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Effect of toothpaste with high fluoride concentration on remineralization of dental substrate with artificial caries

Efeito de dentifrícios com alta concentração de flúor na remineralização de substrato dentário com cárie artificial

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Resumo

Introdução: dentifrícios fluoretados são amplamente utilizados pela população. Foram desenvolvidos dentifrícios com alta concentração de fluoreto de sódio e presença de tricálcio fosfato, fornecendo proteção adicional a pacientes vulneráveis ao desenvolvimento da cárie. **Objetivo:** o objetivo deste estudo foi avaliar a influência de diferentes dentifrícios na dureza superficial, interna e desgaste do esmalte após cárie artificial, ciclagem de pH e escovação. **Material e método:** blocos de esmalte (4x4 mm) foram obtidos a partir de 20 dentes bovinos. Os espécimes foram submetidos à lesão de cárie artificial e, em seguida, à ciclagem de pH e escovação de acordo com o dentifrício: Colgate Total 12 e Clinpro + Tricálcio Fosfato. Após este período, foram submetidos à análise de dureza superficial e interna e perfilometria. Foi realizada microscopia eletrônica de varredura. **Resultado:** os dados obtidos foram avaliados por ANOVA um critério para avaliar a recuperação mineral e perfilometria, ANOVA dois critérios medidas repetidas para avaliar a dureza superficial e interna. **Conclusão:** analisando a dureza superficial, após a indução da cárie houve uma redução significativa na dureza que foi parcialmente recuperada independente do dentifrício utilizado. Para dureza interna, Clinpro obteve valores menores no lado controle e até 90 micrômetros no lado teste. Quanto à perfilometria, o Colgate Total 12 apresentou maior desgaste quando comparado ao Clinpro. Concluiu-se que Clinpro promoveu menor dureza interna, porém, o Colgate Total 12 resultou em maior desgaste superficial do esmalte dentário.

Descritores: Creme dental; esmalte dental; remineralização dentária.

Abstract

Introduction: fluoride toothpaste is widely used by the population. **Objective:** dentifrices with a high concentration of sodium fluoride and the presence of tricalcium phosphate were developed, providing additional protection to patients vulnerable to the development of caries. This study aimed to evaluate the influence of different dentifrices on the surface and internal hardness and enamel wear after artificial caries, pH cycling, and toothbrushing. **Material and method:** enamel blocks (4x4 mm) were obtained from 20 bovine teeth. The specimens were submitted to artificial caries lesion and then to pH cycling and brushing according to the dentifrice: Colgate Total 12 and Clinpro + Tricalcium Phosphate. **Result:** after this period, they were submitted to analysis of superficial and internal hardness and profilometry. Scanning Electron Microscopy (SEM) was performed. The data obtained were evaluated by one-way Analysis of Variance (ANOVA) to evaluate the mineral recovery and profilometry, and two-way repeated measures ANOVA to evaluate the superficial and internal hardness. **Conclusion:** analyzing the surface hardness, after caries induction, there was a significant reduction in hardness that was partially recovered regardless of the dentifrice used. For internal hardness, Clinpro obtained lower values on the control side and up to 90 micrometers on the test side. As for profilometry, Colgate Total 12 showed greater wear when compared to Clinpro. It was concluded that Clinpro promoted lower internal hardness, however, Colgate Total 12 resulted in greater surface wear of tooth enamel.

Descriptors: Toothpaste; dental enamel; dental remineralization.

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INTRODUCTION

Lack of oral hygiene care can worsen the clinical condition of hospitalized patients, as long periods of hospitalization can allow the evolution of pre-existing infections and increase the risk of developing opportunistic infections[1]. Under healthy conditions, the relationship between microorganisms in the oral cavity is symbiosis, in which different species interact beneficially with each other, without harming the oral environment[2]. However, when there are systemic changes, in the standard of oral hygiene or with the use of antimicrobials, the balance between the species is broken and the environment becomes conducive to the expression of pathogenic microorganisms. In this sense, the inclusion of a dental surgeon in the hospital team contributes to reducing the risk of dental caries, and periodontal disease and preventing the oral cavity from becoming a focus of infection and dissemination of microorganisms to the systemic circulation.

Fluoride toothpaste with 1450 ppm of fluoride is widely used by the population; dentifrices with a high concentration of sodium fluoride (5000 ppm) were recently developed for specific indications[3]. Due to their high concentration of fluoride, they are only available under professional prescription for specific cases such as a high risk of developing caries lesions. In this context, due to the ability of phosphates to stimulate the process of mineral balance and deep remineralization of caries lesions, tricalcium phosphate (PTC)[2,4] has been added to certain toothpaste to provide additional protection to patients vulnerable to the development of caries.

This study aimed to evaluate the influence of different dentifrices on the surface and internal hardness, in addition to enamel wear, after artificial caries induction, pH cycling, and brushing. The established null hypothesis was that there would be no difference between the dentifrices in superficial and internal hardness and the profilometry of the dental enamel.

MATERIAL AND METHOD

The project was submitted and approved by the animal research ethics committee (Process 00513-2019). Twenty bovine teeth were selected and stored in 0.1% thymol solution for 30 days. Organic debris was removed with a periodontal curette. Enamel blocks (4x4mm) were obtained through cuts in the mesiodistal and inciso-cervical directions in the central region of the crown with a diamond disk (Buehler, Illinois, USA) mounted on a precision cutter (Isomet 1000, Buehler, Illinois, USA).

Enamel blocks were standardized according to surface hardness, and specimens with values 10% below and above average were excluded[5]. Initial hardness was analyzed at the center of the specimens on a micrometer (Micromet 5114 and OmniMet Software - Buehler, Lake Bluff, Ill, USA), performing 5 indentations with a pyramidal Knoop tip, 50 cm apart, under a static load of 25 g for 10 seconds[5]. Stratified randomization was performed to distribute samples with similar hardness values among the groups, ensuring that the values were statistically similar after the caries challenge.

To induce artificial caries, one hemiface of each sample was protected with acid-resistant varnish (Colorama, São Paulo, BR), creating a control area. The blocks were immersed in 30 ml of demineralizing solution (2 mM Ca (NO_3) 2 × $4H_2O$, 2 mM Na_2HPO_4 × $2H_2O$, acetate buffer 0.075 M, and 0.04 ppm F, pH 4.7, 6 hours/day) and 30 ml of remineralizing solution (1.5 mM $Ca(NO_3)$ 2 × $4H_2O$, 0.9 mM Na_2HPO_4 × $2H_2O$, 1.50 mM KCl, 0.2 M Tris and 0.05 ppm NaF, pH 7.0, 18 hours /day) renewed daily for 7 days[6]. The samples were submitted to surface hardness analysis to verify the reduction of hardness values (DS1).

Then, for pH cycling, the specimens were immersed in 35 ml of demineralizing solution (2.0 mmol L-1 Ca, 2.0 mmol L-1 P, 0.075 mol L-1 acetate buffer, 0.04 g F/mL, with pH 4.7) for 6 hours, and in remineralizing solution (1.5 mmol/L Ca, 0.9 mmol/LP, 0.15 mmol/L KCl, 0.02 mmol/L cacodylate buffer of sodium, 0.05 g of F/mL, with pH 7.0) for 18 hours[7]. For brushing, Colgate Total 12 (CT) and Clinpro + Tricalcium Phosphate (CL) toothpaste were used, described in Table 1. The dentifrices were weighed and diluted in distilled water (1:3); 2 ml was pipetted onto the specimens of each group and brushed manually with an electric brush (Oral B Professional Care 5000 Oral B Schwalbacham

Taunus, DE) equipped with a pressure sensor whose red light turned on when the pressure exerted reached a value of 2N. Brushing was performed twice a day at an interval of 12 hours, with 15 seconds of simulated brushing and immersion in the toothpaste for up to 2 minutes[8].

Table 1. Trade name, fluoride concentration, composition, and manufacturer of the dentifrices used in this study

TRADE NAME	FLUORINE CONCENTRATION	COMPOSITION	MANUFACTURER
COLGATE TOTAL 12 (CT)	1450 ppm	Glycerin, water, hydrated silica, sodium lauryl sulfate, arginine, zinc oxide, cellulose gum, poloxamer 407, tetrasodium pyrophosphate, zinc citrate, benzyl alcohol, cocamidopropyl betaine, sodium fluoride, sodium saccharin, xanthan gum, phosphoric acid, sucralose, eugenol.	Colgate-Palmolive (São Bernardo do Campo, BR) (Lote 9080BR122D)
CLINPRO 5000 (C)	5000 ppm	Sodium fluoride, water, sorbitol, hydrated silica, glycerin, amorphous silica, polypropylene-polyethylene glycol, aroma, polyethylene glycol, sodium lauryl sulfate, titanium dioxide, carboxymethylcellulose, sodium saccharin, and tricalcium phosphate.	3M ESPE (St Paul, EUA) (Lote 11038)

For surface hardness, 5 indentations were made 100 μm apart in the control and test areas[9], to assess whether the dentifrices altered the final surface hardness (SH2)[9]. The percentage recovery of surface hardness (% SH) was calculated by the formula [% RSH = 100 (SH2-SH1) / SH1][9]. For the internal hardness analysis, the specimens were longitudinally sectioned in the central region and embedded in acrylic resin, sequentially polished with silicon carbide sandpaper (#600, #800, and #1200) until the entire enamel surface was exposed. Seven indentations were performed with depth distances of 10, 30, 50, 70, 90, 110, and 220 μm, both on the control side and on the test side, with a Knoop indenter under a load of 5g for 10 seconds[9]. The averages were calculated for each distance and values converted to mineral content (vol% min = 3.66 * (√KHN) + 21.19)[9]. The integrated mineral area of the lesion and healthy enamel was calculated using a trapezoidal rule. The values obtained were subtracted from the integrated area of the post-demineralized enamel, resulting in the integrated mineral recovery (IMR).

Mineral tissue loss was determined using an optical profilometer (Surftest SJ 401, Mitutoyo American Corp)[8]. In the center of the enamel samples, 3 scans (2 mm in length) were performed with an interval of 0.5 mm between them. The scans were interpreted with specific software coupled to the profilometer based on the construction of regression lines between the reference and experimental areas. Tissue loss (μm) was defined from the vertical distance between the regression lines of the reference area (previously protected by varnish) and the area submitted to pH cycling and brushing. The average between the three scans was calculated[8]. Three representative specimens from each group (control and test) were analyzed under a Scanning Electron Microscope (SEM) (EVO LS-15, Carl Zeiss, Oberkochen, DE) at 3000x magnification, to observe the differences structures in healthy and caries-affected enamel after pH cycling and toothbrushing.

The data obtained in this study were submitted to the normality and homogeneity test. One-way Analysis of Variance (ANOVA) was used to assess mineral recovery and profilometry, two-way repeated measures ANOVA to assess surface and internal hardness, and Tukey's test post-test for multiple comparisons. All analyzes were performed with a significance level at 5%.

RESULT

According to the data obtained in the surface hardness analysis (Table 2), when comparing the dentifrices, there was no statistically significant difference in any treatment period. When comparing the surfaces, there was a difference between sound enamel, decayed enamel, and after treatment with the respective dentifrices, with lower values for decayed enamel. Through the calculation of the mineral recovery, we observed that both groups did not present statistically significant differences after the treatments.

Table 2. Mean and standard deviation of surface hardness (KH) and mineral recovery (%) analysis

	CT	CL
HEALTHY	345.04 ± 7.23 Aa	340.94 ± 7.63 Aa
ARTIFICIAL CARIES	57.86 ± 21.17 Ac	54.34 ± 23.00 Ac
TREATMENT	148.18 ± 25.16 Ab	144.36 ± 21.10 Ab
MINERAL RECOVERY	31.05 ± 9.60 A	30.8 ± 10.05 A

Capital letters compare toothpaste. Lowercase letters compare the surfaces.

The results of the internal hardness (Table 3) showed that the CL dentifrice obtained lower values on the control side and up to 90 micrometers on the test side. When evaluating the different depths of each dentifrice on the control side, the CT group showed less hardness for the distance of 10 and 30 micrometers, with a statistical difference for the other measures, stabilizing from 50 micrometers. Likewise, the CL group presented the lowest hardness observed for the distance of 10 micrometers and a gradual increase up to 220 micrometers. When analyzing the side submitted to the challenges, there were statistical differences of up to 50 micrometers for the CT group and of up to 70 micrometers for the CL group. From 70 to 90 micrometers, the CT group approached the deepest distances and upon reaching 110 micrometers, it reached hardness stability, while the CL group no longer showed statistical differences at 110 micrometers. Finally, there was a difference between the control and test sides at the same depth, and toothpaste was only up to 50 micrometers. As for profilometry, CT toothpaste showed a higher enamel wear profile (-47.9 ± 4.9) when compared to CL (-17.5 ± 2.2).

Table 3. Mean and standard deviation of internal hardness (KH) analysis

	CONTROL	
DEPTH	CT	CL
10	206.23±11.49 Ab	183.49±15.51 Bc
30	220.61±16.17 Aab	195.29±18.49 Bbc
50	227.16±12.75 Aa	200.25±19.66 Bbc
70	229.9±16.11 Aa	201.4±14.95 Bbc
90	235.84±12.47 Aa	209.26±13.70 Bab
110	236.64±14.27 Aa	213.30±16.90 Bab
220	244.56±7.72 Aa	224.09±11.74 Ba
	TEST	
10	104.35±4.23 Ae#	68.13±6.15 Bf#
30	163.01±26.61 Ad#	129.24±28.48 Be#
50	200.91±22.08 Ac#	161.25±23.62 Bd#
70	212.37±14.15 Abc	192.83±11.77 Bc
90	229.10±10.75 Aab	209.01±18.44 Bbc
110	232.47±9.8 Aa	216.4±16.08 Aab
220	236.03±9.0 Aa	229.08±20.6 Aa

Capital letters compare toothpaste. Lowercase letters compare depths. #Statistical differences within the same dentifrice and depth after challenges.

Figure 1 represents micrographs obtained by SEM with a magnification of 3000x illustrating the surface appearance of the samples on the control side (A), treated with CT (B), and treated with CL (C). In Figure 1B, it is possible to observe greater disorganization of the surface in Figure 1A and 1C, while Figure 1C is characterized by greater homogeneity of the surface after treatment.

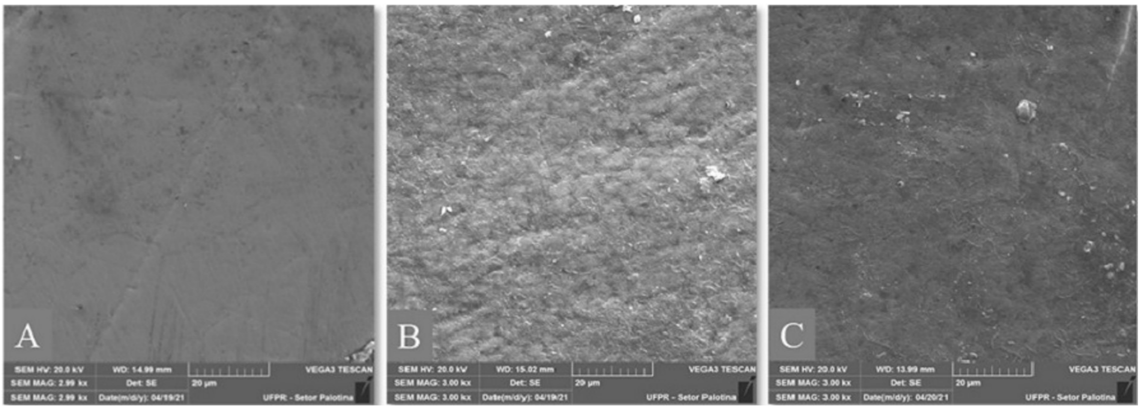

Figure 1. Scanning electron microscopy of the tooth enamel surface on the control side (A), treated with Colgate Total 12 toothpaste (B) and Clinpro toothpaste (C). 3000x magnification.

DISCUSSION

In this study, the enamel surface hardness test was used at three different times (initial, after artificial caries induction, and after treatments) to identify the achieved mineral reduction. Despite having a 96% of inorganic load, the mineral balance of enamel is compromised due to constant exposure to acids, which promote the dissolution of ions and create subsurface lesions into the interprismatic spaces[10]. Through salivary action and adjuvant remineralizing therapies, there is a tendency to recover lost ions; however, recovery may not occur in its entirety and leave unevenness in the tooth structure. For this reason, profilometry was used to identify the enamel wear between the healthy side and the side subjected to artificial caries after brushing with the dentifrices to be analyzed.

The hypothesis of this study was denied, as the dentifrices showed differences in internal hardness and profilometry. After inducing the formation of artificial caries, the enamel showed a significantly reduced hardness in the initial reading, confirming the methodology used to induce artificial caries[6]. In general, the mechanism of action of dentifrices occurs through the inhibition of the demineralization process and increased remineralization, promoting preventive action on healthy substrates and therapy against caries[11]. Also, dentifrices with sodium fluoride act by forming fluorapatite, which is the union of fluoride with hydroxyapatite crystals present in tooth enamel[12]. According to the manufacturer, during the remineralization process, CL promotes a neutral or slightly alkaline pH[13]. With the addition of TCP, the action on subsurface areas is expected to be more effective than toothpaste with sodium fluoride alone. In the toothpaste production process, the ions are protected by a modified carboxylic acid (fumaric acid) that produces β-TCP[14,15]. When this substance came into contact with the aqueous medium, the interface between the acid that protects the ions was disrupted, releasing calcium and phosphate into the medium.

In contrast to this study, there are some *in vitro* and *in situ* evidences on the effects of β-TCP present in solutions, mouthwashes, dentifrices, and varnishes, showing that the association with fluoride improves enamel hardness, fluoride absorption, remineralization of white spot lesions, and release of calcium in saliva[13,16-20].

Some factors may explain the difference between the results of this study in the literature, such as the presence of biofilm, brushing time, and type of storage. In the present study, a chemical process was used to induce artificial caries, unlike models with biofilm where the dentifrice can bind to the acquired film, acting as an additional reservoir to enhance the action of the dentifrice[21]. In addition, the total time of contact of the samples with the dentifrice was 2 minutes, based on the time it takes an individual to brush the teeth[22]. Featherstone et al.[*] indicated that 5 minutes of contact of the dentifrice with the surface is adequate to promote greater fluoride retention[2,*]. It is also known that storage in artificial saliva plays a fundamental role in the remineralization process, which may influence the results of *in vitro* studies that evaluate toothpaste[23].

The advantages of the presence of a high concentration of fluoride and TCP in the CL toothpaste could be evidenced in the profilometry results, as it presented better resistance to degreasing the CT. It is known that in addition to compositional characteristics, abrasiveness can affect the action of dentifrices on enamel wear. In addition to containing active principles, dentifrices have characteristics related to abrasiveness. In this context, measures such as RDA (relative dentine abrasion) and REA (relative enamel abrasion) are present in studies that investigate the effect of toothpaste abrasiveness, showing that dentin is more susceptible to abrasion than enamel. However, not all companies provide RDA and REA values, as well as the relationship between RDA and REA is not necessarily direct, as a toothpaste that has a high RDA value may have a low REA value and vice versa[24]. The CL toothpaste used in the present study had an RDA of 62.15 and REA of 3.49, while the CT toothpaste had an RDA value between 70 and 78 and an unspecified REA value[25]. It is noteworthy that representative SEM images demonstrated the superior roughness promoted by CT toothpaste compared to CL (Figure 1A and 1B).

Correlating the results of internal hardness and profiling, it is speculated that the superiority of the CT results about the CL is due to the removal of enamel weakened by the artificial caries process. The effect of artificial caries associated with the treatments promoted a porous surface, mainly in the CT group. There is a condition called lamination, in which the acid diffuses through the porosities without plugging them, resulting in the demineralization of the previously treated area[26]. It is noteworthy that this condition varies according to the pH cycling model and the fluorine concentration in the dentifrice. Although the surface was rougher on the CT dentifrice, as seen in Figure 1B, the interaction between sodium fluoride and the available minerals was able to neutralize the acids and create an effective barrier against demineralization. The initial distances are fundamental to detect the differences found in the hardness values, and in this study, it was evident that the CL toothpaste traveled a greater distance to achieve stability in the internal hardness. Other reported factors also contribute to the surface appearance, such as the presence of abrasive silica, incorporated to increase the cleaning potential, daily contact time with acids, strength, and abrasiveness promoted by brushing, and relative abrasiveness of the dentifrice. As this is an *in vitro* study where some variables are subject to control, the total time of contact with the acid was followed according to the protocol, and the strength and abrasiveness during brushing were also considered adequate since the electric toothbrush used has a pressure sensor that is activated in the face of excessive force[23]. On the other hand, it was not the objective of the study to quantify abrasives and other components in the substrates.

As limitations of this study, the artificial caries model, brushing time and type of storage may have enabled us to find results that are different from those found in the literature and that use protocols with biofilm or longer brushing time. Future studies that combine β-TCP with titanium dioxide or other metallic oxides may make it more stable[14-16]. An alternative is to functionalize it with organic and/or inorganic molecules, allowing the creation of barriers that prevent premature interactions of fluorine-calcium and facilitating the availability of ions when applied to teeth through dentifrices, varnishes, and other means.

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CONCLUSION

Given the data presented, we concluded that on the surface of the enamel, the dentifrice with the highest concentration of fluoride promoted lower internal hardness, however, the conventional dentifrice resulted in greater surface enamel wear.

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CONFLICTS OF INTERESTS

The authors declare no conflicts of interest.

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