Original Research Article

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In vitro study to evaluate the efficacy of DENTE91® Remineralizing Gel in oral health

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Abstract

Background: Dental enamel is vulnerable to erosion, microbes, and damage, leading to issues like caries, sensitivity, and discoloration. Conventional treatments target individual problems. There is a growing need for multifunctional solutions that address multiple oral health concerns together.

Objectives: The objective of the study was to evaluate the *in vitro* efficacy of DENTE91® remineralizing (RM) gel across varying oral health concerns.

Materials and Methods: Six independent *in vitro* studies were carried out. (1) Antimicrobial activity was tested against four microorganisms through colony formation unit analysis after 2- and 5-min treatment exposure. (2) Remineralization was investigated on lesions using 8-day pH cycling for surface repair and mineral gain. (3) Cavity healing was assessed by fibroblasts using a colorimetric assay. (4) Desensitizing effect was tested on acid-exposed dentine disk and assessed for tubule closure. (5) Cavities protection was evaluated using 8-day pH cycling, scanning electron microscopy, and mineral content analysis. (6) Tooth whitening was tested using lux meter.

Results: (1) DENTE91® RM gel exhibited 99.99% antimicrobial efficacy with <0.01% survival rate. (2) Dentine tubule occluded by 37.5% along with 109.73% and 107.56% increment in calcium and phosphate levels, respectively, indicating strong remineralization. (3) It promoted NIH/3T3 cell proliferation at 0.01% and 0.05% concentration. (4) 66.53% teeth sensitivity reduction was noted within 15 days. (5) DENTE91® RM gel boosted enamel minerals (Ca − 110.7%, $P = -108.2\%$), strengthening defense against caries. (6) 7-day use led to 87.07% teeth whitening improvement.

Conclusion: This *in vitro* study demonstrated that DENTE91® remineralization gel is effective in promoting remineralization and also provides antimicrobial, desensitizing, and teeth-whitening benefits. These findings suggest its potential for use as a comprehensive oral care solution.

Keywords: Dental carries, dentin sensitivity, tooth remineralization, tooth whitening

Introduction

Oral health is a crucial aspect of overall well-being, but dental problems like caries, erosion of enamel, and hypersensitivity are highly prevalent globally. They are caused by the progressive loss of tooth structure by acids in the diet, oral hygiene practices, and microbial action. If not treated, they can cause pain, impairment of function, aesthetic sensitivity, and compromised quality of life at all ages. Oral diseases affect nearly 3.5 billion people globally, with untreated dental caries in permanent teeth being the most common health condition. The burden is particularly high in

low- and middle-income countries due to limited access to preventive care and dental services. Oral diseases also share common risk factors with other non-communicable diseases such as diabetes and cardiovascular conditions, further underscoring the need for integrated oral health strategies within primary healthcare systems.[1]

Dental enamel, the outermost layer of the dental crown, is the hardest and most water-resistant substance in the human body, protecting teeth from physical, chemical, and thermal forces.[2] Despite its durability, enamel is acellular and incapable of self-regeneration once damaged.[3] One of the most prevalent and irreversible forms of damage is enamel erosion, defined as the progressive loss of enamel due to chemical processes, particularly acid exposure, not involving bacterial activity.[4] However, acidic by-products from bacterial metabolism also contribute to enamel degradation through demineralization. Repeated acid exposure from dietary acids, gastroesophageal reflux, or poor oral hygiene can lead to dental caries, hypersensitivity, tooth discoloration, and periodontal issues, with the process often beginning with surface softening and progressing to deeper structural loss. Epidemiological data suggest enamel erosion affects 6–50% of preschoolers, 14% of school-aged children, up to 100% of adolescents, and 4–82% of adults, with males slightly more affected and incidence increasing by up to 27% over time.[5] Enamel is composed of approximately 85% calcium-deficient carbonated hydroxyapatite, with the remaining space filled by water (12%) and organic material (3%), where demineralization and remineralization occur.[6] If demineralization is left untreated, it can result in cavities and deeper structural damage, as dentine has smaller crystals and a lower mineral content (47%), making it more vulnerable.

The body's natural remineralization process can reverse early-stage enamel damage, but this process is often slow and not sufficient in a chronically acidic environment. Therefore, there is a need of therapeutic agent to enhance this process.[7] Conventional treatment involves invasive procedures such as crowns, filling and root canal, and direct restoration.[8] These methods have short- to mid-term success rates of about 85–90% over 5–10 years, but it requires removal of healthy tooth, and underlying diseases process cannot be addressed.[9]

Recently, several mineralizing systems have been developed, including crystalline calcium phosphate, unstabilized amorphous calcium phosphate (unstable-ACP), and stabilized ACP. Crystalline calcium phosphates release calcium and phosphate ions but have low solubility. Unstabilized ACP or ACP with fluoride releases calcium and phosphate ions quickly but is unstable. Stabilized ACP stabilizes calcium and phosphate ions that keep them bioavailable, but limited penetration into deeper layers. Other remineralization approaches include self-assembling peptides and natural proteins.[7] Fluoride-based products promote remineralization but may cause fluorosis and less effective in low-saliva condition.[10] Xylitol-based products limit bacterial acid production, but very poor remineralization effect.[11]

DENTE91® remineralizing (RM) gel is a unique and powerful formulation, designed specifically to protect, preserve, and strengthen the enamel. It prevents and reduces tooth sensitivity, fight dental caries by remineralization. Nano-hydroxyapatite (n-HAP), lactoferrin, and potassium nitrate exhibit synergistic pharmacological effect. n-HAP promotes remineralization by depositing apatite nanoparticles in enamel defects.[12] Lactoferrin inhibits bacterial and fungal growth; it also combats gum diseases and reduces bad breath.[13,14] Potassium nitrate reduces hypersensitivity and desensitizes nerves by depolarizing nerve fibers.[15,16]

The aim of the present study is to test multifunctional oral health benefits of DENTE91® RM gel, through a series of *in vitro* models. Specifically, the study sought to assess its antimicrobial activity, enamel remineralization, caries protection, cavity healing, sensitivity relief, and teeth whitening efficacy.

Materials and Methods

This *in vitro* study investigated therapeutic potential of DENTE91® RM gel using validated laboratory methods, suitable biological substrates including human teeth, dentine disk, and NIH/3T3 cell line. Several laboratory prepared solutions were used, including demineralizing solution (2.2 mM calcium chloride, 2.2 mM sodium phosphate, 0.05M acetic acid, 1M potassium hydroxide), RM solution (1.5 mM calcium chloride, 0.9 mM sodium hydrogen phosphate, 0.15M potassium chloride, 1M potassium hydroxide) for pH cycle stimulation along with cell culture media, acidic agents and peptone water.

Antimicrobial activity

The antimicrobial activity of DENTE91® RM gel was evaluated against *Streptococcus mutans*, *Pseudomonas aeruginosa*, *Candida albicans*, and *Porphyromonas gingivalis* using pour plate method. Cultures were prepared in Soyabean casein digest agar, Sabouraud dextrose agar, and blood agar, activated, and diluted to 10^6 colony-formation unit (CFU)/mL. One gram of DENTE91® RM gel was added in 9 mL of 0.1% peptone water, vortexed, and inoculated with microbial suspension. After 2- and 5-min of treatment exposures, mixtures were filtered, washed, serially diluted, plated, incubated, and CFUs were counted in comparison to controls. The acceptance criteria required that the survival rate not exceed 0.01% after 2 min and 0.001% after 5 min of exposure, with the gel demonstrating at least 99.9% microbial kill efficiency.

Remineralization effect

Healthy teeth were cleaned and demineralized for 96 h to induce lesions. An 8-day pH-cycling regimen was followed, which included 5 min DENTE91® RM gel application before and after 6 h acid challenge, rinsing, and 16 h remineralization. Control group did not receive DENTE91® RM gel treatment. Effects were assessed through visual inspection, dentinal tubule morphological changes using scanning electron microscopy (SEM), and mineral content analysis through inductively coupled plasma–optical emission spectroscopy (ICP-OES).

Dental cavity healing potential

Dental cavity healing effect was assessed using the dimethyl thiazole diphenyl tetrazolium bromide (MTT) assay on NIH/3T3 mouse fibroblast cells, cultured in α-minimum essential medium with 10% fetal bovine serum. Cells were treated with five concentrations (1%, 0.5%, 0.1%, 0.05%, and 0.01%) of DENTE91® RM gel in triplicate (R1-R3). Optical density at 570 nm was used to measure cell proliferation and compared to controls.

Effect on hypersensitivity

The desensitizing effect was tested on dentine disks exposed to lemon juice. A 5-min treatment was applied daily, and samples were examined on days 1, 7, and 15 corresponding to 5-, 35-, and 75- min total exposure, respectively. Samples were analyzed for tubule closure by SEM.

Dental carries protection

Artificial carious lesions were created using 96 h demineralizing solution treatment, and a similar 8-day pH cycling regimen was followed as used in the remineralization study. Treated and control (without DENTE91® RM gel treatment) teeth were evaluated by visual inspection, SEM analysis, and ICP-OES.

Tooth whitening

Stained human teeth were treated with DENTE91® RM Gel for 5 min daily, and evaluated on Days 1, 5, and 7, corresponding to cumulative exposures of 5, 25, and 35 min, respectively. Tooth whitening was assessed using blue laser light reflection and a lux meter.

Data interpretation

Antimicrobial efficacy was evaluated by comparing CFU counts between treated and control groups. For remineralization, surface microhardness and SEM images were analyzed to assess mineral

deposition. The cavity healing potential was analyzed based on cell proliferation rate and morphological features *in vitro*. The effect on hypersensitivity was interpreted through SEM-based examination of dentinal tubule occlusion. Protection against dental caries was assessed using artificially induced carious lesions, with outcomes evaluated by visual inspection, SEM analysis, and mineral quantification through ICP-OES. Teeth whitening efficacy was interpreted by measuring changes in reflected light intensity using a lux meter under blue laser illumination.

Results

Antimicrobial activity

DENTE91® RM gel demonstrated potent antimicrobial efficacy against key oral pathogens: *S. mutans*, *P. aeruginosa*, *C. albicans*, and *P. gingivalis*, all displayed >99.99% killing efficiency within 5 min. The highest efficacy (100%) was observed against *C. albicans* at 5 min [Table 1].

Remineralization effect

DENTE91® RM gel substantially reduced the progression of demineralization and enhanced the remineralization process. As shown in Figures 1a and b, the teeth treated with DENTE91® RM gel displayed a considerable color difference from a yellowish tone to opaque white with fewer dental surface lesions compared to initial or control teeth. SEM analysis revealed that the diameter of open dentine tubules substantially reduced from 3.950 µm (control) to 2.648 µm (treated), indicating a 37.51% reduction [Table 2]. Mineral analysis further supported the remineralization effect of DENTE91® RM gel. The calcium content increased from 16.45% in the control group to 34.50% in the treated group, indicating a remarkable improvement of 109.73% over the control [Table 3]. Similarly, the phosphate content increased from 8.86% in the control group to 18.39% in the treated group, indicating an improvement of 107.56% over the control [Table 3].

Table 1: Antimicrobial efficacy of DENTE91® Remineralizing Gel

Organism	Exposure time (in min)	Percentage survival	Percentage efficacy
Streptococcus mutans	2	0.0036	99.996
	5	0.0006	99.999
Pseudomonas aeruginosa	2	0.0031	99.997
	5	0.0007	99.999
Candida albicans	2	0.0039	99.996
	5	0.0005	100.000
Porphyromonas gingivalis	2	0.0027	99.997
	5	0.0008	99.999

Dental cavity healing potential

DENTE91® RM gel exhibited a dose-dependent cellular proliferation of NIH 3T3 cells. While higher concentrations of DENTE91® RM gel (1% and 0.5%) reduced proliferation, the lowest concentration (0.01) enhanced cellular proliferation by ~10% over the vehicle control, indicating optimal healing activity at lower doses.

Effect on hypersensitivity

The surface scan of the dentine disk treated with DENTE91® RM gel demonstrated substantially reduced lesions compared to control dentine disks [Figure 2]. SEM analysis displayed a progressive reduction in dentine tubules over time, starting from a 10.08% reduction on day 1, 43.51% on day 7, and 66.53% on day 15 [Table 4]. These findings indicate effective tubule occlusion and potential alleviation of hypersensitivity with continued use of DENTE91® RM gel.

Protection against dental carries/ tooth decay

Data from SEM analysis revealed that the diameter of open dentine tubules substantially reduced from 3.489 µm (control) to 1.821 µm (treated), indicating a 47.81% reduction [Figure 3]. Furthermore, the calcium content increased from 16.63% in the control group to 35.04% in the treated group,

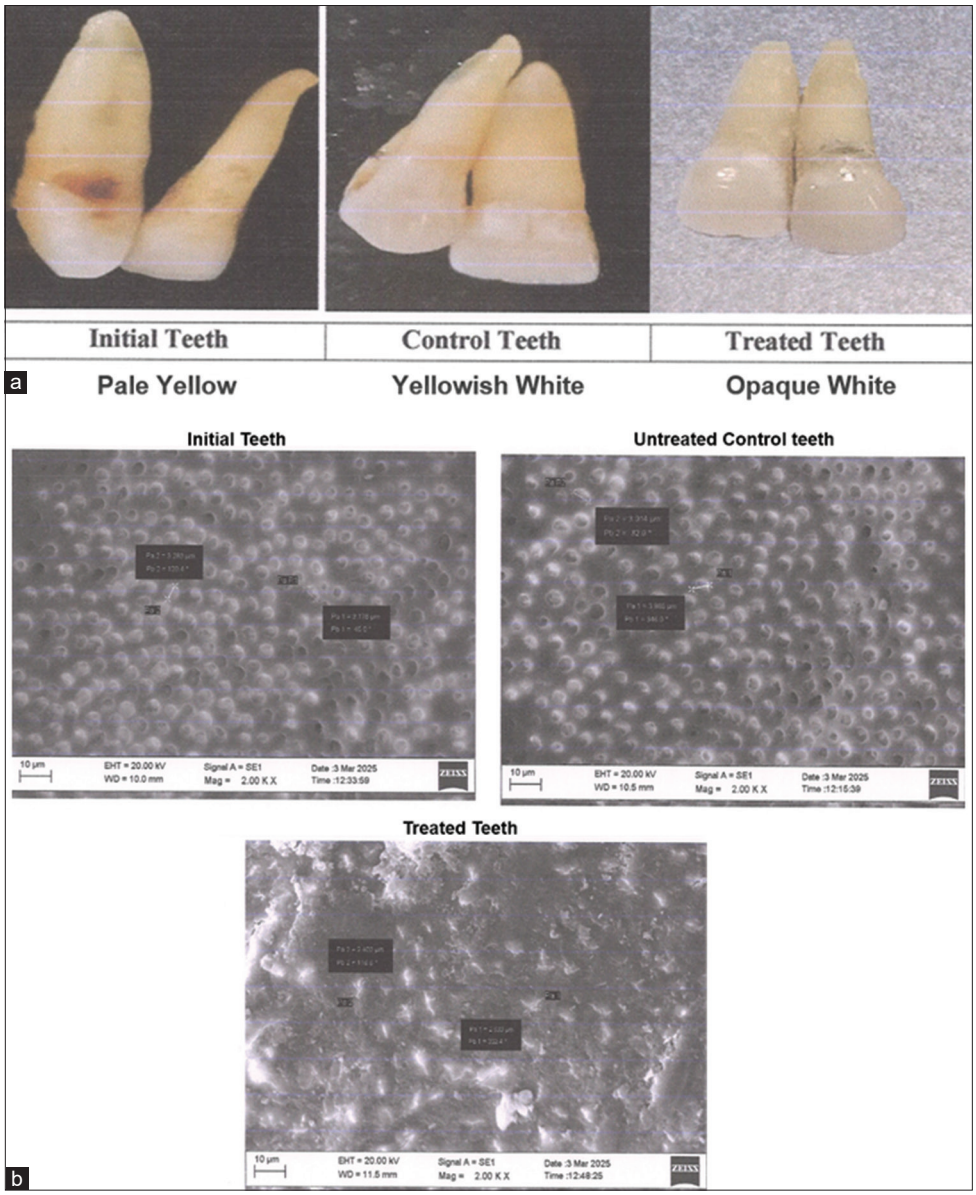

Figure 1: Remineralizing effect of DENTE91® Remineralizing Gel. (a) The color change of the teeth by visual inspection pre-and post-treatment of DENTE91® Remineralizing Gel. The lower panel shows initial teeth pale yellow in color, control teeth yellowish white in color, and teeth treated with DENTE91® Remineralizing Gel opaque white in color. (b) Images of teeth specimens under scanning electron microscopy to visualize remineralization effects. The left image shows Initial teeth before treatment, the right image shows control teeth without any gel treatment, and the bottom image shows teeth treated with DENTE91® Remineralizing Gel

indicating a remarkable improvement of 110.70% over the control. Similarly, the phosphate content increased from 8.75% in the control group to 18.22% in the treated group, indicating an improvement of 108.23% over the control. The data showed suggests DENTE91® RM gel effectively

Table 2: Diameters of open dentine tubules in the control versus DENTE91® Remineralizing Gel-treated group (remineralization effect)

Diameters	Initial teeth	Control teeth	Treated teeth	Reduction in diameter (control vs. treated)
Avg. diameter open dentine tubule (µm)	3.230	3.950	2.468	37.51%

Table 3: Mineral composition of teeth in the control versus DENTE91® Remineralizing Gel-treated group

Minerals	Initial teeth (%)	Control teeth (%)	Treated teeth (%)	Percentage improvement (control vs. treated) (%)
Calcium	21.67	16.45	34.50	109.73
Phosphate	11.61	8.86	18.39	107.56

Table 4: Diameter of open dentine tubules and % reduction post DENTE91® Remineralizing Gel-treatment (desensitization effect)

Day of treatment	Average diameter of open dentine tubules (µm)		Percentage reduction in diameter
	Control group	Treated group	
1st day	3.176	2.856	10.08
7th day		1.794	43.51
15th day		1.063	66.53

prevents demineralization and supports enamel repair.

Tooth whitening

Data from lux meter readings displayed a substantial increase in brightness of teeth treated with DENTE91® RM gel compared to control teeth. As shown in Figure 4, control teeth exhibited a yellowish tone and a minor improvement in the brightness of 14.32%. While teeth treated with DENTE91® RM gel showed progressive whitening with 39.31%, 65.99% and 87.07% improvement in brightness on day 1, 5, and 7, respectively.

Discussion

The present *in vitro* study evaluated multiple effects of DENTE91® RM gel, a novel product formulated to address a wide range of oral health concerns including antimicrobial protection, remineralization, cavity healing,

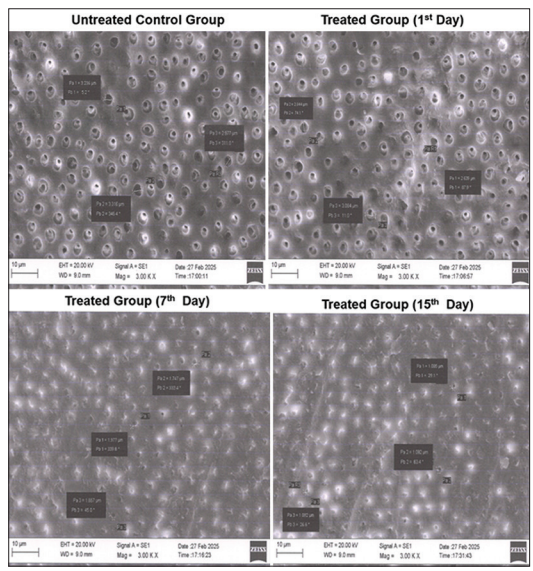

Figure 2: Images of dentine disks under scanning electron microscopy to visualize the effect of DENTE91® Remineralizing Gel on hypersensitivity. Panel A shows the image of the dentine disk in the untreated control group. Panels B, C, and D show the image of dentine disks in DENTE91® Remineralizing Gel -treated group (1st day, 7th day, and 15th day), respectively

dental hypersensitivity reduction, prevention of carries, and tooth whitening. Unlike conventional treatment options that typically target only a single function, DENTE91® RM gel was designed to offer comprehensive therapeutic benefits for better patient-centered care.

In the antimicrobial assay, significant efficacy was noted against Gram-positive (*S. mutans*),

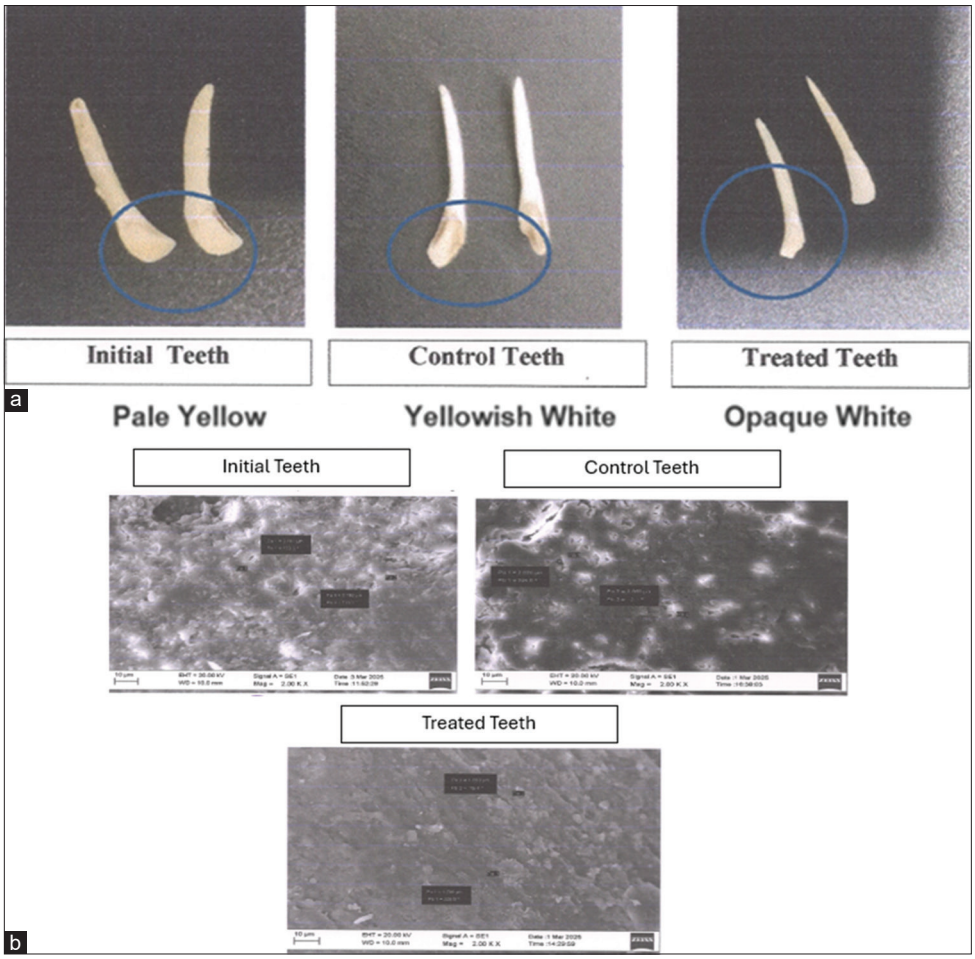

Figure 3: Protective effect of DENTE91® Remineralizing Gel against dental caries/tooth decay. (a) The color change of the teeth by visual inspection pre-and post-treatment of DENTE91® Remineralizing Gel. The lower panel shows initial teeth pale yellow in color, control teeth yellowish white in color, and teeth treated with DENTE91® Remineralizing Gel opaque white in color. (b) Images of teeth specimens under scanning electron microscopy to visualize remineralization effects. The left image shows Initial teeth before treatment, the right image shows control teeth without any Gel treatment, and the bottom image shows teeth treated with DENTE91® Remineralizing Gel

Gram-negative (*P. aeruginosa, P. gingivalis*), and fungi (*C. albicans*). Oral health conditions such as dental caries, gingivitis, and halitosis are associated with these bacteria.[17-19] Halitosis is often caused by Sulphur-producing gram-negative anaerobes like *P. gingivalis*.[19] Moreover, its 100% efficacy against *C. albicans*- the most common cause of oral candidiasis- indicates potential anti-fungal action.[20] The observed 99.99% microbial reduction after DENTE91® RM gel treatment indicates its broad-spectrum antimicrobial activity. This suggests its utility in not only preventing demineralization but also protection against various oral health infections.

The observed enamel remineralization in SEM analysis demonstrated strong therapeutic potential, especially with regular use. Tubule occlusion and the increase in calcium and phosphate content align with prior studies in terms of similar enamel repair benefits using n-HAP, casein phosphopeptide-amorphous (CPP)-ACP,

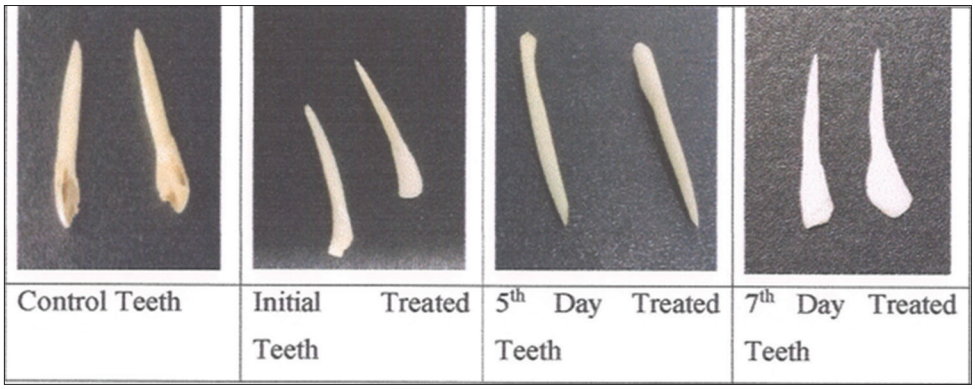

Figure 4: Effect of DENTE91® Remineralizing Gel on tooth whitening activity. Image shows the color change in the control versus DENTE91® Remineralizing Gel-treated group

and bioactive glass systems.[21-23] In contrast to conventional fluoride therapy, which carries a risk of fluorosis, DENTE91® RM gel utilizes n-HAP to promote safe and effective enamel remineralization.

The DENTE91® RM gel stimulated fibroblast proliferation, causing up to 113.92% growth compared to controls, which demonstrates significant regenerative capability and no cytotoxicity. These results are consistent with previously shown findings that calcium- and phosphate-based systems increase cellular stimulation and healing process.[24,25] Dental hypersensitivity was effectively reduced overtime with treatment, likely due to progressive sealing of dentin tubule. This process appears consistent with Brännström's hydrodynamic theory, which established a connection between pain and fluid movement in exposed tubules.[26,27] Similar evidence has been shown with established desensitizing agents such as arginine, calcium carbonate, and potassium nitrate, which also act by sealing tubules and reducing fluid movement.[28]

In the caries protection model, treatment greatly improved enamel remineralization as evidenced by occluded dentinal tubules and higher calcium and phosphate concentrations. These findings support previous evidence for fluoride, CPP-ACP, and bioactive glass; all of which promote mineral deposition and enhancement of enamel during acidic conditions. Fluoride supports the uptake of ions,[6] CPP-ACP stabilizes calcium-phosphate pools on the enamel surface,[29] and bioactive glass generates hydroxyapatite layers, which positively affect microhardness and seal tubules.[30] Thus, it is plausible that DENTE91® RM gel affects similarly.

Enamel brightness increased by 87.07% on day-7, compared to only 14.32% in the water-treated control group, with visible improvements in shade and surface smoothness. These findings align with whitening properties of n-HAP, which enhances enamel reflectance by filling microdefects and smoothing surface irregularities.[31] However, unlike peroxide-based whitening agents—which may provide whitening but can also erode the enamel and cause hypersensitivity—mineral-based approaches are a gentler yet effective alternative. Overall, these *in vitro* data indicate that DENTE91® RM gel provides multifunctional oral care benefits such as antimicrobial protection, structural repair, sensitivity relief, and cosmetic benefit. While the evidence is compelling, clinical studies will be essential to confirm its effectiveness in a real-world situation and patient outcomes.

Conclusion

This *in vitro* study demonstrated that DENTE91® RM gel is effective in promoting remineralization and provides antimicrobial, desensitizing, and teeth-whitening benefits. These findings suggest

its potential for use as a comprehensive oral care solution.

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Conflicts of Interest

This study was sponsored by ENAVANT RESEARCH, the manufacturer of DENTE91® RM Gel. However, the authors declare that the sponsor was not involved in the data interpretation.

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