

Influence of desensitizing and anti-erosive toothpastes on dentine permeability: An in vitro study



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ABSTRACT

Objective: This study analyzed the effect of desensitizing and/or anti-erosive toothpastes on dentine permeability.

Methods: One-mm dentin discs were prepared from human molars and exposed to EDTA solution (5 min, 17%). Initial dentine permeability was measured, under constant pressure. Specimens were randomly allocated into 10 groups: four anti-erosive toothpastes (calcium silicate + sodium phosphate, potassium nitrate, stannous chloride + chitosan, oligopeptide-104); four desensitizing toothpastes (arginine + calcium carbonate, calcium sodium phosphosilicate, strontium acetate, stannous fluoride); and two controls (regular fluoridated toothpaste, and human saliva). They were submitted to a 5-day erosion-abrasion cycling model. Erosion consisted of immersion in citric acid (2 min, 0.3%, natural pH ~ 2.6, 4x/day), followed by 1 h exposure to human saliva. Specimens were brushed for 15 s (2 N, 45 strokes) with the toothpaste slurries (total exposure time of 2 min). After 5 cycles, the final dentine permeability was determined. Dentine permeability change was calculated as a percentage of the initial hydraulic conductance (%Lp). Data were analyzed with one-way ANOVA and Tukey tests ($\alpha = 0.05$).

Results: The toothpastes calcium silicate + sodium phosphate and potassium nitrate, showed significant decrease in %Lp, with no difference between them. The regular fluoridated toothpaste also decreased the %Lp, not differing from potassium nitrate. No desensitizing toothpaste showed change in %Lp. Human saliva, oligopeptide-104 and stannous chloride + chitosan presented significant increase in %Lp, without difference between them.

Conclusion: Calcium silicate + sodium phosphate, potassium nitrate, and the regular fluoridated toothpaste decreased dentine permeability, whereas the desensitizing toothpastes tested did not.

Clinical relevance: Toothpastes had distinct impacts on dentine permeability, which may reflect a variable effect on the treatment of dentine hypersensitivity. Within the limitations of a laboratory-based study, toothpastes with an anti-erosive claim could also be effective in reducing the pain in dentine hypersensitivity.

1. Introduction

Dentine hypersensitivity (DH) is a short and sharp pain that occurs in open and patent dentinal tubules in response to external stimuli [1,2]. The most accepted theory for the mechanism of pain in DH is the hydrodynamic theory, in which the flow of the dentinal fluid within its

tubules changes in view of the stimuli at the dentine surface [3]. The change in the dentine's fluid flow movement can be analyzed in vitro using a hydraulic conductance system that simulates the intrapulpal pressure and is influenced by the patency of the dentinal tubules [4]. Any reduction of the dentinal lumen or in the patency of the tubules will interfere on the fluid flow movement, and consequently on the

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Table 1
Details of the groups; names, active ingredients, claims and pH of toothpaste slurries.

Groups	Active Ingredients	Claim	Retail name	pH (slurry)
HS (Human Saliva)		Control		7.64
Regular	1450 ppm F ⁻ (MFP and NaF)	Control	Colgate® Caries Protection ^a	7.07
Arginine	1450 ppm F ⁻ (MFP) Arginine and calcium carbonate	Desensitizing	elmex® Sensitive Professional ^c	8.85
CSP	1450 ppm F ⁻ (NaF) Calcium sodium phosphosilicate (CSP)	Desensitizing	Sensodyne® Repair and Protect ^b	8.60
Strontium	1040 ppm F ⁻ (NaF) Strontium acetate	Desensitizing	Sensodyne® Rapid Relief ^d	6.91
Stannous	1450 ppm F ⁻ (SnF ₂ and NaF) 3436 ppm Sn ²⁺	Desensitizing	Blend-a-Med® Complete Protect Expert ^e	6.04
Oligopeptide	1450 ppm F ⁻ (MFP) Oligopeptide-104	Anti-erosion	Candida® Protect Professional ^f	7.44
Stannous-chitosan	1400 ppm F ⁻ (AmF and NaF) 3500 ppm Sn ²⁺ Chitosan (0.5%)	Anti-erosion	elmex® Erosion Protection ^c	6.35
Potassium	1450 ppm F ⁻ (NaF) Potassium nitrate	Anti-erosion	Sensodyne® Pronamel ^d	7.49
CSSP	1450 ppm F ⁻ (MFP) Calcium silicate and sodium phosphate (CSSP)	Anti-erosion	Regenerate ^g	9.01

Manufacturer; country of acquisition.

^a Colgate-Palmolive; Switzerland.

^b GlaxoSmithKline; France.

^c Colgate-GABA; Switzerland.

^d GlaxoSmithKline; Switzerland.

^e Procter and Gamble; Switzerland.

^f Migros; Switzerland.

^g Unilever; France.

intensity of the pain [5].

Most of the treatments for DH aims to block the opened dentinal tubules, preventing the external stimuli to provoke the rapid movement of the dentinal fluid [6–8]. In-office treatments or home-care products can be used with this goal [7,9]. The advantage of in-office treatment is its instant effect, however it could be gradually removed by erosion-abrasion challenges [10], uncovering the dentine tubules. In view of this, in-office treatment would be an option for immediate management of the pain, but not for a long-term treatment, where the frequent exposure to products containing the active ingredients responsible for blocking the tubules would be ideal.

The use of toothpastes is a convenient option to allow frequent exposure of the dentine surfaces to the active ingredients [11]. Currently, there are many toothpastes available on the market claiming to have a desensitizing effect. A recently systematic review on this topic showed that many active ingredients are capable of diminishing DH, without any substantial differences between them [12]. In fact, this review pointed out that there is a high heterogeneity among the studies, which are related to the variability in patient response, and to the different methods of evaluation used (type of stimuli), in addition to the lack of studies not sponsored by companies.

One of the predisposing factors for DH is erosive tooth wear, which is the loss of dental hard tissues due to demineralization caused by the frequent contact of non-bacteria acids associated to mechanical forces, such as abrasion [13,14]. In dentin, demineralization occurs in the peri- and intertubular area, resulting in increased diameter of the lumen of dentinal tubules [15], which is also influenced by toothbrush abrasion with different toothpastes [7]. Thus, preventing erosive tooth wear would also avoid the opening of dentinal tubules. Nowadays, there are toothpastes with anti-erosive claim available in the market, which aim to increase the resistance of the tooth against the erosive acids. We supposed that these toothpastes could have an additional effect on dentine permeability. Although the literature shows a range of studies testing the effect of toothpastes on dentine permeability and tubule occlusion in vitro [16–20], none of them tested the effect of anti-erosive toothpastes. Furthermore, there is a lack of studies analyzing the effect of the toothpastes on reducing dentine permeability when they are

applied regularly, during an abrasion challenge and between several erosive challenges.

In view of the above, the present study aimed to evaluate the effect of desensitizing and/or anti-erosive toothpastes on dentine permeability when applied during an erosion-abrasion cycling model, simulating the clinical conditions. The null hypothesis was that no toothpaste is able to decrease dentine permeability.

2. Material and methods

2.1. Ethical consent/aspects

In the present study, human molars and human stimulated whole saliva were used, so an approval from the local Ethics Committee on Research with Human Beings was necessary. Accordingly, this study was performed after approval was obtained (process number: 1.402.193).

2.2. Specimen preparation

One hundred sound human molars, previously stored into 0.1% of thymol solution, were selected. Dentine discs of 6 mm diameter were prepared from the central area of the tooth crowns, using a circular cutting machine. To standardize the area of the crown from where the discs were obtained, the pulpal surfaces were first removed with silicon carbide paper of #400 grit in a polishing machine (Ecomet 3, Buehler Ltd, USA), under constant cooling. Then, with the same paper grit, the occlusal enamel was removed. After, the occlusal surfaces of the specimens were polished, using carbide paper of #600 grit, until discs of 1 mm-thickness were obtained. Between the different paper grits and after the polishing, the specimens were sonicated with distilled water for 3 min.

2.3. Opening of dentinal tubules

To simulate a sensitive dentine, the dentinal tubules were opened by immersing the discs for 5 min in EDTA solution (17%, pH 7.4). After,

the discs were abundantly rinsed with deionized water [10]. The initial dentine permeability of the specimens was analyzed, and considered as reference for the dentine permeability change of each specimen after the erosion-abrasion cycles. Then, the specimens were randomly distributed among the experimental groups ($n = 10$). Table 1 shows the details of the groups.

2.4. Human saliva collection

Human stimulated whole saliva was collected from volunteers that have agreed to donate saliva and signed a written informed consent term, in accordance with the regulation of the local ethics committee. They were instructed not to eat or drink for at least 1 h before the collection, which was carried out always in the morning, for 10 min. During this time, the volunteers had to chew a parafilm, and all stimulated saliva was collected in an iced-chilled bottle. After each collection, saliva of all volunteers was pooled and immediately centrifuged (20 min; 4 °C; 3226 g-force). After, the supernatant was separated from the pellet and divided in tubes that were stored at -80 °C. The amount of saliva needed for each cycle was thawed and kept at room temperature for at least 2 h before using [10].

2.5. Erosion-abrasion cycles

The toothpastes were applied during the abrasion challenges, twice per cycle, 30 min after the first and the last acid challenge. Toothpaste slurries were prepared right before using, by mixing one part of toothpaste with three parts of human saliva. The abrasion was performed using an automatic brushing machine with standard toothbrushes (Odeme Equipamentos Médicos e Odontológicos Ltda; 45 strokes, 2 N force), totalizing 2 min of exposure of the specimens to the toothpaste slurries. Moreover, the specimens were immersed 4 times in citric acid (2 min; 0.3%; natural pH \sim 2.6), followed by 60 min immersion in human saliva, under constant agitation (shaker table, TS-2000^A VDRL Shaker, Biomixer). This was repeated 5 times, with one cycle per day (Fig. 1). Between the cycles, the specimens were kept in human saliva, under constant agitation. After the last cycle, the specimens were immersed in human saliva for 60 min and then kept in 100% humidity chamber at 4 °C, until the final dentine permeability analysis.

2.6. Dentine permeability

The dentin permeability was performed as described in previous study [10]. Shortly, the specimens were placed with the occlusal

surface facing up in the chamber of a specific machine, which was kept with a constant pressure of 10 psi, simulating the intrapulpal pressure. An air bubble was introduced in the system and its displacement through a microcapillary (100 μ l) was recorded for 3 min. This process was repeated 3 times and the average of the 3 records was transformed to flow volume (μ L min^{-1}). The hydraulic conductance (L_p) was calculated taking into consideration the area analyzed in the center of the specimen (area = 0.058 cm^2), the pressure in the system and the flow volume. For each specimen, dentine permeability was calculated as a percentage of the initial hydraulic conductance (% L_p): % $L_p = L_{p\text{final}} \cdot 100 / L_{p\text{initial}}$. For the analysis of decrease or increase in dentine permeability, 100% was considered as zero.

Illustrative micrographs were obtained with scanning electron microscope (FEI, QuantaFEG 650, Czech Republic), under high vacuum, 20Kv, and magnifications of 1,500 \times and 2,400 \times . Illustrative transversal micrographs of the fractured specimens were also obtained (3,500 \times magnification).

2.7. Statistical analysis

Shapiro-Wilk and Brown-Forsythe tests showed that the data was neither normally distributed nor homogeneous. So, the data was transformed in Log_{10} and positive results for normality and homoscedasticity were obtained. One-way ANOVA and Tukey tests were performed, considering a significance of 5%. The analyses were performed with the software SigmaPlot 13 (Systat Software Inc.).

One sample t -test was performed to compare a single sample mean (% change in dentine permeability) to a specific constant (in this case zero), which corresponds to the initial dentine permeability. The groups Oligopeptide and Stannous were not normally distributed, so related-samples Wilcoxon signed rank test was performed. The significance was also set at 5% and the analyses were performed using SPSS (IBM Statistics version 22).

3. Results

The experimental groups presented significant differences between each other ($p < 0.05$). Fig. 2 shows the differences between groups and the percentage of decrease or increase in dentine permeability after 5 erosion-abrasion cycles. At Figs. 3–5, illustrative micrographs both of the surfaces and longitudinal surfaces for each group can be seen. The immersion of the specimens in 17% EDTA solution for 5 min resulted in open dentinal tubules (Fig. 3). In general, it is possible to observe that none of the products tested were able to complete occlude dentinal

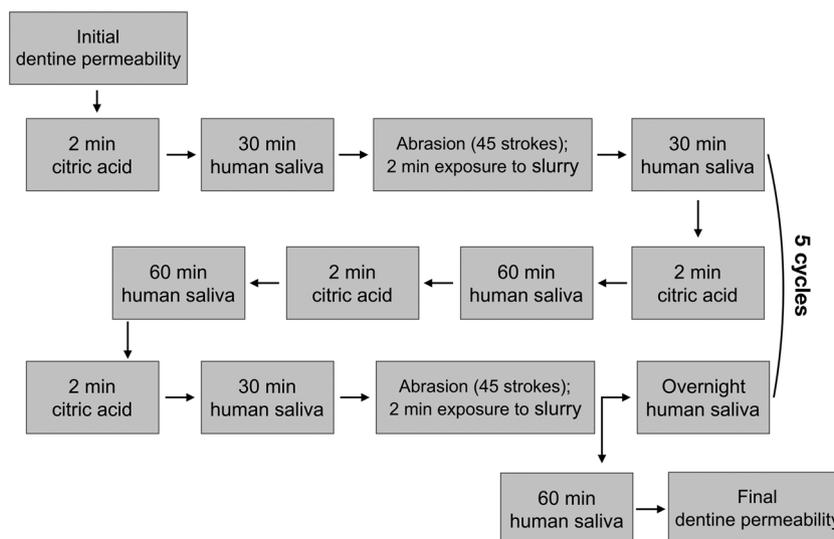


Fig. 1. Flowchart of the erosion-abrasion cycles.

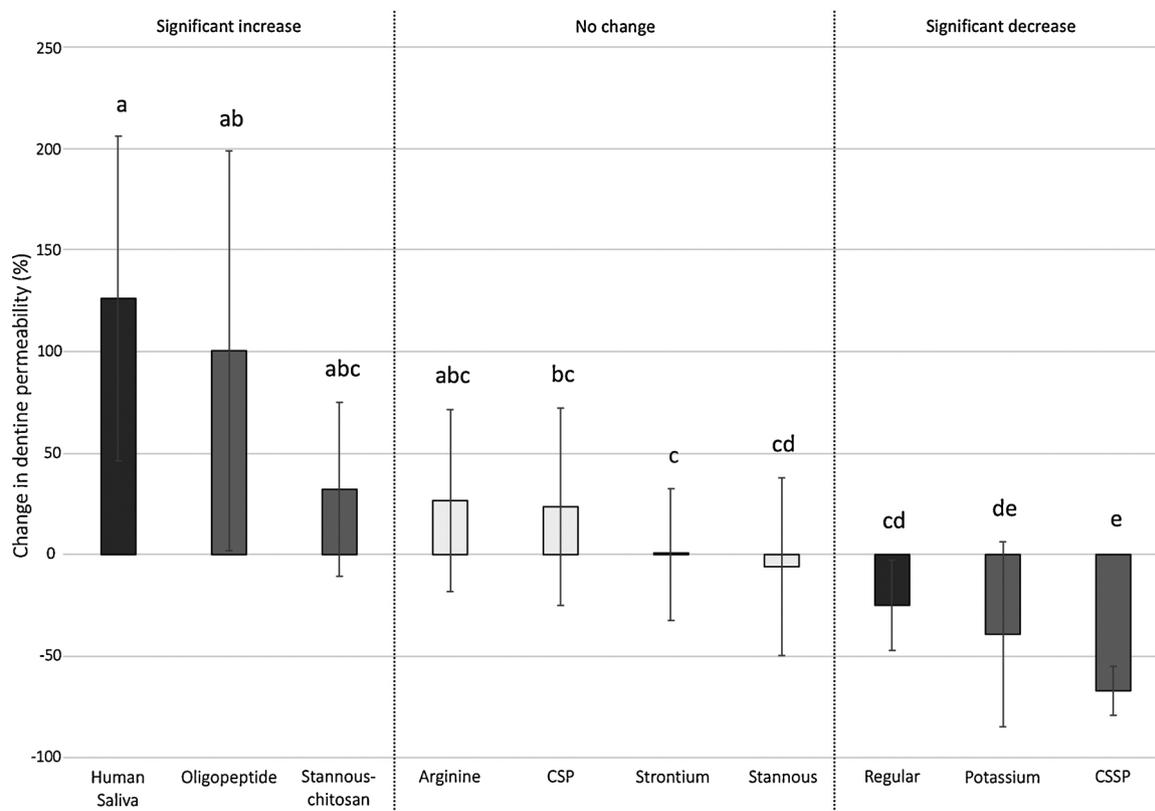


Fig. 2. Percentage change in dentine permeability after 5-day erosion-abrasion cycles. The groups with significant increase or decrease in dentine permeability, according to One sample *t*-test and Wilcoxon signed rank test, are separated by dotted lines. Different letters denote significant differences between groups ($p < 0.05$). Dark grey boxes = control groups; medium grey boxes = toothpastes with main claim as anti-erosive; and light grey boxes = toothpastes with main claim as desensitizing.

tubules after the erosion-abrasion cycles, since open tubules with different sizes are observed. The surfaces of the groups brushed with toothpastes are more irregular, however open tubules still observed and deposits on the dentine surfaces are present only in some groups.

Human Saliva (SH) showed the highest increase in dentine permeability, whereas Regular showed significant decrease. The former was not different from Oligopeptide, Stannous-chitosan and Arginine, and the later did not differ from all toothpastes, except from Oligopeptide that showed significant increase in dentine permeability, and from CSSP that showed significant decrease. All desensitizing toothpastes did not show any significant change in dentine permeability, whereas the anti-erosive toothpastes showed conflicting results: two of them (Oligopeptide and Stannous-chitosan) presented significant increase and two (CSSP and Potassium) presented a significant decrease in dentine permeability.

4. Discussion

The present study evaluated in vitro the effect of toothpastes containing different active ingredients on dentine permeability. As the recommendation of use of toothpastes as an oral care product is twice daily, a model following this recommendation was used. Previous studies have analyzed the effect of desensitizing toothpastes after a single application on tubule occlusion and dentine permeability reduction [16,18]. They observed that immersion in citric acid or the contact with saliva can impair their effect, as they removed the deposits formed on dentine surface. Thus, in the present study, frequent exposure to citric acid and exposure to saliva was performed to verify the retention of the potential deposits formed on dentine surface.

Interestingly, significant decrease in dentine permeability was observed for two anti-erosive toothpastes, CSSP and Potassium. So, the null hypothesis could be rejected. The CSSP toothpaste acts by forming hydroxyapatite and depositing particles of calcium silicate on the tooth

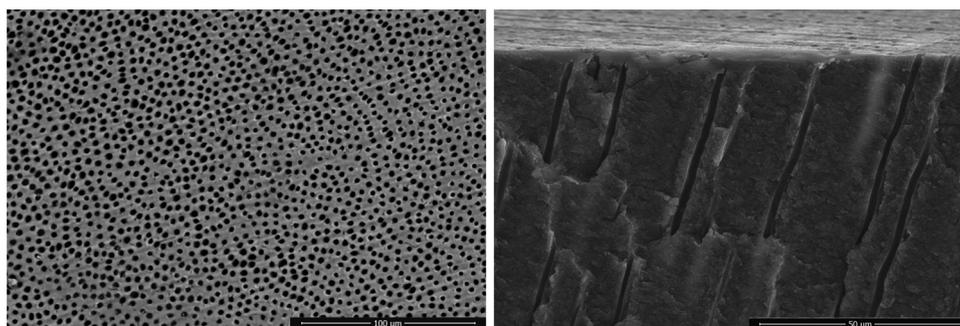


Fig. 3. Illustrative micrographs (superficial and transversal) of dentin surfaces after opening of dentinal tubules (5 min immersion in 17% EDTA solution).

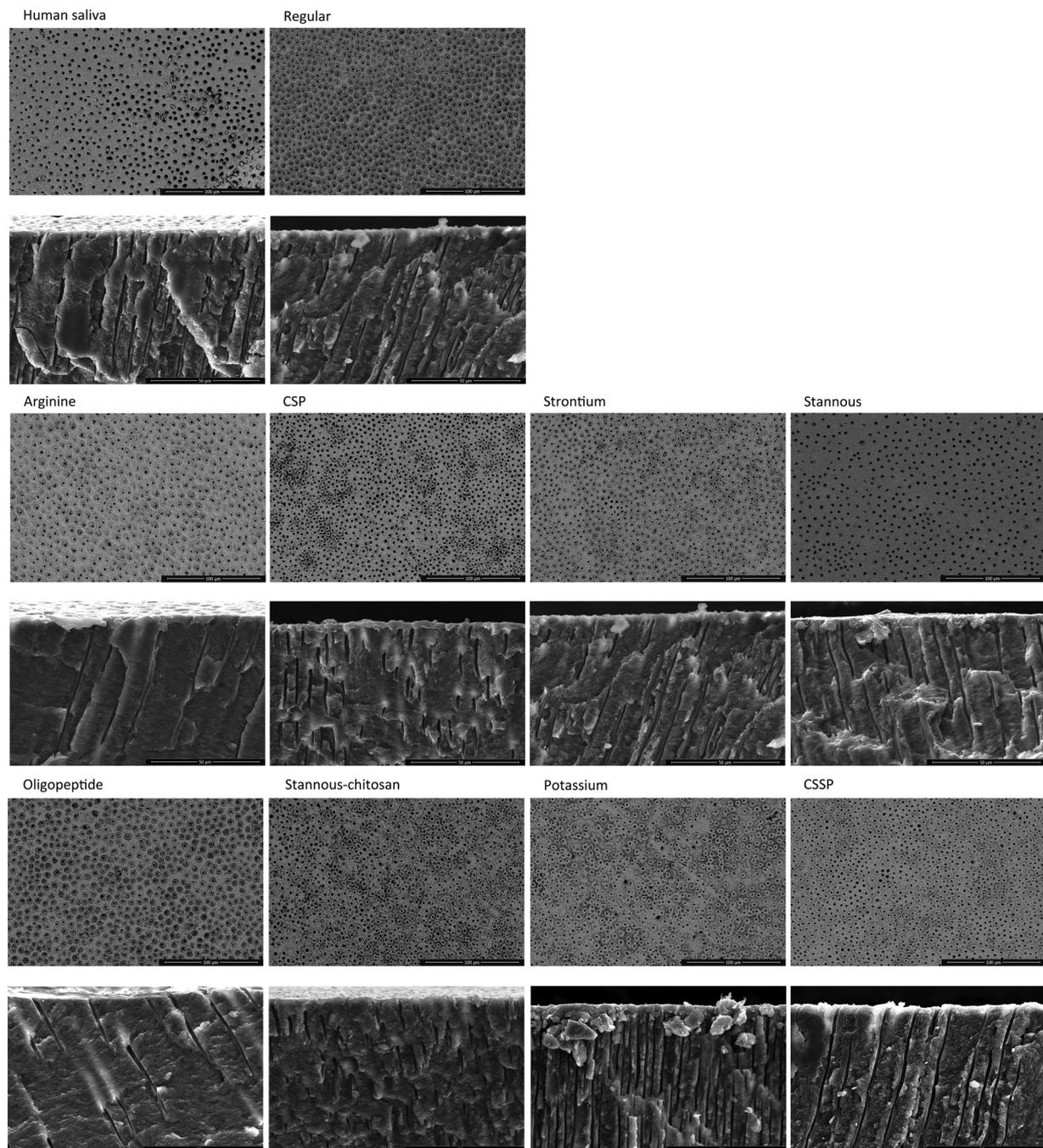


Fig. 4. Illustrative micrographs (superficial and transversal) of dentin surfaces for each group after 5-day erosion-abrasion cycles.

surface, protecting it from acid challenges [21,22]. Although studies verified this effect only on enamel, we suppose that these particles are also deposited on dentine surfaces, leading to tubule occlusion and to a decrease in dentine permeability (Fig. 5). This toothpaste also presents big solid particles ($> 50 \mu\text{m}$) [23]. These particles can be deposited on the surface of the dentine, thus most probably covering the opening of the dentinal tubules, whose diameters are around $1\text{--}3 \mu\text{m}$. This, in turn, leads to a considerable reduction in the flow of the dentinal fluid, because, according to Poiseuille's law, the flow of a fluid through a capillary will be dependent on the radius of the capillary to the power of 4 [24]. This means that if the diameter of the dentine tubule is reduced in half, there will be a 16-fold decrease in the flow of the dentinal fluid, thus reducing the pain.

The Potassium toothpaste claims to protect the tooth against dental erosion, and for that, it contains high concentration of available

fluoride and low abrasivity [25]. The decrease in dentine permeability observed for this toothpaste may be explained by its protective effect against dental erosion, preventing dentine demineralization and, consequently, the opening of dentinal tubules. This toothpaste contains potassium nitrate, which acts on pulpal nerves desensitization [25,26], and thus, it is also effective for the treatment of DH. However, in vitro, it is not expected that this component would affect the dentine permeability. Nevertheless, other studies showed tubular occlusion after application of toothpastes containing potassium ions and related this effect to deposition of solid particles from the toothpastes rather than the influence of potassium [16,27,28]. Indeed, particles can be seen at the transverse micrograph of this group (Fig. 4). This is important, since the effect of potassium ions on pulpal nerves takes longer to reduce DH [7].

The other two anti-erosive toothpastes, Oligopeptide and Stannous-

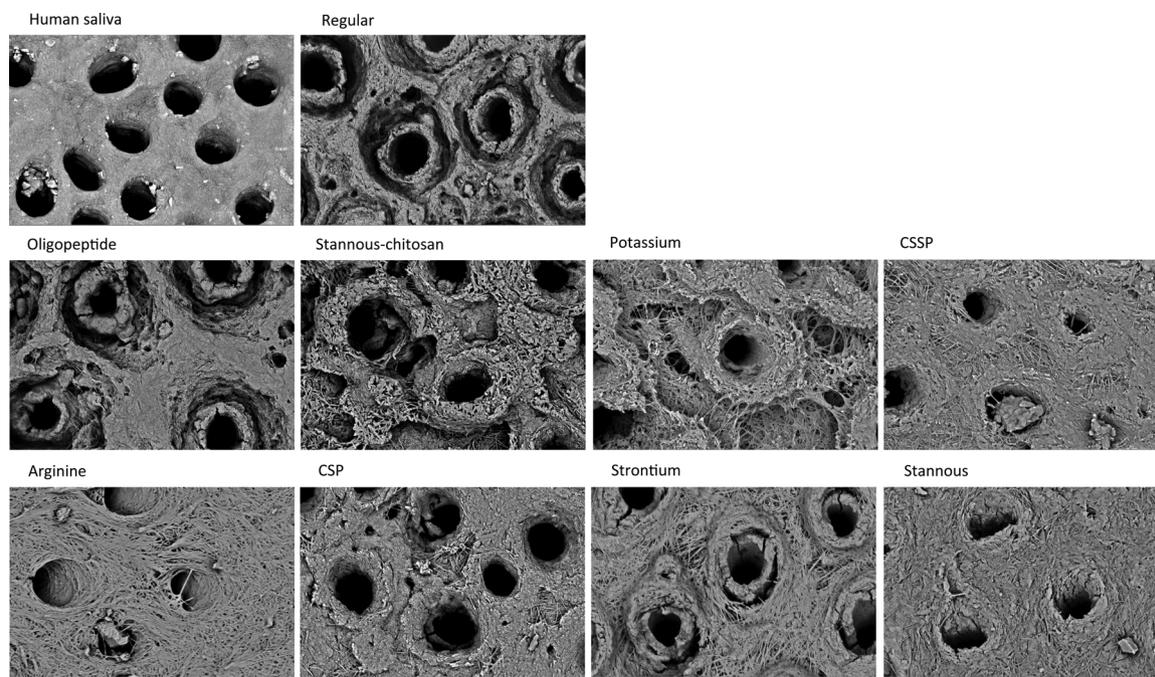


Fig. 5. Illustrative micrographs of dentin surfaces for each group after 5-day erosion-abrasion cycles, higher magnification (24,000 \times).

chitosan, resulted in increased dentine permeability. The Oligopeptide toothpaste contains a self-assembling peptide that may bind to collagen and increase its resistance against proteolytic activity [29], besides enabling hydroxyapatite growth and tubule occlusion [30]. Although positive results in treating DH has been shown after application of a gel containing a self-assembling peptide, which resulted in a layer occluding the dentinal tubules [31], the toothpaste containing this component was not able to reduce dentine permeability and the transverse micrograph did not show surface deposits. In contrast, it even increased the dentine permeability. The toothpaste containing chitosan and stannous ions acts forming an acid-resistant layer on the dentine surface, with precipitates that are retained on the surface and underlying surface of the dentine, protecting it against acid challenges [32,33]. Moreover, studies have shown tubule occlusion with toothpastes containing stannous fluoride [34–36]. Despite that, in the present study, the toothpastes containing stannous were not able to decrease dentine permeability. We can suppose that the erosive-abrasive model used here, with frequent exposure to citric acid, could have influenced this result, by removing the deposits formed on the dentine surface. Still, no study testing the Stannous-chitosan formulation for dentinal tubule occlusion was found until now.

Surprisingly, all desensitizing toothpastes (Arginine, CSP, Strontium and Stannous) showed no change in dentine permeability. These toothpastes contain arginine and calcium carbonate, calcium sodium phosphosilicate, strontium acetate and stannous fluoride, respectively. Previous studies have shown tubule occlusion and/or dentine permeability reduction with the application of these compounds [16,17,19,20,36]. The resistance of the tubule occlusion was usually verified after one or few acid challenges or after immersion in saliva for a period of time [16,20,36–38]. However, no study tested these agents under an erosion-abrasion cycling model, with frequent erosive challenges, as done in the present study. The frequent acid challenges performed here may have removed deposits of the toothpastes, and acted on the opening of the dentinal tubules, explaining the difference in the results from the other studies.

A previous study showed that there is an instability of the occlusion formed by the active ingredients present in desensitizing toothpastes, which were easily removed by acid challenge [18]. Immersion in saliva was also shown to increase dentine permeability, by rinsing away the

deposits formed on the surface [16]. Thus, any deposition of particles on the dentine surfaces that may have occurred could have been easily detached from the surface after the erosion challenges and/or contact to human saliva. Although no decrease in dentine permeability was observed for these groups, they also did not increase dentine permeability, even in view of the successive erosive challenges. Thus, we can suppose that the action of the active ingredients was somehow resistant to the repeated challenges. Perhaps these toothpastes may have an effect also on the protection of dentine from future demineralization, but this should be further investigated.

As expected, the HS showed a significant increase in dentine permeability. It does not contain any active ingredient or solid particles that would form strong deposits on the dentine surface that would significantly occlude the tubules. Moreover, the frequent acid challenges must have further opened and enlarged the dentinal tubules, which in turn resulted in the increased permeability. Although human saliva could have acted as a natural tubule occluding agent by the formation of a salivary pellicle on the dentine surface or by creating mineral deposits [39], this was not sufficient to show a substantial effect here.

Despite not having a specific claim to treat DH or prevent dental erosion, the Regular toothpaste showed significant decrease in dentine permeability. This toothpaste contains only fluoride as active ingredient. Although the other toothpastes also contain fluoride besides other active ingredients, they were not different from this toothpaste, excepted for CSSP and Oligopeptide. The later showed a significant increase in dentine permeability, not differing from HS. The former, in turn, showed a significant decrease in dentine permeability. The reason for a positive result with the use of the Regular toothpaste cannot be straight addressed. The deposition of a significant number of CaF_2 -like particles on the surface can be ruled out, as the pH of this toothpaste slurry is not acidic (pH 7.07). Besides, all toothpastes analyzed contain fluoride, indicating no further effect of this compound in dentine permeability reduction. We can assume that other factors of this toothpaste may have protected the dentine surface against dental erosion or resulted in less abrasion.

The hydraulic conductance system used for the analysis is based on the movement of a liquid inside a capillary tube, and is influenced by the opening of the dentinal tubules [4]. The application of treatments

should cause a reduction in the liquid flow through the capillary tube, which is associated to the reduction of the dentine permeability [40]. An advantage of this method is the possibility to differentiate the efficacy of deposits that are strongly attached to the dentine surface from the ones that are only weakly attached, since the liquid through the dentine might remove the weak deposits.

It should be mentioned that even though we standardized the thickness of the dentine discs, the place of the crown from where they were obtained, and the method of opening the dentine tubules, a high variation was observed in dentine permeability. This variation was already addressed when using a hydraulic conductance system and is explained by the difference between the natural morphology of the teeth [41]. Accordingly, we can extrapolate the results, albeit within the limitations of this laboratory study, to the variability in DH that occurs in the clinical scenario, where different responses to the stimuli can also be observed. Moreover, this can explain the fact that one treatment may not work in the same manner for all patients [1].

5. Conclusion

No desensitizing toothpaste showed a change in dentine permeability when applied during an erosive-abrasive model, whereas the groups that showed significant decrease in dentine permeability (CSSP and Potassium) have anti-erosive as the main claim. This is an important finding, since erosive tooth wear is a predisposing factor for DH. So, a toothpaste that protects the tooth against dental erosion and is also effective for reducing the pain is encouraging.

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Declaration of Competing Interest

None.

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