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Original Article

The Remineralizing Potential of Coral Calcium Nano Silver Versus MI Paste Plus Toothpaste on Early White Spot Lesions of Primary Molars: In-Vitro Study

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Abstract

Aim: The aim of this study is to evaluate the remineralization potential of Coral Calcium Nano Silver toothpaste (Calcium Carbonate-Nano Silver) in comparison with MI Paste Plus (Casein PhosphoPeptide-Amorphous Calcium Phosphate Fluoride) toothpaste on management of white spot lesions of primary molars.

Methodology: Two equal groups (Group A and Group B) were created from a total of sixteen extracted or exfoliated human primary molar teeth. Eight primary molars in group (A) received treatment with Coral Nano Silver toothpaste. Eight primary molars in group (B) received treatment with MI Past Plus toothpaste. Pre-mineralization Energy dispersive X-ray (EDX) analysis was performed. After creating white spot lesions for 72 hours, the samples were exposed to the tested agents twice a day for three minutes each. Two weeks were spent on the remineralization procedure. Following demineralization and post-remineralization, the measurements were taken again.

Results: After 14 days, EDX measurements revealed no significant variations in the remineralization capability between Coral Nano Silver and MI Paste Plus ($P>0.05$).

Conclusions: Both MI Paste Plus and Coral Nano Silver demonstrated effective remineralization of artificially induced enamel lesions in primary molars.

Keywords: MI Paste Plus, Coral Nano Silver, Energy dispersive X-ray, Remineralization potential.

INTRODUCTION

The process of dental caries is dynamic. According to **Lacruz *et al.,* 2017**, it is a chemical dissolution caused by metabolic activity in a microbial deposit (biofilm) that covers a tooth surface at any given time. Even while demineralization is the initial stage, it can be reversed to retain enamel integrity by promoting remineralization, which is crucial for tooth enamel preservation **(Featherstone and Chaffee., 2018)**.

In relation to the mineral phase of enamel, the quantities of calcium and phosphate ions in oral fluids are supersaturated under normal physiological conditions. As a result, these ions are continuously added to the enamel's surface or replenished in places where they have disappeared. Saliva facilitates this natural defense system, which helps to preserve the mineral integrity of the mouth's enamel **(Rajesh *et al*., 2019)**.

The primary issue preventing enamel from remineralizing is still the availability of calcium. Furthermore, the remineralization process is highly complicated because of the chemical heterogeneity of enamel ***(*Jin., 2013)**. It has been suggested that "the non-invasive treatment" of early carious lesions through enamel remineralization could greatly improve the clinical management of the condition. This process has been studied for around a century **(Nagarathana *et al*., 2015)**.

In clinical dentistry, the possibility of remineralizing hard dental tissues may help close the gap between surgical and preventative procedures. The natural healing process for non-cavitated lesions is called remineralization, which uses calcium and phosphate ions along with fluoride to rebuild a new surface on crystal remnants that remain in subsurface lesions after demineralization **(Philip., 2019)**.

Fluoride is a two-edged sword: at optimal levels, it reduces the risk of dental cavities, but at greater concentrations, it can have negative side effects, such as skeletal and dental fluorosis. Dental research has been working on creating newer, safer, non-toxic, anti-cariogenic compounds to be utilized as alternatives to fluoride, which is still the mainstay of non-invasive caries prevention **(Duraisamy *et al.,* 2017)**.

To get around fluoride's disadvantages, numerous non-fluoride remineralizing chemicals have been created to help in remineralization. These agents include sodium calcium phosphosilicate (bioactive glass), calcium carbonate carrier SensiStat, sugar substitution carriers, casein phosphopeptides-amorphous calcium phosphate, and most recently, coral calcium nano silver.

Fluoride is combined with calcium and phosphate in a product called MI Paste Plus® (MPP, Tooth Mousse Plus®), which is ideal for creating fluorapatite deposits in enamel. An essential part of the product is the milk-derived protein casein phosphopeptide (CPP), which stabilizes amorphous calcium phosphate (ACP). This is changed by the fluoride present into fluorapatite, which is subsequently deposited in enamel **(Beerens *et al.,* 2018)**.

Coral Nano Silver toothpaste, a remineralizing natural fluoride-free product, recently hit the market. It is made up of alkaline calcium carbonate, which raises the pH of saliva, xylitol, which acts as an antibacterial agent, and nano silver solution, which has strong antimicrobial activity against Klebsiella pneumonia and Staphylococcus aureus. It also has anti-inflammatory and antifungal properties. According to **Abdelnabi *et al.,* 2019**, this product is thought to be useful in controlling enamel demineralization and encouraging the remineralization of subsurface enamel lesions **(Abdelnabi *et al*., 2019)**.

Therefore, the aim of this study is to evaluate the remineralization potential of Coral Calcium Nano Silver toothpaste (Calcium Carbonate-Nano Silver) in comparison with MI paste plus (Casein PhosphoPeptide-Amorphous Calcium Phosphate Fluoride) toothpaste on management of white spot lesions of primary molars.

MATERIALS AND METHODS

This invitro study was conducted in Pediatric Dentistry and Dental Public Health Department, Faculty of Dentistry, Cairo University, Egypt. The study was reviewed and approved by the Research Ethics Committee of the Faculty of Dentistry, Cairo University, on 26/6/2023, no. 13623. This study was conducted to evaluate the remineralization potential of Coral Calcium Nano Silver toothpaste in comparison with MI paste plus toothpaste on management of white spot lesions of primary molars.

Sample Size Calculation

A power analysis was designed to have adequate power to apply a two-sided statistical test of the null hypothesis that there is no difference between different tested groups. By adopting an alpha level of (0.05) a beta of (0.10) i.e. power=90% and an effect size (d) of (1 .89) calculated based on the results of **Abdelnabi *et al.*, 2019**, the predicted sample size (n) was total of (8) samples for each group (with a total sample size 16 for both). Sample size calculation was performed using G*Power version 3.1.9.7.

Collection Of Teeth

At the end of each day, newly extracted primary molars were gathered from the Pediatric Dentistry Department's outpatient clinic at Cairo University's Faculty of Dentistry. After brushing the teeth under running tap water to get rid of biological waste, the teeth were inspected under a magnifying glass to check for abnormalities, caries, and fissures on the buccal surface. If there were, they were thrown away. (9g NaCl, 0.24g CaCl2, 0.43g KCL, 0.2g NaHCO3, 1 L of water) was used to keep the specimens in daily fresh artificial saliva **(Kamal *et al.,* 2020; Alattar *et al.,* 2023)**.

Materials

The materials which were used in the present study, compositions and manufacturers are listed in **Table (1)** shown in **figure (1)** and **figure (2)** and the laboratory prepared solutions are present in **Table (2)**.

Samples Preparation

The coronal part of the teeth was detached from the roots at the dentin-enamel junction using a diamond disc which was attached to a micro motor straight handpiece (NSK, Japan) with water coolant. Specimens were then immersed in epoxy resin with their buccal surface facing upwards **Figure (3)**. Each tooth sample was covered with acid-resistant nail varnish, leaving just a little window (2 x 2 mm) in the middle of the buccal surface of enamel exposed to the demineralising solution, which caused a lesion resembling caries **(Hamba *et al*., 2020; Alattar *et al*., 2023)**. An elemental (Ca & P) was measured before any cariogenic challenge.

Sample Grouping

Each epoxy resin block was given a number (1-8) inside the group, being written by inerasable marker on one surface of the resin block together with the symbol of the group. Such demarcation was made to allow for assessment at pre-mineralization, after demineralization and post treatment. Then the numbered samples were stored in artificial saliva till subjected to EDX evaluation. Human primary molars, anonymously sourced and extracted, were randomly allocated into two groups (Group A, Group B) to evaluate their remineralization potential **(Alattar *et al*., 2023)**.

Group A: Primary molars which were treated with Coral calcium Nano silver toothpaste (Intervention group).

Group B: Primary molars which were treated with MI paste plus toothpaste (Comparator group).

Lesion Formation

A 12 mL newly made demineralizing solution (0.2 ppm fluoride, 2.2 mM CaCl2, 2.2 mM NaH2PO4, and 0.05 mM lactic acid) was added to each sample in a sterile test tube. To create synthetic carious lesions, the pH was brought down to 4.5 using 4% NaOH and kept at 37°C for 72 hours **(Alattar *et al*., 2023; Rafiei *et al*., 2020)**. Since deionized water has no remineralizing properties, it was used to thoroughly wash the samples for one minute, letting them dry after the lesion formed.

Application of Remineralizing Toothpaste

Following the manufacturer's recommendations, samples from each group were treated twice a day for 14 days with 0.03g of the specified undiluted remineralizing agent. Using a cotton tip applicator, the agents were applied for three minutes. This ensured consistency in the application technique across all samples, leading to more reliable results.

Cotton tips provide precise and uniform application of the remineralizing agent. In contrast, toothbrush bristles can vary in pressure, angle, and contact with the surface, making it difficult to control the amount and distribution of the tested product. The samples were then cleaned with deionized water and submerged in artificial saliva, which was changed every twenty-four hours. In order to evaluate changes, the mineral content, more specifically (Ca, phosphate [P]) was evaluated using EDX after 14 days **(Alattar *et al.*, 2023)**.

Statistical Analysis

Microsoft Excel 2016, Graph Pad Prism®, and SPSS 20® were used for statistical analysis. The mean, standard deviation, and lowest and maximum values were used to display all quantitative data. As a result, the Independent t test is used to compare the intervention group to the comparator group, and the Repetitive One-Way ANOVA is used to compare different intervals.

RESULTS

Intragroup Comparison in Intervention Group (Coral Calcium Nano Silver Toothpaste)

Table (3) and Figure (4) show the calcium, phosphorous, and calcium phosphorous ratios at baseline, after demineralization, and after remineralization in the intervention group, along with the minimum, maximum, mean, and standard deviation.

To compare baseline, demineralization, and remineralization, a repetitive one-way ANOVA test was used. The results showed a significant difference in calcium, phosphorous, and calcium phosphorous ratio ($P<0.05$).

Intragroup Comparison In Comparator Group (MI Paste Plus Toothpaste)

Table (4) and Figure (5) show the calcium, phosphorous, and calcium phosphorous ratios at baseline, after demineralization, and after remineralization in the comparator group, together with the minimum, maximum, mean, and standard deviation.

To compare baseline, demineralization, and remineralization, a repetitive one-way ANOVA test was used. The results showed a significant difference in calcium and phosphorous, as well as the calcium/phosphorous ratio, with a as ($P<0.05$).

Intergroup Comparison Between Intervention Group and Comparator Group

Table (5) and Figure (6) show the mean and standard deviation of the calcium, phosphorous, and calcium phosphorous ratios for the intervention and comparator groups at baseline, after demineralization, and after remineralization.

The Independent t test was used to compare the intervention and comparator groups, and the results showed that there was no significant change in the calcium, phosphorous, and calcium phosphorous ratio between the two groups at baseline, after demineralization, and after remineralization ($P>0.05$). phosphorous, and calcium phosphorous ratios for the intervention and comparator groups at baseline, after demineralization, and after remineralization.

Table (1): Specifications, compositions and manufacturers of the used materials.

Materials	Composition	Manufacturer
Coral Nano Silver®	Coral Calcium, Nano Silver Solution, Xylitol, Hydrated Silica, Sodium Cocoyl Glutamate, SodiumaMagnesium Silicate, Extract, Xanthan Gum, Hydrastis Canadensis (Goldenseal)Extract, Ginko Biloba Leaf Extract	Coral LLC. Carson City Nevada, United States
MI Paste Plus®	Pure water, glycerol, CPP-ACP, sorbitol, CMC-Na, propylene glycol, silicone dioxide, titanium dioxide, phosphoric acid, sodium fluoride (900ppm), flavoring, Sodium saccharin, ethyl p-hydroxy benzoate, Propyl p-hydroxy benzoate, Butyl p-hydroxy benzoate, Hydroxyapatite	GC Europe N.V. Interleuvenlaan, Leuven, Japan

Table (2): The Laboratory Prepared Solutions Used In The Study.

Solution	Composition	Used for	pH
Demineralizing Solution	0.2 ppm fluoride, 2.2 mM $CaCl_2$, 2.2 mM NaH_2PO_4, 0.05 mM lactic acid	Artificial sub-surface lesion formation.	4.5
Artificial Saliva	9g NaCl 0.24g $CaCl_2$ 0.43g KCL 0.2g $NaHCO_3$ 1 L of water	Storage medium for the sample.	7.0

Fig. (1): Picture showing Coral Nano silver® Toothpaste

Fig. (2): Picture showing MI Paste Plus® Toothpaste

Fig. (3): Embedding of specimens in epoxy resin with their buccal surface facing upwards.

Table (3): The comparison of calcium, phosphorous, and the calcium/phosphorous ratio for the intervention group at baseline, following demineralization, and following remineralization.

	Group A	Minimum	Maximum	Mean	Standard Deviation	P value
Ca	Baseline	42.3	50.06	46.35	2.34	0.0001*
	After demineralization	28.09	37.62	32.05	2.96	
	After remineralization	37.19	46.38	40.58	3.21	
P	Baseline	16.72	20.87	18.62	1.55	0.003*
	After demineralization	14.66	17.64	16.19	1.12	
	After remineralization	15.94	19.71	18.12	1.28	
Ca / P ratio	Baseline	2.17	2.74	2.49	0.51	0.001*
	After demineralization	1.64	2.57	1.98	0.17	
	After remineralization	1.97	2.75	2.24	0.11	

**Significant difference as P<0.05.*

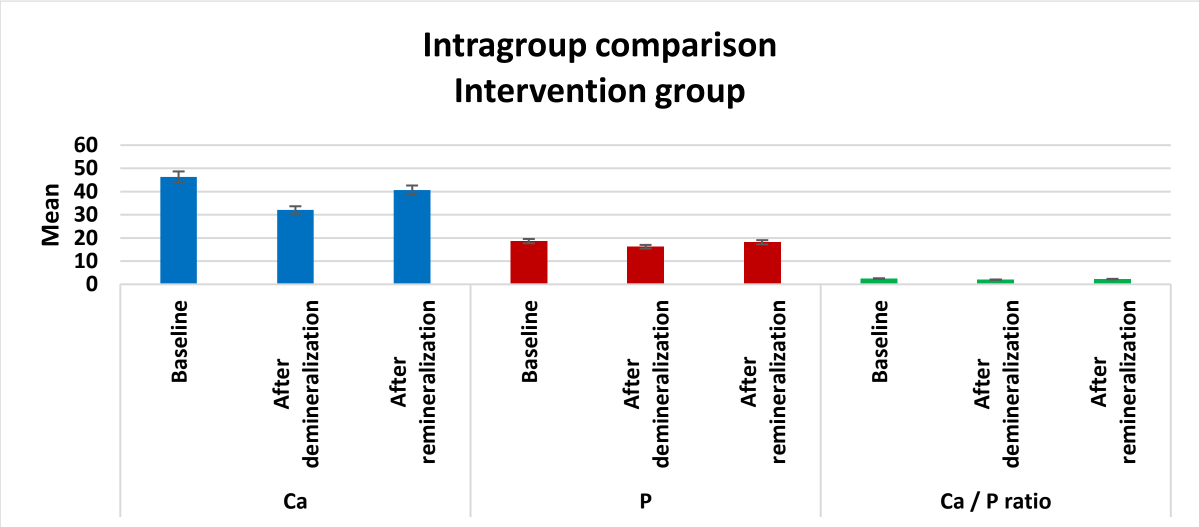

Fig. (4): Bar chart for intervention group showing calcium, phosphorous, and calcium / phosphorous ratio at different intervals.

Table (4): Descriptive results for comparison of calcium, phosphorous, and calcium/ phosphorous ratio regarding comparator group at baseline, after demineralization, and after remineralization.

	Group B	Minimum	Maximum	Mean	Standard Deviation	P value
Ca	Baseline	40.44	51.12	47.09	3.99	0.001*
	After demineralization	25.69	38.85	32.75	4.64	
	After remineralization	33.87	45.52	41.02	3.99	
P	Baseline	14.96	19.78	18.51	1.6	0.0004*
	After demineralization	14.02	17.01	15.06	1.2	
	After remineralization	14.99	19.51	17.17	1.52	
Ca / P ratio	Baseline	2.18	3.32	2.54	0.14	0.05*
	After demineralization	1.51	2.47	2.17	0.16	
	After remineralization	2.07	2.79	2.39	0.16	

**Significant difference as P<0.05.*

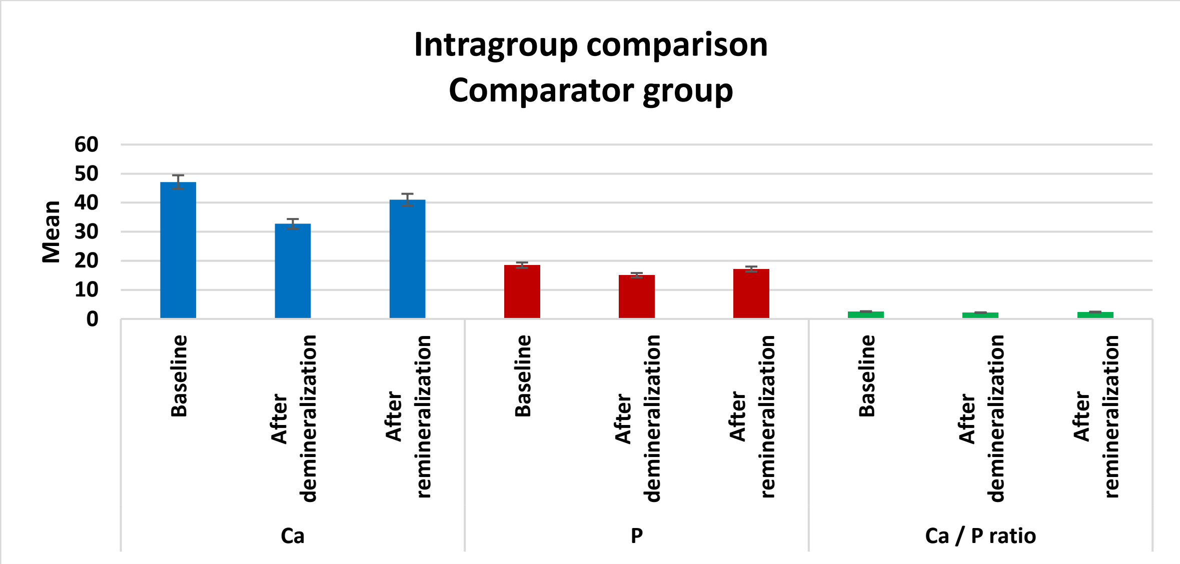

Fig. (5): Bar chart for comparator group showing calcium, phosphorous, and calcium / phosphorous ratio.

Table (5): Comparison between intervention and comparator groups regarding Ca, P, and Ca/P ratio at different intervals.

		Intervention group		Comparator group		Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference		P value
		Mean	Standard Deviation	Mean	Standard Deviation			Lower	Upper	
At Baseline	Ca	46.35	2.34	47.09	3.99	0.74	1.64	-2.74	4.24	0.65
	P	18.62	1.55	18.51	1.6	0.11	0.78	-1.79	1.57	0.89
	Ca/P	2.49	0.51	2.54	0.14	0.05	0.18	-0.35	0.45	0.79
After demineralization	Ca	32.05	2.96	32.75	4.64	0.71	1.94	-3.47	4.87	0.72
	P	16.19	1.12	15.06	1.2	1.16	0.58	-2.37	0.11	0.07
	Ca/P	1.98	0.17	2.17	0.16	0.19	0.08	-0.012	0.36	0.051
After Remineralization	Ca	40.58	3.21	41.02	3.99	0.44	1.81	-3.44	4.32	0.81
	P	18.12	1.28	17.17	1.52	0.95	0.71	-2.45	0.55	0.19
	Ca/P	2.24	0.11	2.39	0.16	0.15	0.06	-0.002	0.29	0.06

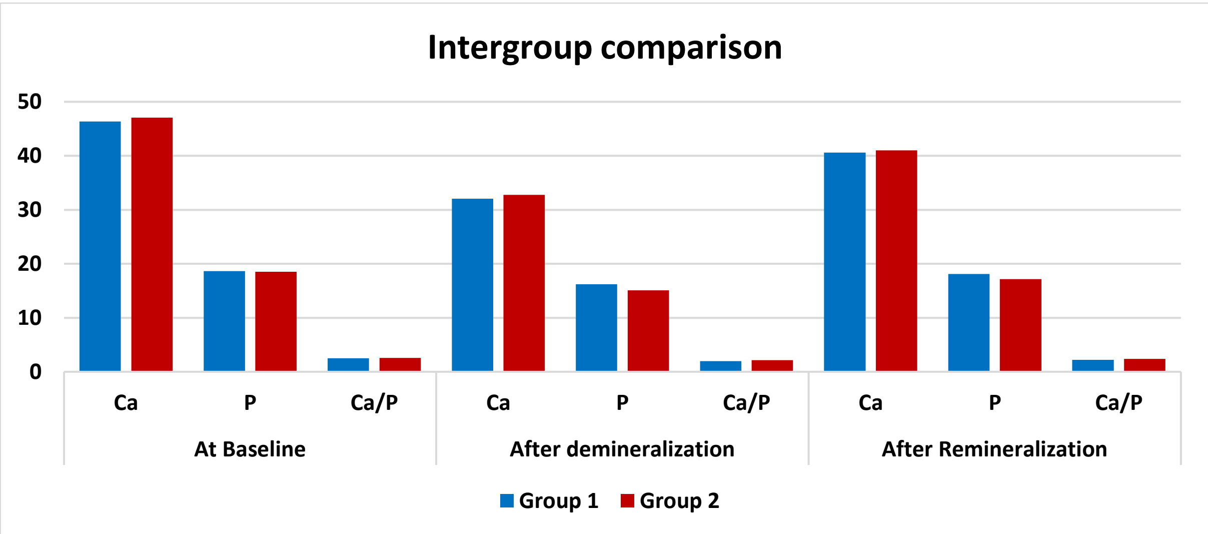

Fig. (6): Bar chart showing intergroup comparison between intervention and comparator groups.

DISCUSSION

Dental caries is still a major public health concern because it causes obvious white-spot lesions through molecular changes in tooth apatite crystals. According to **Abou Neel *et al.*, 2016**, the caries process is caused by an imbalance between protective and detrimental components, which dissolves apatite crystals and leads in a net loss of calcium, phosphate, and other ions. Modern dentistry places a high priority on non-invasively managing non-cavitated lesions by remineralisation in order to slow the disease's progression and enhance the tooth's strength, appearance, and functionality **(Cochrane *et al.*, 2010)**.

This current in-vitro study was carried out to assess the remineralization potential of Coral Nano Silver versus MI Paste Plus on artificially induced early enamel lesions in primary teeth. CPP-ACPF has a synergistic anticariogenic effect, releasing calcium, phosphate, and fluoride ions that promote remineralization. MI Paste Plus contains amorphous calcium and phosphate stabilized by casein phosphopeptide, which helps localize the ions at the enamel surface and enhances hydroxyapatite crystal density **(Behrouzi *et al.*, 2020)**.

Coral nano silver consists of natural calcium carbonate (CaCO3) particles capable of adhering to mineral surfaces. When calcium carbonate dissolves, it releases calcium that can remineralize lost minerals, while the carbonate release may slightly increase local pH, helping to fill superficial enamel lesions **(Arifa *et al.*, 2019)**. Similarly, **Abdelnabi *et al.*, 2019** study stated that coral calcium demonstrated a remineralization ability comparable to nano hydroxyapatite across all groups, with the highest effect observed at a 20% concentration.

In the present study, each sample was embedded in an epoxy resin block for easy handling, leaving only the buccal surface of the sample exposed. The hardened epoxy enhanced the microstructure, providing durability during mechanical preparation and preventing debris accumulation **(Kjellsen *et al.*, 2003)**. The samples were divided into two equal groups at random to prevent operator bias, make the groups comparable, and provide each group an equal chance of getting the treatment **(Lim and In., 2019)**.

In order to replicate an early enamel lesion that only turns white when dry, specimens were immersed in a demineralizing solution for 72 hours at 37°C. This resulted in a subsurface demineralization that was about 150μm broad and had an intact surface. Demineralization was performed as described by **Lata *et al.*, 2010; Alattar *et al.*, 2023**. Deionized water was chosen for washing of specimens because of its nature to lack any remineralizing capability and to remove any remnants of the used materials **(Behrouzi *et al.*, 2020)**.

Following the manufacturer's directions, the remineralization regimen was applied twice daily for three minutes every twenty-four hours for two weeks. comparable to the study by **Shirahatti *et al.*, 2007,** in which treatment pastes were applied twice daily for three minutes throughout a fourteen-day period. The remineralization protocol lasted 14 days, with artificial saliva being replaced every 24 hours. to preserve the proper pH of the solution and ionic equilibrium **(Alattar *et al.*, 2023)**.

The current study's findings demonstrated that there was no statistically significant difference between the two groups' mean weight percentages of calcium and phosphate before and after demineralization (sound teeth). In the MI paste plus group, the Ca (wt%) decreased significantly from 47.09 ± 3.99 at baseline to 32.75 ± 4.64 after demineralization, and the P (wt%) decreased significantly from 18.51 ± 1.6 at baseline to 15.06 ± 1.2 after demineralization. In the Coral nano silver group, the Ca (wt%) decreased significantly from 46.35 ± 2.34 at baseline to 32.05 ± 2.96 after demineralization, and the P (wt%) decreased significantly from 18.62 ±

1.55 at baseline to 16.19 ± 1.12 after demineralization. Following demineralization, the mineral content in both groups significantly decreased, with approximated values. This finding was a logical outcome because the sound samples had nearly similar mineral percentage and after application of the same demineralizing solution, the percentage of mineral loss was also close **(Omran *et al.*, 2021)**.

However, the current study's findings demonstrated that both groups' post-treatment mineral content significantly increased when the two distinct remineralizing toothpaste types were used. This indicates that in the MI paste plus group, Ca (wt%) significantly increased to 41.02 ± 3.99 and P (wt%) significantly increased to 17.17 ± 1.52. And the Coral nano silver group, Ca (wt%) increased significantly to 40.58 ± 3.21 and P (wt%) increased significantly to 18.12 ± 1.28. This result suggests that MI Paste Plus and Coral Nano Silver significantly remineralize enamel caries, hence raising the mineral content in WSLs. This may be because the constituent's Ca^{2+} and PO_4^{3-}ions in these kinds of toothpaste were able to infiltrate enamel pores to serve as templates during the precipitation process, drawing a significant quantity of Ca^{2+} and PO_4^{3-} from the remineralisation solution to the enamel surface to fill any vacancies left by the enamel calcium crystals **(Soares *et al.*, 2017)**. MI Paste Plus is thought to be able to keep the calcium and phosphate supersaturated across the surface of the enamel. Furthermore, MI Paste Plus's fluoride concentration increases the remineralizing capacity of CPP-ACP by working in concert with it.

The deposition of calcium ions from the calcium carbonate in Coral toothpaste may be the cause of Coral calcium's ability to remineralize demineralized enamel. Additionally, the high calcium concentration of the toothpaste causes the pH to change from acidic to alkaline, which promotes mineral deposition **(Kumar *et al.*, 2016)**. By increasing the ionic mobility of anions such as phosphate and hydroxyl, this change in alkalinity supplies more ions for the remineralization of enamel. On the other hand, a low pH in the remineralizing solution indicates a greater concentration of H+ ions, which limit the number of ions available for remineralization via binding to anions. Furthermore, the inclusion of silica facilitates the gel's adherence to the surface of the tooth **(Abdelnabi *et al.*, 2019)**.

After remineralization, the mean calcium and phosphate weight percentage of several toothpastes showed insignificant difference between groups. This study's results concurred with those of **Ebrahimi *et al.*, 2017**. They claimed that there was no discernible difference between MI Paste Plus, Remin Pro, and NaF's efficacy in treating children's regressive WSLs. This outcome was also consistent with **Alattar *et al.*, 2023** study, which evaluated the remineralization potential of MI Paste Plus and Remin Pro on artificially created white spot lesions in primary molars. In summary, it was discovered that both treatment groups improved the remineralization of primary molars' caused demineralized enamel. This could be because remineralizing agents were applied infrequently during the brief trial period.

The results displayed that both Coral Nano Silver and MI Paste Plus used in the present study effectively enhanced remineralization of enamel by forming deposits and creating a protective coating on demineralized enamel surface. The most plausible explanation for these results might be that the findings could be attributed to the fact that the microporosities formed in the subsurface enamel due to demineralization offer areas prone to the redeposition of materials with higher mineral content, comparable to what happens in arrested caries, high calcium concentrations have been previously demonstrated to be effective in dental remineralization, high calcium concentration can lead to rapid absorption in the surface layers, and hence, reduced remineralization in deeper lesion layers, these findings had been in accordance to **Alattar *et al.*, 2023**. Additionally, gel ion components can penetrate deeper into demineralized enamel due to its higher porosity compared to sound enamel. This larger surface area facilitates greater interaction with enamel minerals, promoting the deposition of calcium from the coral calcium gel onto the enamel surface. Coral calcium's high calcium carbonate content encourages calcium ion deposition via a concentration gradient, which probably blocks surface pores and increases remineralization **(Abdelnabi *et al.*, 2019)**.

LIMITATIONS

This in vitro study faces challenges in replicating the complex conditions of the oral cavity, such as the presence of plaque, saliva, and bacterial biofilms. Additionally, variability among samples from different donors, influenced by environmental factors like diet, may have affected the results. The short experimental period for remineralization does not reflect real-life scenarios, emphasizing the need for further research with longer durations.

CONCLUSIONS

Both MI Paste Plus and Coral Nano Silver toothpastes significantly increased the mineral content of demineralized enamel when used twice daily for two weeks. There is no significant difference in remineralizing potential of white spot lesions between MI Paste Plus and Coral Nano Silver.

To further validate these findings, it is recommended that further in vivo investigation studies are needed to examine the efficacy of the remineralizing agents in the highly challenging oral environment. Additionally, more conclusive results can be obtained through further studies must be done on the formation and chemical structure of enamel crystals using advanced quantifying techniques and on the acid solubility resistance of these remineralized crystallites. Finally, it is crucial to investigate the remineralization potential of MI Paste Plus and Coral Nano Silver over a longer duration to determine their long-term effectiveness.

Conflict of interest:
The authors declare no conflict of interest.

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Ethics:
This study protocol was approved by the ethical committee of the faculty of dentistry-Cairo university on: 26/6/2023, approval number: 13623.

Data Availability:
Data will be available upon request.

CRediT statement:
Author 1: Conceptualization, Data curation, Formal analysis, Investigation, Resources, Writing - original draft preparation.

Author 2: Conceptualization, Data curation, Formal analysis, Project administration, Writing - review and editing.

Author 3: Conceptualization, Data curation, Formal analysis, Methodology, Supervision, Writing - review and editing.

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