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Comparative Evaluation Of Two Different Toothpastes On Microhardness Of Artificially Induced White Spot Lesions In Primary Teeth Using Vickers Hardness Tester – An In Vitro Study.

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ABSTRACT

Aim and background: *This study aimed to assess and compare the remineralization potential of Fluoridated (Tricalcium phosphate paste) and non-fluoridated (Calcium sucrose phosphate paste) toothpastes using the Vickers hardness tester.*

Materials and methods: *Sixty enamel samples were prepared by embedding the crown of extracted or exfoliated primary teeth in acrylic resin blocks leaving the buccal surface exposed. After developing the initial caries lesions using 37% phosphoric acid gel for 3 minutes, the samples were divided into three groups (n = 20). Samples in Group A were treated with fluoridated (Clinpro 3M ESPE) and in Group B with non-fluoridated (Enafix) calcium phosphate toothpaste. The control group C received no treatment. Toothpaste was applied to samples for 4 minutes twice daily for 10 days. Samples were kept in artificial saliva throughout the study. The enamel surface microhardness (SMH) was measured at baseline, post-demineralization, and post-treatment using a Vickers hardness tester. The data obtained were analyzed using ANOVA for intergroup comparison followed by pairwise comparison by Tukey's post hoc test.*

Results: *No statistically significant difference was found for mean microhardness among the three groups at baseline with p=0.516 and at demineralization with p=0.562 but a highly significant difference was found at remineralization with p<0.001. Multiple comparisons between every two groups showed a highly statistically significant difference at remineralization with Clinpro toothpaste being the best of them in terms of remineralization potential.*

Conclusion: *The fluoridated (Clinpro 3M ESPE) toothpaste was more effective in remineralizing early enamel lesions than non-fluoridated (Enafix) toothpaste.*

Clinical significance: *The present study suggests the non-invasive treatment for white spot lesions in primary teeth which promotes net mineral gain through the process of remineralization.*

Keywords: *Vickers hardness, white spot lesion, toothpaste, in vitro, calcium phosphate, primary teeth*

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I. INTRODUCTION

Dental caries is defined as an irreversible microbial disease of the calcified tissues of the teeth, characterized by demineralization of the inorganic portion and destruction of the organic portion of the tooth, which often leads to cavitation.[1] Demineralization can be described as the loss of calcium and phosphate minerals from the tooth surface below critical pH and in turn decreases the hardness of the tooth.[2] The initial carious lesions are the so-called "white spot" lesions, which implies that there is a subsurface area with a decrease in mineral loss beneath a relatively intact enamel surface.[3] Thus white spot lesion can be considered a demineralized lesion. These white spot lesions are known to be reversible if intervened with novel non-invasive effective methods through the process of remineralization.

Remineralization of dental enamel is the reconstitution of the lost mineral content in teeth. Dentifrices-containing remineralizing agents are known to be effective in remineralization of early enamel lesions. Various remineralizing toothpastes containing agents such as casein phosphopeptide, and calcium phosphate are available in the market to yield daily remineralization and prevention against dental caries. Fluoride has been

known to be the most common and effective remineralizing agent. Although the remineralizing efficacy of fluoride is substantially justified, the material is not able to surpass the high caries challenge posed by few individuals and this highlights the need to find newer methods to enhance the remineralization process.[4]

Studies have shown that fluoride drives the process of remineralization only if there is an adequate supply of calcium and phosphate.[5] Clinpro (3M ESPE) is an anticaries tricalcium phosphate (beta-TCP) and sodium fluoride (NaF) dentifrice. The combination of fluoride with beta-TCP provides greater remineralization in terms of fluoride absorption and microhardness.[6]

Since the process of remineralization is limited by the availability of calcium and phosphorous ions, calcium phosphate-based remineralization systems like Anticay® which is a mixture of calcium sucrose phosphate with inorganic amorphous calcium phosphate are commercially available.[7,8] These newly introduced calcium phosphate-based systems are known to have remineralizing potential as their solubility in water provides high concentrations of free calcium and phosphate ions several times higher than normally present in saliva.[9] They are easily available in the market in the form of both fluoridated and non-fluoridated toothpastes. However, the use of a greater amount of fluoride may increase the risk of toxicity, for example, dental fluorosis, especially among children <6 years of age.[10] And also it has been proved that children who brushed with low-fluoride toothpaste may increase the risk of caries.[11] Therefore, more studies should be done to determine whether children should be prescribed fluoridated or non fluoridated toothpaste. Thus this study aimed to comparatively evaluate fluoridated and non fluoridated calcium phosphate(CP) based toothpaste on microhardness of artificially induced white spot lesions in primary teeth using Vickers hardness in terms of remineralization potential.

II. MATERIALS AND METHODS

Ethical approval and trial design:

This in vitro clinical trial was conducted at the Department of Pediatric and Preventive Dentistry, MGV's KBH Dental College and Hospital, Nashik, Maharashtra, India. Ethical approval for the study was obtained from the institutional research committee.

Test agents used in this study:

Two commercially available toothpastes and artificial saliva were used in this study-

- Tricalcium phosphate toothpaste - Clinpro™ Toothpaste (3 M ESPE, USA).
  Tooth cream containing tricalcium phosphate and 0.21% w/w sodium fluoride (950 ppm).
- Calcium sucrose toothpaste – EnaFix (Group Pharmaceuticals, Malur, India).
  5% calcium sucrose phosphate with inorganic amorphous calcium phosphate (Anticay®)
- Artificial saliva – Wet mouth (ICPA health products LTD, India).
  Contains water, glycerin, cellulose gum, sodium saccharin, parabens, and flavor.

Sample size:

The sample size was determined using the mean and standard deviation values from the literature using the formula

$$n = \frac{2 (Z_\alpha + Z_\beta)^2 [s]^2}{d^2}$$

where Z_α is the z variate of alpha error i.e., a constant with a value 1.96, Z_β is the z variate of beta error i.e., a constant with value 0.84.

The sample size calculated was 60 for this study using the power calculation $\alpha = 0.05$ and $\beta = 0.20$ with 80% being the power of the study.

Method of Selection of study subjects:

Inclusion criteria: Caries free extracted or exfoliated primary molar tooth
Exclusion criteria: Cavitated tooth, Restored tooth, Teeth with any other enamel defects

Randomization:

This was an analytical study.
Caries-free extracted or exfoliated primary molar teeth was selected for the study. The samples were randomly divided into 3 groups by using lottery method according to treatment modalities as follows:
Group A- Fluoridated Calcium phosphate toothpaste (Clinpro™ 3M ESPE)
Group B- Non fluoridated Calcium phosphate toothpaste (Enafix)
Group C- Control group (Artificial saliva – Wet mouth)
Each sample received only one treatment modality.

Preparation of test samples:

Sixty caries-free extracted or exfoliated primary molar teeth were selected for the study. The tooth specimens were thoroughly cleaned with an ultrasonic scaler to remove all soft-tissue remnants, calculus, and plaque and after polishing with pumice paste and rubber cup specimens were stored in the normal saline. The roots of the teeth were removed up to the cementoenamel junction by using a diamond disc at 15,000 rpm, attached to a slow-speed straight handpiece in a micromotor with constant water coolant. Specimens were placed in a plastic mould and embedded in self-cure acrylic resin, in such a way that the buccal portion of the crown of the tooth will be projected. (Fig. 1) The enamel samples from all the groups were kept in artificial saliva throughout the study. Following this, all the samples were tested for surface microhardness at different stages.

White spot lesion stage:

All samples were demineralized with 37% phosphoric acid gel (BestEtch™, Waldent) (Fig. 2) which was applied on buccal surface of teeth for 3 minutes. After 3 minutes it was washed with distilled water and allowed to dry. This created artificial white spot lesions just mimicking the initial carious lesions.

Clinical interventions:

GROUP A – Fluoridated CP toothpaste. (Clinpro 3M ESPE) (Fig. 3)
It was applied for 4 min twice a day for 10 days using a cotton applicator tip.
GROUP B – Non fluoridated CP toothpaste. (Enafix) (Fig. 4)
It was applied for 4 min twice a day for 10 days using a cotton applicator tip.
GROUP C – Artificial saliva. (Control group)
Samples were rubbed using a cotton applicator tip without any toothpaste for 4 min twice a day for 10 days. After 4 min the samples were washed with distilled water.

Fig. 1 Human extracted or exfoliated primary teeth embedded in acrylic block (60 samples)

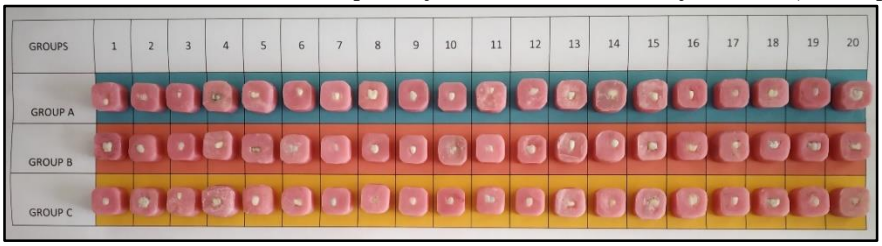


Fig. 2 Application of 37% phosphoric acid gel

Fig. 3 Group A: Application of Clinpro toothpaste to tooth surface using applicator tip

Fig. 4 Group B: Application of Enafix toothpaste to tooth surface using applicator tip

Fig. 5 Vickers hardness tester

Recording of readings:

Enamel microhardness assessment was done for each group by Vickers Microhardness tester (Prima German, model no. 73/Marz/0119/02) with a load of 100 gm for 15 seconds. On each sample, three indents were made, and the mean value was calculated. (Fig. 5) Microhardness was measured-

a) At base level
b) At white spot lesion stage
c) After 10 days using remineralizing agent

Statistical analysis:

All the data was entered into Microsoft Excel 2010. Statistical analysis of the results of the experiments was performed using descriptive statistics, and the data were expressed as mean and standard deviation. Inter group comparison of various parameters among three groups was done for Analysis of Variance (ANOVA). All the results were considered significant with a probability p-value <0.05. Multiple pairwise individual comparisons among the groups were done by Post hoc test.

III. RESULTS

No statistically significant difference was found among the three groups at baseline and demineralization ($p<0.05$) whereas a statistically highly significant difference was found at remineralization ($p<0.001$) among the three groups using ANOVA. (Table 1)

The mean microhardness at remineralization for Group A, Group B, and Group C was 373.15, 309.28, and 279.02 respectively which indicated Group A had the highest mean microhardness at remineralization. (Table 2)

There was a significant reduction in mean microhardness from baseline to demineralization and an increase in mean microhardness values from demineralization to remineralization approaching the baseline values

in both groups. The maximum demineralization-remineralization mineral gain was found in Group A followed by Group B and then Group C. (Table 3)

As ANOVA was significant at remineralization, multiple pairwise comparisons were done at the remineralization level using Tukey's post hoc test. Multiple comparisons between every two groups showed highly significant differences at remineralization with $p<0.001$. (Table 3, Graph 1)

Table 1 Comparison of Micro-hardness among three groups at Baseline, Demineralization, and Remineralization by Analysis of Variance

Sr no	**Groups**	**Baseline**		**Demineralization**		**Remineralization**	
		Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**
1	GROUP A	406.625	3.3359	264.425	2.6620	373.150	4.4959
2	GROUP B	407.575	2.9077	264.550	2.6552	309.275	4.8054
3	GROUP C	406.450	3.6379	265.300	2.9886	279.025	3.8061
ANOVA	F VALUE	0.670		0.583		2397.371	
	P VALUE	0.516		0.562		<0.001*	

Group A – Clinpro, Group B – Enafix, Group C – Artificial saliva
Significance: *p < 0.05; SD: Standard deviation

Table 2 Pairwise comparison of Micro-hardness among three groups at Remineralization by Tukey's Post hoc test

Multiple Comparisons						
Dependent Variable: Remineralization Tukey HSD						
(I) Groups	(J) Groups	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
GROUP A	GROUP B	63.8750*	1.3879	<0.001*	60.535	67.215
GROUP A	GROUP C	94.1250*	1.3879	<0.001*	90.785	97.465
GROUP B	GROUP C	30.2500*	1.3879	<0.001*	26.910	33.590
*. The mean difference is significant at the 0.05 level.						

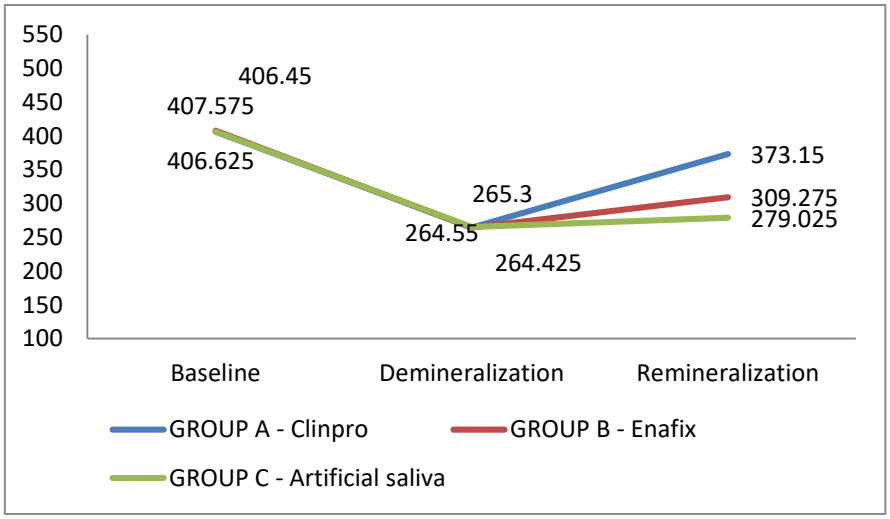
Group A – Clinpro, Group B – Enafix, Group C – Artificial saliva

Table 3 Pairwise comparison of Micro-hardness among three groups at Remineralization by Tukey's Post hoc test.

Sr no	**Groups**	**Baseline**		**Demineralization**		**Remineralization**	
		Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**
1	GROUP A	406.625	3.3359	264.425	2.6620	373.150	4.4959
Mean Change	Baseline- Demineralization Reduction	142.20 ± 4.94					
	Demineralization-Remineralization Gained			108.72 ± 5.29			
2	GROUP B	407.575	2.9077	264.550	2.6552	309.275	4.8054
Mean Change	Baseline- Demineralization Reduction	143.02 ±4.25					
	Demineralization-Remineralization Gained			44.73 ± 5.38			
3	GROUP C	406.450	3.6379	265.300	2.9886	279.025	3.8061
Mean Change	Baseline- Demineralization Reduction	141.15± 3.54					
	Demineralization-Remineralization Gained			13.73 ± 6.13			

Group A – Clinpro, Group B – Enafix, Group C – Artificial saliva

Graph 1 Comparison of Micro-hardness among three groups at Baseline, Demineralization, and Remineralization



IV. DISCUSSION

Due to the increased availability of novel remineralizing agents in the market, many clinical trials have been carried out to acknowledge the most effective and technique-sensitive remineralizing agent which can be used routinely especially for children e.g., toothpaste. This study was carried out to evaluate whether the remineralizing efficacy of non-fluoridated calcium phosphate toothpaste is similar to that of fluoridated toothpaste so that to determine if only a prescription of non-fluoridated toothpaste is sufficient. Thus, this in vitro study aimed to evaluate the remineralizing potential of two different toothpastes (Fluoridated and non-fluoridated) in the treatment of initial carious lesions considering the side effects of increased intake of fluoride by children accidentally especially below 6 years of age.

The white spot lesions can be intact for 6 to 7 years, which either become arrested or revert to sound enamel in 75% of cases whenever there is the availability of calcium and phosphate ions in an oral environment and only 25% cases proceed to cavitations.[12] Remineralization starts when the salivary pH increases beyond the critical pH level.[9] Non-invasive remineralization methods like dentifrices help to restore the dissolved mineral content of teeth thus preventing further advancement of the carious process.

In the demineralization process, there is a loss of mineral content from the tooth surface thus in turn reducing the hardness of the tooth. However, remineralization refers to a reconstitution of lost mineral ions thus increasing the microhardness of tooth structure.[2] Thus in this study to determine and assess microhardness, a Vickers microhardness tester machine was used and surface microhardness was measured at baseline, post-demineralization, and post-remineralization stage. Surface microhardness pyramid shaped indentation provides a proportionately simple and accurate method with high precision in demineralization and remineralization studies in materials of fine microstructure, non-homogenous, or prone to cracking such as dental enamel.[13] In the present study, Group A with Clinpro toothpaste showed better remineralization potential (373.15 VHN) over Group B with Enafix (309.28 VHN), $p<0.001$.

In order to create an artificial demineralized lesion, 37% phosphoric acid was used, as suggested by Sorozini.[14] Within the limitations of this study, this was considered sufficient, as it has been shown that absolute simulation of oral conditions is almost impossible due to other variables, including the speed of saliva flow and its buffering ability, dynamic pH cycles in the mouth, and behavioral changes.[15] As expected, the application of acid led to a significant decrease in microhardness values due to mineral loss, lowering the values in each group to similar levels.

Clinpro contains 0.21% NaF (950 ppm fluoride) and facilitates remineralization, prevents demineralization, and caries progression. According to Rao et al., Clinpro crème was noted in a report as a new material obtained using a milling technique incorporating beta TCP and sodium lauryl sulfate or fumaric acid. This idea behind the Clinpro formulation was hypothesized to provide a "functionalized" calcium and a "free" phosphate designed to drive fluoride remineralization effectiveness.[6] The significant remineralizing effect of TCP can be explained by increased calcium levels in plaque and saliva after its application, the presence of free calcium and phosphorus ions, as well as the presence of fluoride ions in saliva, which provided a suitable remineralizing solution to facilitate the remineralization of initial carious lesions.[16,17]

Alfeel J et al concluded that, Clinpro Tooth Creme had a remineralizing effect on white-spot lesions while oral health care itself was not enough to be able to remineralize them as combining TCP and fluoride could

have a greater impact than just applying fluoride topically. When there is an acid challenge nearby, the anticariogenic activity of Tri Calcium Phosphate's benefit of supplying calcium and phosphate to the enamel-surrounding media.[18] In accordance with the present study, Sreekumar P et al.[19] and Nalini P et al.[20] found Clinpro as a promising agent for remineralizing primary teeth and also concluded that TCP-containing dentifrices could remineralize teeth in a significant manner.

Anticay® is a mixture of calcium salts of sucrose phosphate esters, complexed with inorganic calcium orthophosphate. It is composed of 10-12% calcium and 8-10% phosphorous by weight.[9] Anticay® in Enafix – Quickly breaks down and releases calcium, phosphate, and sucrose phosphate ions into the saliva, thus increasing the rate of remineralization through the common ion effect.[21] An important feature of Anticay® is that it allows for the creation of aqueous solutions containing very high concentrations of calcium and phosphate without precipitation occurring. It prevents acid dissolution of enamel by depositing a layer of sucrose phosphate ion layer over the exposed hydroxyapatite of the tooth. The sucrose phosphate ions are adsorbed on the enamel surface which helps in decreasing the rate of acid dissolution of hydroxyapatite.[7] Calcium sucrose phosphate also prevents plaque accumulation thus reducing demineralization activity.[22] In addition, Calcium Sucrose Phosphate application was also found to have a beneficial in restoring the color of white spot lesions to that of normal enamel.[17,23]

Anticay®-based dentifrice can be an alternative for fluoride dentifrices, especially in children below 6 years of age who are at risk for dental fluorosis due to their tendency to swallow dentifrices.[10,24,25] According to Thomas et al (2015), CaSP containing dentifrices gave higher microhardness values compared to CPP-ACP and calcium sodium phosphosilicate.[26] The remineralization potential of CaSP in terms of a significant increase in microhardness after 7 days of use was reported by Kshirsagar et al.[27]

In the present study, the mean microhardness was in the range of 404-408VHN at baseline. However, after demineralization using 37% phosphoric acid, there was a significant reduction in microhardness in all the groups which indicated the production of artificial caries-like lesions. The mean microhardness was 373.150 for Group A, 309.275 for Group B, and 279.025 for Group C posttreatment which concluded that Group A (Clinpro) showed a significant difference in post-demineralization and post-remineralization values with definite better remineralization potential than Group B (Enafix). It can be highlighted that the microhardness value at the remineralization stage surpassed the value of the demineralized state for both the study groups which suggests net mineral gain can be established with both toothpastes. Also, it was noted that even artificial saliva showed slight remineralizing efficacy. Recently Shivani PS et al conducted similar type of study and concluded that Functionalised β TriCalcium Phosphate containing paste (Clinpro Tooth Crème) has superior remineralizing efficacy compared to Enafix and Clinpro tooth crème can be considered as a promising future agent for remineralization within the subsurface body of incipient carious lesions.[23]

During the experimental procedure, all samples were immersed in the artificial saliva which was regularly replaced every 24 hours. Samples were also kept safely inside an incubator (37^0C) during the remineralization process. These procedures were done to ensure a constant temperature and humidity, as well as create an oral cavity-like environment by maintaining pH.[28]

A drawback of our study was a shorter period of remineralization of 10 days, which could not remineralize artificial caries completely as remineralization increases over time. The remineralization process in vitro is quite different than in vivo in the oral cavity. Thus, there is a need for studies with clinical conditions to evaluate if only the recommendation of non-fluoridated dentifrice is adequate.

V. CONCLUSION

- The present study concluded that both fluoridated (Clinpro) and Non-fluoridated toothpaste (Enafix) were indeed effective in the remineralization of initial white spot lesions. Thus, both dentifrices can be recommended in clinical practice for children.
- Clinpro showed a significantly pronounced remineralization efficacy than Enafix dentifrice.
- Non-fluoridated Enafix toothpaste can be prescribed to young children who are at high risk of fluorosis.
- However, further in vivo studies are required to reassure the superiority and safety of Clinpro over Enafix for a longer period of time.

Clinical significance

This in vitro study highlights the non-invasive treatment of white spot lesions in primary teeth. Both fluoridated (Clinpro) and Non-fluoridated toothpaste (Enafix) can be prescribed to children routinely for the management of incipient lesions. For children who are at risk of fluorosis, Enafix toothpaste can be recommended as it does not contain fluoride.

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Declaration of conflict of Interest
The authors declare that there is no conflict of interests.

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