was taken into account.

Microhardness was assessed due to its strong correlation with enamel mineral content and caries lesion severity.[20] The findings indicated greater mineral loss in the cervical region compared to the distal region, likely due to increased plaque accumulation and reduced brushing effectiveness in these areas.

In the current investigation, participants were randomly assigned to various groups, with each group receiving only one specific agent. This was based on baseline clinical, radiological, salivary, and laser fluorescence data, which indicated that all participants had an equivalent risk for demineralization. Pascotto et al. explained that enamel hardness is reduced in the cervical region of the bracket compared to the occlusal region.[30] In this trial, greater mineral loss was observed in the cervical area, followed by the distal region, as indicated by DIAGNOdent® values. This pattern can be attributed to increased plaque and debris accumulation, along with less effective brushing in these regions. The samples subjected to remineralization were evaluated with a laser fluorescence device (DIAGNOdent®) at three time points: before bracket placement, after bracket placement, and after 20 days. The changes in fluorescence readings for samples from groups I, II, and III indicated that a significant level of remineralization had occurred. It is well-known that demineralized enamel becomes more porous, and even a minor surge in porosity results to changes in the optical properties of enamel, resulting in increased light scattering (Pascotto et al.).[30,31] Thus, the changes in fluorescence were expected to correspond with the DIAGNOdent® digital readings. The microhardness evaluation produced similar results. After 20 days, the teeth were extracted and stored in gauze soaked in 2% formalin, ensuring that the pH was maintained at 7. This step was taken to prevent further changes in mineral content during the storage period. The 20-day duration was chosen because demineralization can begin as early as 2–3 weeks after bracket placement.[20] The microhardness tester, which is a sensitive and reliable tool, was used to assess lesion remineralization, as has been reported in earlier studies.[13,30] This method also produces minimal artifacts, thereby reducing the likelihood of inaccurate results. As such, the microhardness tester, in combination with the laser fluorescence device, was employed. Statistically significant differences in microhardness were found between the tested materials and the control. The study's findings demonstrate that applying agents of remineralization can effectively prevent demineralization. However, additional long-term *in vivo* research is necessary to understand the long-term effects of these agents.

Conclusion

From the findings of the study, it can be suggested that laser fluorescence can be an effective adjuvant to monitor remineralization, particularly *in vivo*. With the advent of most advanced techniques to detect caries at the earliest stages and the use of remineralizing agents can favorably retard demineralization and enhance remineralization. It is possible to intercept caries in such a way that the caries process can be reversed favorably to heal the dental tissues as well as prevent demineralization in removable and fixed orthodontic treatments.

Clinical Significance

Remineralizing agents were of great significance in cases of preventive, interceptive, and corrective orthodontics as well as in incipient caries to prevent demineralization of teeth.

Importance for Pediatric Dentistry

- Laser fluorescence device, DIAGNOdent Pen® can be used as a chairside technique to access demineralization.
- The pediatric patients are highly beneficial from these remineralizing agents as they consume high amount of sucrose in the form of sweets, snacks, and also as part of medications (syrups).
- The remineralizing agents, especially GC Tooth Mousse® can act below the critical pH (5.5) which is almost to a pH of 4.

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