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Effect Of Calcium Silicate, Sodium Phosphate, and Fluoride on Dentinal Tubule Occlusion and Permeability in Comparison to Desensitizing Toothpaste: An In Vitro Study.

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CLINICAL RELEVANCE

Although initially promoted as antierosive or enamel remineralizing toothpaste, calcium silicate, sodium phosphate, and fluoride salts have the ability to reduce dentin permeability more than some of the commercially marketed desensitizing TPs.

SUMMARY

This study compared the ability of a calcium silicate-, sodium phosphate-, and fluoride-based (CSSPF) toothpaste (TP) in promoting dentinal tubule occlusion and reducing dentin permeability with that of other commercially available antisensitivity TPs. Seventy-eight dentin discs (1.0±0.1 mm thick) were prepared from the midcoronal area and were treated with 37% phosphoric acid for 2 minutes; then they were randomly divided into six groups according to treatments: No treatment [positive control (PC)], entirely covered with nail varnish [negative control (NC)], hydroxyapatite (HAP)-containing TP [Desensin Repair (DES)], NovaMin-based [Sensodyne Repair & Protect (SEN)], CSSPF-based TP [Regenerate Advanced (REG)], sodium monofluorophosphate, potassium citrate, zinc citrate TP [Signal Sensitive Expert (SIG)]. Dentin permeability was tested by the dye percolation method (DP%). Scanning electron microscope (SEM) micromorphological and energy dispersive X-ray elemental analysis (EDX) of the dentin surfaces were done following each treatment. Results were analyzed using one-way analysis of variance (ANOVA) followed by Tukey post hoc test at a 95% confidence level (α=0.05). All the tested groups showed higher DP% than NC

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and lower percolation than the PC (*p*<0.05). REG and SIG were statistically comparable, and showed significantly lower DP% (*p*<0.05) than SEN and DES. None of the TPs tested was able to obliterate the lumen of the dentinal tubules (DT) completely. REG exhibited the highest weight percentage of calcium deposition, followed by SEN. Compared to the tested desensitizing TPs, CSSPF-based TPs demonstrated equal or less dentin permeability and better DT occlusion.

INTRODUCTION

Dentin hypersensitivity (DH) has been described as the short sharp pain caused by exposed dentin that cannot be ascribed to any other dental disease.[1,2] Brännström and others proposed the hydrodynamic theory to explain DH as the fluid movement in open dentinal tubules (DT) when they are exposed to thermal, evaporative, tactile, osmotic, or chemical stimuli, which activate mechanoreceptors that cause pain and discomfort.[3,4] Gingival recession or loss of enamel due to abrasion, erosion, or abfraction may cause the exposure of DT.[5] Pain arising from exposed DT may hamper the patient's maintenance of good oral hygiene.[6] It was noticed that the increased number of exposed DT were closely correlated to the increased sensitivity.[7] Two methods were proposed to desensitize dentin: 1) Block out or modulate the response of intradental nerves to fluid movements or 2) mechanically occlude the exposed DT to reduce dentin permeability and prevent fluid movement.[8]

Potassium ions present in some types of toothpastes (TPs) in the form of 5% potassium nitrate may reduce tooth sensitivity by decreasing the excitability of A-fibers around the odontoblasts.[9] However, dentinal tubule occlusion is the most common therapeutic method.[8] Most of the home-use desensitizing products belong to the second group and include a wide range of active elements. One of these active elements is Bioglass. It was initially developed to stimulate new bone formation. It was also shown by scanning electron microscopy (SEM) that it occludes DT when applied to the exposed dentin by forming a hydroxycarbonate apatite (HCA) layer over the tubules.[10] NovaMin, which is based on the original 45S5 Bioglass, is the active ingredient in Sensodyne Repair & Protect dentifrice; a number of clinical and laboratory studies showed the ability of this product to block DT and relieve sensitivity.[11-18]

The combination of arginine and calcium carbonate demonstrated the ability to occlude DT by the precipitation of calcium phosphates. However, these precipitates are soluble and unstable under acid challenge.[19] Clinical studies have demonstrated a significant reduction in DH after the use of arginine and calcium carbonate TPs immediately and up to 8 weeks after treatment.[20,21] Another approach to treat DH is the use of stannous fluoride, which is characterized by water and acid-resistant precipitate, which demonstrated effective treatment of DH in many randomized controlled clinical trials.[22,23]

Another novel approach is the use of nanoparticles as desensitizing agents.[24, 25] Nanoparticles may easily penetrate DT and block fluid movement due to their small size. A recently introduced formulation containing calcium silicate, sodium phosphate, and fluoride (CSSPF), promoted initially as a remineralizing or antierosive TP for the repair of demineralized enamel, was found to deposit calcium silicate particles onto the enamel surface and nucleate HAP formation.[26] This mechanism of action can be very appealing to use for the obliteration of the DT and the treatment of DH. There are few reports in the literature on the potential repair of dental enamel by CSSPF formulations[27,28]; however, no information is available on their effect on dentin lesions. Therefore, the objectives of this study were to compare the ability of CSSPF formulations to promote dentinal tubule occlusion and reduce dentin permeability, with that of other commercially available antisensitivity TPs. The null hypothesis was that there is no difference between CSSPF-based TP and the antisensitivity TPs tested in their ability to occlude the DT and reduce dentin permeability.

METHODS AND MATERIALS

Preparation of Dentin Samples

Seventy-eight caries-free freshly extracted human third molars were obtained from the oral surgery clinic after the patient's informed consent was obtained. The teeth were cleaned from soft tissue remnants with an ultrasonic scaler and stored in 0.1% thymol solution for one month before use. Seventy-eight dentin discs with a thickness of 1.0 ± 0.1 mm were prepared from the midcoronal area by sectioning over the cementoenamel junction (CEJ) using a low-speed, water-cooled diamond saw (IsoMet 1000, Buehler Ltd, Lake Bluff, IL, USA). The dentin discs were inspected under the stereomicroscope to exclude the presence of pulp horn exposures or remnants of enamel. The disc samples were collected and polished with 600-grit silicon carbide paper to create a standardized smear layer, and then the samples were trimmed using a diamond finishing bur to adjust their diameter to 8.5 ± 0.1mm.

Table 1: *Materials Tested in This Study*

Product	Abbreviation	Manufacturer	Active ingredient	LOT
Desensin Repair	DES	Dentaid, Spain	Nano hydroxyapatite (HAP), potassium nitrate	K2011
Sensodyne Repair & Protect	SEN	Glaxo Smith Kline, Weybridge, Surrey, UK	Glycerin, silica, calcium sodium phosphosilicate (Novamin), sodium monofluorophosphate 1.08% w/w (1450 ppm fluoride)	077G L1
Regenerate Advanced	REG	Unilever, UK	Glycerin, calcium silicate, hydrated silica, trisodium phosphate, sodium phosphate, sodium monofluorophosphate (1450 ppm fluoride)	L4274CCC
Signal Sensitive Expert	SIG	Unilever, UK	Sodium monofluorophosphate (1450 ppm fluoride), potassium citrate, zinc citrate, HAP	B21

Dentin Permeability (Dye Percolation Test)

A circular paper sticker with 5.5-mm diameter was placed on each prepared dentin disc's surface, and nail varnish was applied to the exposed dentin around the sticker. The nail varnish was left for 5 minutes to dry, then the sticker was removed, and the upper and lower surfaces of the dentin discs were treated with 37% phosphoric acid gel for 2 minutes to remove the surface smear layer and attain patent tubules of dentin. The specimens were rinsed with distilled water and maintained wet to evaluate the maximum permeability. The dentin discs were randomly divided into six groups, 13 samples each, and received one of the following treatments:

- Group 1 [positive control (PC)]: No treatment
- Group 2 [negative control (NC)]: Samples were entirely covered with nail varnish.
- Group 3 (DES): Brushed with potassium nitrate-, HAP nanoparticles-containing TP.
- Group 4 (SEN): Brushed with NovaMin bioactive glass (BG)-containing TP.
- Group 5 (REG): Brushed with a calcium silicate-, sodium phosphate-, and fluoride- containing TP.
- Group 6 (SIG): Brushed with sodium monofluorophosphate-, potassium citrate-, zinc citrate-containing TP.

The composition of the materials tested are listed in Table 1. Each TP (a slurry of 1 g of TP and water in 1:2 ratio) was applied for 2 minutes two times a day for 7 days, using a soft brush and minimal pressure; the dentin surface was rinsed with distilled water after every application and kept immersed between the applications in artificial saliva (composition: 0.4 g NaCl, 0.4 g KCl, 0.795 g $CaCl_2{\cdot}2H_2O$, 0.78 g $NaH_2PO_4{\cdot}2H_2O$, 0.005 g $Na_2S{\cdot}9H_2O$, 1 g urea, and 1000 mL distilled water).

Sixty plastic vials (Eppendorf tube, Eppendorf AG, Hamburg, Germany) were cut at 5 mm from the vial's tip, using a cutter, and the inner surfaces of the vials were sandblasted with 25-μm aluminum oxide particles. The vials were cleaned with distilled water and dried, and a resin bonding agent (Scotchbond Universal, 3M Oral Care, St. Paul, MN, USA) was applied at the inner surface of the vials at a level of 5 mm from the vial's opening. Ten dentin discs from each group (n=10) were randomly selected and placed in the vials at the level of 5 mm, and flowable composite (Filtek Z350 XT, 3M Oral Care, St. Paul, MN, USA) was used to seal the interface between the side of the disc and the inner wall of the vials. The composite was light-cured using an LED light-curing unit (Elipar, 3M Oral Care, St. Paul, MN, USA). The dentin disc divided the vial into an upper compartment and a lower compartment (Figure 1). The vials were numbered, the lower compartments were filled with distilled water, and the caps were closed. The lower compartments were checked for the presence of any air bubbles in the water, and, if a bubble was detected, injection of water through the vial's wall using a fine needle syringe occurred, and the puncture site was closed with paraffin wax.

A two-toned dye (Plaquesearch, Oral Dent Ltd, UK) was used to test dentin permeability. Different concentrations of the dye were made, considering the undiluted as 100%, and serial dilutions were made from 100%-3.125% (Figure 1). The absorbance of the different concentrations of the dye was red in a multimode microplate reader (Varioskan Flash, Thermo Fisher Scientific, Vantaa, Finland) at a wavelength of 630 nm and plotted to generate a calibration curve. The calibration curve was optimized to get a straight line by including the dilutions from 0.39% to 3.125% only. 100 μl of 3.12% dye was added to the upper compartment of the vial, on top of 10 samples from each group (n=10), and kept undisturbed for 24 hours. The readings were taken in the microplate reader, and, using the calibration curve, the equivalent dye percentage of the readings was recorded.

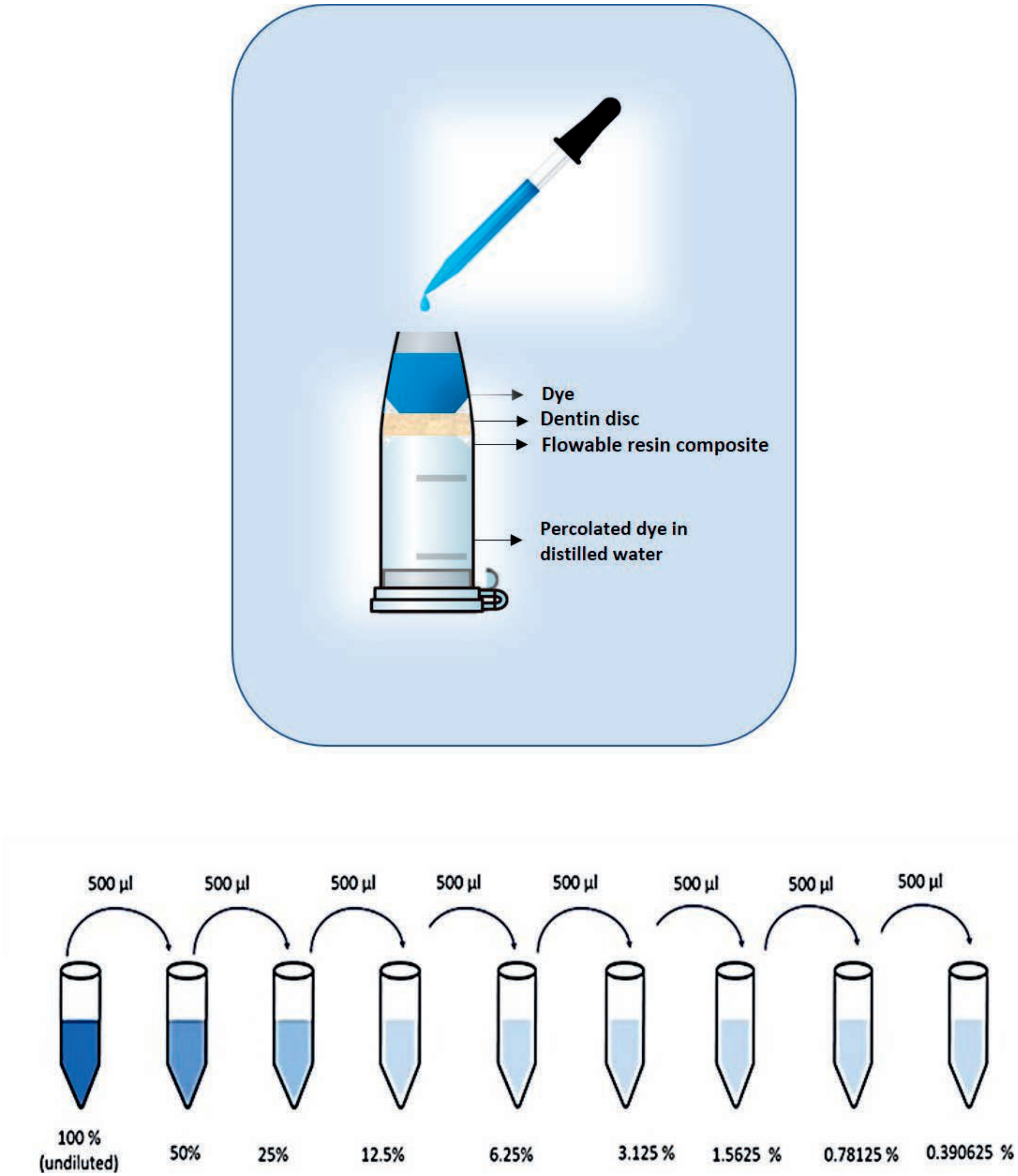

Figure 1. *Schematic representation showing the sample set-up for the dye percolation (DC) test and the different dilutions of dye for making the calibration curve (considering the undiluted solution as 100%).*

Table 2: *Dye Percolation (DC) (Mean%±Standard Deviation) and Energy Dispersive X-ray Elemental (EDX) Analysis of Major Components of Element Surface Composition (wt%) of the Dentin Surface after Treatment with the Tested Materials*

Material	Percentage Dye Percolation (DC%)	Elemental Surface Composition (wt%)				
		Ca	P	Si	C	O
NC	0.003 ± 0.002 a	0.0	0.0	0.7	26.5	17.4
SIG	0.054 ± 0.028 b	9.85	4.6	0.9	43.6	27.5
REG	0.064 ± 0.020 b	21.6	10.1	0.9	27.2	39.2
DES	0.108 ± 0.025 c	12.9	8.4	1.8	29.5	39.9
SEN	0.126 ± 0.040 c	19.1	8.6	1.8	30.1	38.4
PC	0.195 ± 0.050 d	8.0	3.6	1.3	59.9	20.5

Mean values with different lowerase letters are statistically significantly different ($p<0.05$).

Micromorphological and Energy Dispersive X-Ray Analysis (SEM-EDX)

The three remaining dentin discs samples from each group (n=3) were dehydrated in a desiccator containing dehydrated silica gel at room temperature for 24 hours. Samples were sputter-coated with 100 Å gold-palladium (EMS 7620 Mini Sputter Coater, Hatfield, PA, USA) to create a conductive specimen surface and reduce electron charging, which may reduce the quality of the image. The treated surfaces of the samples were analyzed, and one sample from each group was fractured using a #15 scalpel blade to reveal the cross-section of the samples and study the penetration of the TP into the dentinal tubules. Observations were performed under different magnifications up to 5000×, using a scanning electron microscope (SEM) (VEGA3 XM—TESCAN, Kohoutovice, Czech Republic) operating at 10-20kV acceleration voltage and 10-27 mm working distance.

Elemental analysis of the samples from each group was done using a SEM-coupled energy dispersive X-ray microanalyzer (EDX - TESCAN, Kohoutovice, Czech Republic), operating at a take-off angle of 35° with map mode. The average main element percentage weight content for each TP (silicon, fluoride, calcium, and phosphorus) was calculated.

Statistical Analysis

The power analysis of the study was performed after a pilot study to determine adequate sample size. One-way analysis of variance (ANOVA) and Tukey post hoc tests were used to detect pairwise differences among experimental groups. A 95% confidence level was applied for all the statistical tests, and the power of the analysis with a=0.05 (b=0.10, f=0.40) was 0.90. The statistical analysis was performed by the IBM SPSS Statistics software (SPSS version 20.0, SPSS Inc, Chicago, IL, USA).

RESULTS

Dentin Permeability (Dye Percolation Test)

The dentin permeability results, expressed as dye percolation percentage (DP%), are shown in Table 2. The one-way ANOVA test revealed that the type of TP significantly affected dentin permeability ($p<0.0001$). Compared to the NC group, all the tested groups showed statistically higher DP% ($p<0.05$). Meanwhile, all the tested materials exhibited significantly less percolation than the PC group (0.195±0.05). There were no statistically significant differences ($p>0.05$) in DC results among REG and SIG (0.064±0.02 and 0.054±0.028, respectively), which have shown significantly less DC ($p<0.05$) than SEN (0.126±0.04), and DES (0.108±0.025).

Micromorphological and Energy Dispersive X-Ray Analysis (SEM-EDX)

The SEM microphotographs of aerial views of sample surfaces and cross-sectional views of the fractured samples for each group are illustrated in Figure 2. The PC samples showed open DT with a complete absence of smear layer and plugs, while the analysis of the NC group revealed a 10- μm-thick nail varnish layer on the surface with up to 15-μm-long intact smear plugs filling the DT. In comparison to the NC group, none of the TPs tested in this study was able to obliterate the lumen of the DT completely. Deposition of crystal-like and granular structures on the dentin surface and in the lumen of the tubules brushed with SEN, SIG, REG, and DES resulted in a reduction of the tubule lumen diameters (arrow) and complete obliteration of some tubule openings. A longitudinal view of the fractured samples revealed poor penetration of the TPs into the DT, except for REG and SIG, which showed deeper penetration into the DT up to 15 μm.

EDX micrographs are presented in Figure 2, and the analysis of major components of the surface

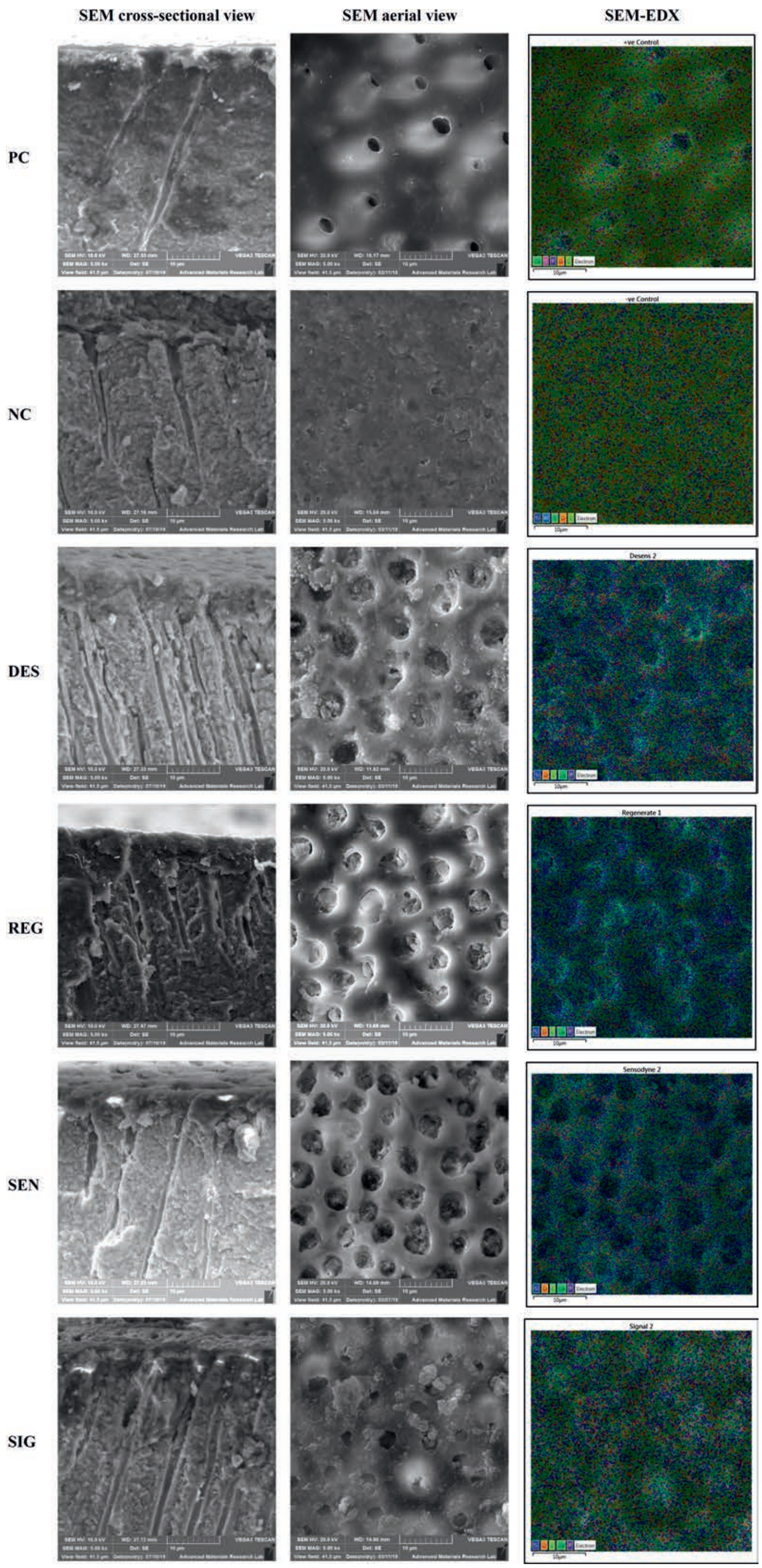

Figure 2. *Scanning electron microscope (SEM) (cross-sectional view and aerial view) and energy dispersive X-ray elemental analysis (EDX) micrograph (5.0 kx magnification) of dentin disc, after 37% phosphoric acid-etched dentin surface (Positive Control, PC), fully covered with nail varnish (Negative Control, NC), and after treatment with Desensin Repair (DES), Regenerate Advanced (REG), Sensodyne Repair & Protect (SEN), and Signal Sensitive Expert (SIG) toothpastes.*

elemental composition of the dentin disc surfaces is shown in Table 2. Some elements, including phosphorus (P), silicon, (Si), chlorine (Cl), sodium (Na), and magnesium (Mg), were detected, but the most predominant element was calcium (Ca), with REG exhibiting the highest weight percentage of Ca (21.6 %) followed by SEN (19.1 %).

DISCUSSION

Fluid conductance in the DT is the main contributing factor to DH; therefore, one of the fundamental approaches to manage DH aims at occluding the exposed DT and consequently preventing the movement of fluid in the tubule, and thereby reducing the pain and discomfort associated with DH. The current study investigated the efficacy of an antierosive calcium silicate/sodium phosphate salts/fluoride TP [Regenerate Advanced (REG)] in comparison to three different anti-sensitivity TP preparations in occluding the DT.

There are various methods available in the literature to test the dentin permeability.[29,30] Pashley and others described one of the most widely used methods in which a fluid filtration system and split-chamber unit were used to measure the dentin permeability.[31] In this method, the movement of an air bubble is measured, and the linear displacement is translated into a dentin permeability value. Several other *in vitro* studies utilized SEM topographical examination to measure the percentage of dentinal tubule occlusion.[32] Knight and others described testing dentin permeability through the bacterial migration model, in which a chemostat system provides a constant supply of *Streptococcus mutants* that passes through the dentin discs. The permeability is assessed through optical density measurement and is proportional to the bacterial growth in the nutrient broth.[33]

In our study, we have used a DC method, which calculated the percentage dentin filtration of a known concentration of a specific dye through the DT. The dye concentration is measured utilizing a microplate reader at a particular wavelength and compared against a calibration curve to obtain the percentage of dye filtration through the dentin disc. When compared to Pashley and Knight methods, the DC method is easier to set up, reasonably reliable, reproducible, and more cost-effective. The results of the current study showed that all four types of TPs tested were found to significantly decrease the dentin permeability when compared to the PC group. Therefore, the null hypothesis should be rejected. Out of the four TPs, REG and SIG exhibited significantly less DC ($p<0.05$) than the two other materials. Most of the studies reported on calcium silicate/sodium phosphate/fluoride (REG) were on the antierosive effect or enamel remineralization capacity of this TP.[26,27]

The only study that tested the REG efficacy on dentin permeability is a recent study by João-Souza and others, where REG showed a significant decrease in dentin permeability when compared to all desensitizing TPs (arginine, calcium sodium phosphosilicate, strontium acetate, and stannous fluoride) tested.[34] The results of our study are in agreement with the reported findings of the João-Souza study. We found that REG effectively reduces dentin permeability, similar to the desensitizing TPs or even better.

The ability of REG to reduce the dentin permeability is mainly attributed to the effective dentinal tubule occlusion, as seen in the SEM topographical analysis (Figure 2), and the unique composition of multiple salts that enhance the deposition of complex crystals in the tubules and possible chemical interaction with the dentinal minerals. Several studies have described the mode of action of REG on enamel remineralization, which is based on the dual-phase gel system containing calcium silicate and phosphate, with 1450 ppm fluoride ion from the sodium fluoride and sodium monofluorophosphate—a system that favors ion exchange, and the nucleation and growth of HAP crystals on enamel.[26,35] We postulate that a similar mode of action occurs when brushing REG on dentin. The pH for unbuffered CaSi-water rises to a pH of 9.1. This alkaline environment in the presence of sodium phosphate salts enhances the deposition of calcium silicate in the DT. This postulation is confirmed by the EDX elemental analysis (Figure 2), which showed that among all the tested TPs, the highest calcium contents were reached with REG.

Although SEN has a similar composition to that of REG (calcium sodium phosphosilicate, sodium monofluorophosphate, and 1450-ppm fluoride), it exhibited significantly higher DC. Meanwhile, SIG, which has potassium citrate, zinc citrate, and HAP as active components, has shown comparable results to REG, significantly higher than SEN and DES ($p<0.05$). Jena and others reported similar results when they compared a TP containing potassium citrate and zinc citrate (Pepsodent Pro-sensitive Relief and Repair), with Sensodyne Repair & Protect showing significantly higher dentinal tubule occlusion on the former than the latter.[36] Farooq and others demonstrated superior dentinal tubule occlusion by HAP-containing TPs and BG-containing TPs compared to acid-etched control and fluoride TPs.[37] The findings of the current study support the results of these reports, as DES (HAP-containing TP) and SEN (BG-based TP) were found to reduce the DC in comparison to the PC significantly. Yuan and others have shown a significant improvement in dentinal tubule occlusion by adding HAP to ordinary TP in their study.[38] A novel BG–ceramic, which contains sodium-calcium phosphate and HAP, was compared to commercial BG-containing TP (NovaMin) regarding their dentin permeability reduction capability; no significant difference was observed, as both of them were found to reduce dentin permeability and occlude DT.[39]

One limitation of this study was the application of the desensitizing TPs for a limited time of 7 days only, and that the specimens were stored in artificial saliva between applications. Longer application of the TPs or subjecting the samples to acidic challenges may result in different outcomes. Supporting the findings of this research with more clinical studies is recommended for future investigations.

CONCLUSIONS

Although all the tested TPs were able to reduce the fluid percolation through the dentin and occlude the DT to various extents, the antierosive calcium silicate-, sodium phosphate-, fluoride-containing TP showed significantly better results than some of the commercially marketed desensitizing TP. The superior performance of this TP may be attributed to the combination of different salts in a highly alkaline media that promote remineralization and crystal formation, and subsequently tubule occlusion.

Conflicts of Interest

The authors of this manuscript certify that they have no proprietary, financial, or other personal interest of any nature or kind in any product, service, and/or company that is presented in this manuscript.

Regulatory Statement

This protocol was approved by the University Research Ethics Committee (approval number: REC-17-11-19-01) and was performed in conformity with the University's guidelines for handling biological tissues.

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