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IN VIVO EVALUATION OF ELECTROPHORESIS-AIDED REMINERALIZATION ON MICROHARDNESS OF DEMINERALIZED ENAMEL

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ABSTRACT

Objective: evaluate the electrophoresis effect on the micro-hardness of demineralized enamel in comparison to traditional remineralization using different remineralizing agents. **Subjects and Methods:** Initial enamel lesion was produced in rabbits with an acid etching, then, on a labial surface; three remineralizing agents were placed.; nano-hydroxyapatite (n-HAP), casein phosphopeptide amorphous calcium phosphate (CPP-ACP), and bioactive glass (BAG) with traditional technique and electrophoresis technique. Surface micro-hardness using a Vickers test at baseline, demineralization, and after remineralization at different times was calculated. The normality of the data evaluated using the Shapiro-Wilk and Kolmogorov-Smirnov tests. $P \leq 0.05$ was used to compare different variables using the ANOVA test and Tukey's post-hoc analysis. **Results:** The enamel hardness was greatly raised by all three remineralizing agents utilized in the study following application periods. For the traditional method n-HAP shows the highest remineralizing effect with, the lowest impact revealed in BAG material after two and five weeks. Moreover, in electrophoresis n-HAP material revealed the highest remineralizing effect, followed by CPP-ACP material with the most insufficient effect shown in BAG material after three and five hours. **Conclusion**: the application of the used different remineralizing agents enhances enamel remineralization, has an influential effect on enamel surface hardness, extended time produces an additive effect in the remineralization process and electrophoresis can both strengthen and re-hardening effects on demineralized enamel, also expedite the remineralizing agents' effect.

KEYWORDS: Enamel remineralization, electrophoresis, microhardness.

INTRODUCTION

The most mineralized and hard tissue in the human body is the tooth. The dentin-pulp complex is shielded from external stimuli by the enamel, which is the top layer of the teeth and contains hydroxyapatite in the shape of a well-organized prism pattern that can withstand chewing forces(1,2). Tooth demineralization is a prevalent condition around the world, and modern dentistry aims to control non-cavitated white spot lesions, stop further disease progression, and maintain the structural integrity of the tooth substrate(3). Remineralization of hard dental tissue is the process by which calcium and phosphate ions are introduced from an external source to the tooth to cause ion deposition into the demineralized enamel to restore net minerals(4,5). Alternatives to fluoride as nano-hydroxyapatite (n-HAP), casein phospho-peptide amorphous calcium phosphate

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(CPP-ACP), and bioactive glass (BAG) have been proposed for their remineralization [6,7]. CPP-ACP nano-complex, is a triple multi phosphorylated casein peptide, may maintain a high concentration of calcium and phosphate ions in the solution.

As a calcium-phosphate reservoir, CPP-ACP can improve remineralization and lessen the demineralization of enamel [8,9]. One of the most bioactive and biocompatible materials, n-HAP has gained widespread acceptance in recent years in both dentistry and medicine. Applying nano-hydroxyapatite to biomimetic repair of damaged enamel directly has been given considerable consideration in current dentistry research because of its chemical and structural similarity to enamel minerals [10]. One of the proposed remineralizing agents is bioactive glass which can be used in remineralizing tooth structure [11]. The active ingredient in BAG attaches to the tooth surface once touch with saliva or other fluids, triggering the remineralization process on the enamel by supplying calcium, phosphorous, and others ions to the tooth structure [12]. It is noteworthy that the rate of precipitate growth is prolonged, which may limit the effectiveness of these materials [13]. Ions can move across a gel or solution more quickly with electrophoresis, and more particularly, with ionophoresis. Furthermore, it was claimed that by using an electric field and a little amount of electrical current voltage, electrophoresis also allows ions to migrate in a specific one-dimensional path [14].

The null hypnosis of this research is: the electrophoresis remineralization method and the traditional method will not differ significantly from one another.

MATERIALS AND METHODS

1. **Casein phosphopeptide-Amorphous calcium phosphate (CPP-ACP)** remineralizing agent in the form of (tooth mousse paste, GC International, Itabashi- Ku, Tokyo, Japan.).
2. **Nano Hydroxyapatite (n-HAP)** remineralizing agent in the form of (Apagard Royal toothpaste, Sangi, CO., LDT., Jaban).
3. **Bioactive glass** remineralizing agent in the form of (Biomin C toothpaste, Bielefeld, Germany).
4. **Demineralizing agent** in form of 37% phosphoric acid for enamel demineralization (Ivoclar, vivadent AG).

Grouping of teeth:

A total of 84 teeth were randomly split into two equal primary groups (n=42) according to the remineralizing technique traditional or electrophoresis followed by division into three equal subgroups (n=14) according to the used remineralizing agent, each subgroup was further divided into two equal divisions (n=7) according to the remineralization period for traditional remineralization subgroups were divided into 2 weeks and 5 weeks while for electrophoresis remineralization subgroups were divided into 3 and 5 hours.

Intervention:

New Zealand rabbits were anesthetized by intramuscular injection in the quadriceps femoral muscle using 3.3 cm of Xyla-ject solution at a concentration of 30.0 mg/kg. Throughout the experiment, an additional dose of 10 mg/kg will be provided as required to keep the rabbits under anesthesia [15]. This study was approved by the ethical committee of the Faculty of Dental Medicine, Boys, Cairo, Al-Azhar University. (120192\3\32). All the animal experimental procedure were being taken care of according to the protocol of Canadian Counion Animal Care and in coherence with the three Rs [16].

Sample Preparation:

Forty-two rabbits' model the maxillary incisors were acid-etched for one minute with 37% phosphoric acid (Ivoclar) to produce white spot lesions (WSLs) that mimic caries and about 100–120 μm deep among the selected teeth [17].

Animal coding for traditional remineralization technique:

Identification of the animals was done to distinguish between them during the application of materials. Coding was done by painting the inner ear of each rabbit. The rabbits were coded with black color for n-HAP, red color for CPP-ACP, and green color for BAG.

Surface treatment:

All remineralizing agents' pastes were included as commercial products. For the traditional method, applied to demineralized enamel with a micro brush on the labial surface of demineralized specimens, brushing procedures were carried out in each group using a soft toothbrush (Oral-B) and minimal pressure thrice daily with undiluted toothpaste (approximately 1gm) for 3 minutes. Specimens were cleaned with deionized water for 15 seconds following each brushing procedure. The treatment procedure was repeated daily for 2 and 5 weeks [18,19]. To load remineralizing agents for the electrophoresis technique, a customized mold with an opening cavity on the labial surface was built. The electrophoresis apparatus used a two-electrode setup, with the anode linked to the rabbit's skin and the cathode inserted into a loaded custom-made mold with CPP-ACP, n-HAP, and BAG. The electric current was used for 3 or 5 hours. The maxillary incisors were extracted after each remineralization procedure [20] figure (1).

Evaluation technique:

A custom-made cylindrical plastic mold with an interior diameter of 30 mm and a height of 15 mm was created [21]. Surface Microhardness was determined using Digital Display Vickers Microhardness Tester (Model HVS-50, Laizhou Huayin Testing Instrument Co., Ltd. China) with a Vickers diamond indenter and a 20X objective lens. The specimens' surfaces were subjected to a 50g load for 10 seconds. On the surface of each specimen, three indentations were created, evenly spaced around a circle and at least 0.5 mm apart from one another. The following equation was used to calculate micro-hardness: **HV=1.854 P/d2** Where HV is Vickers hardness in Kgf/mm2, P is the load in Kgf and d is the length of the diagonals in mm.

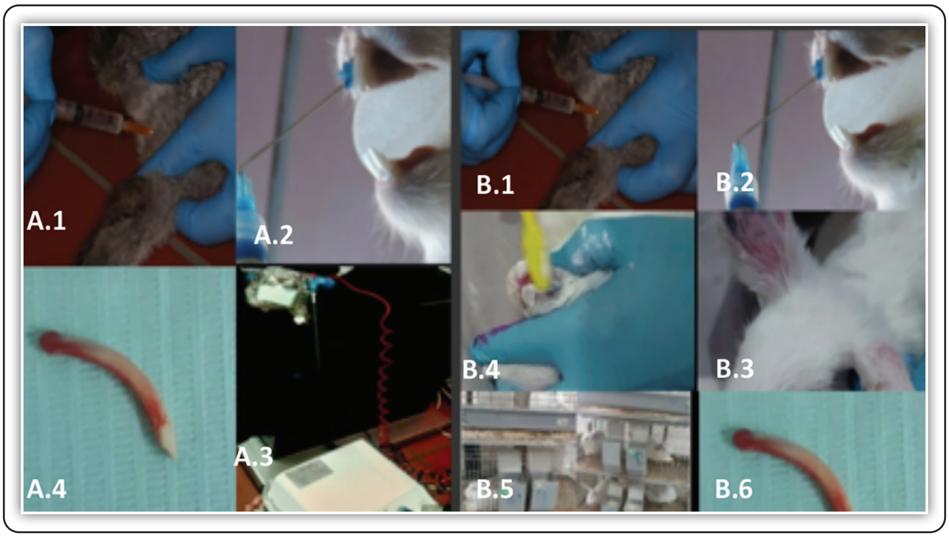

FIG (1) Surface treatment procedure (A: Electrophoresis technique, A1: Anesthesia, A2: Enamel lesion, A3: Electrophoresis application, A4: Extraction – B: Traditional technique, B1: Anesthesia, B2: Enamel lesion, B3: Color coding, B4: Remineralizing agent application, B5: Animal care, B6: Extraction).

RESULTS

The mean and standard deviation values for each group were calculated. Using the Kolmogorov-Smirnov and Shapiro-Wilk tests, the normality of the data was examined, and a parametric (normal) distribution was found. The ANOVA test and Tukey's post-hoc analysis was used to compare different variables. The cutoff for significance was chosen at P 0.05. With IBM® SPSS® Statistics Version 24 for Windows, a statistical analysis was carried out.

Regarding the traditional remineralization technique, n-HAP material revealed the highest remineralizing effect (180.4±55.25) (202.6±62.05) followed by the CPP-ACP material (175.5±53.75) (199.3±61.04) with the lowest impact revealed in BAG material (117.4±35.96) (180.7±55.34) after two and five weeks respectively, as listed in the table (1) and showed in figure (2).

Regarding the electrophoresis remineralization technique, n-HAP material revealed the maximum remineralizing effect (199.5±61.10) (221.7±67.90) followed by the CPP-ACP material (187.5±57.43) (200.1±61.29) with the lowest impact revealed in BAG material (97.2±29.77) (101.6±31.12) after three and five hours respectively, as listed in the table (1) and showed in figure (2).

With the help of the electrophoresis technique, the n-HAP group had the greatest mean value of surface microhardness, followed by CPP-ACP group with aid of an electrophoresis technique. Then n-HAP group with traditional technique and the most negligible mean value was observed in the BAG group with the electrophoresis technique.

TABLE (1) Microhardness of base line and demineralizing groups.

Time \ Material	n-HAP (N)	CPP-ACP (C)	BAG (B)
	Remineralization Technique M ± SD		
Baseline		245.7±59.14	
Demineralization		67.5±21.48	
P-value		<0.0001*	

TABLE (2) Mean & standard deviation (SD) values of surface microhardness with different variables.

Material \ Time	Traditional Remineralization Technique (T)		Electrophoresis Remineralization Technique (E)	
	(W2) Mean ± SD	**(W5) Mean ± SD**	**(H3) Mean ± SD**	**(H5) Mean ± SD**
n-HAP (N)	180.4±55.25[a]	202.6±62.05[a]	199.5±61.10[a]	221.7±67.90[a]
CPP-ACP (C)	175.5±53.75[b]	199.3±61.04[b]	187.5±57.43[a]	200.1±61.29[a]
BAG (B)	117.4±35.96[b]	180.7±55.34[c]	97.2±29.77[b]	101.6±31.12[b]
p-value	**0.2105(ns)**	**0.7626(ns)**	**0.0028***	**0.0018***

*SD; Standard Deviation, P; Probability Level *; significant (p<0.05). The same superscript letters in the same column indicate insignificant differences while different superscript letters in the same column indicate significant differences using Tukey`s post hoc test for multiple comparisons.*

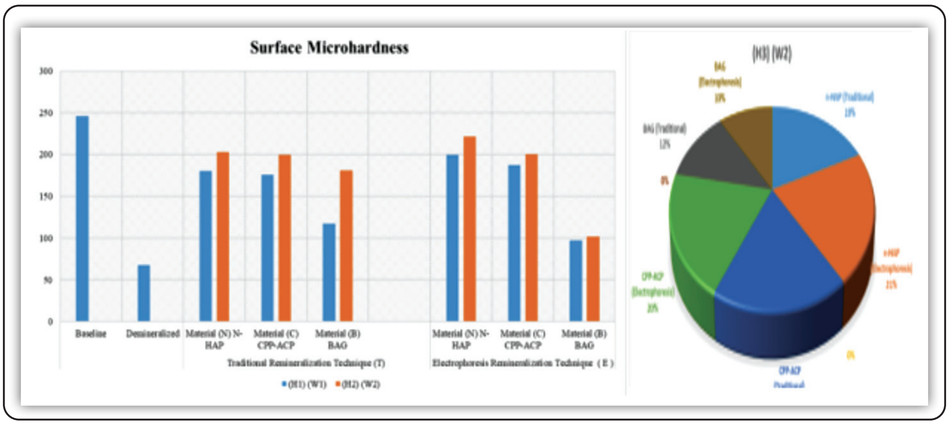

FIG (2) Bar and pie chart representing mean values of surface microhardness of different variables.

DISCUSSION

White spot lesions are the first macroscopic indicators of developing caries, it will eventually collapse into a full cavity [20]. As a result of their electrical charge, the crystals in the demineralized enamel can easily pull calcium and phosphate ions from the remineralization solution to reduce surface energy [20]. Until recently, the traditional approach of treating all caries-attacked teeth involved removing the damaged tissues and replacing them with a restorative material. Today, a modern Fluoride treatment has been demonstrated to remineralize white spot lesions, although it is only effective in the first 10 to 30 mm of the lesion, necessitating the development of alternative treatments to enable a remineralization of deeper areas [22].

Enamel, is a good candidate for microhardness assessment as it possesses a delicate, non-homogenous microstructure and is prone to breaking. Vickers hardness is non-destructive, trustworthy, rapid, and economical when compared to another hardness tests [23].

Based on the results of the present study, the null hypothesis was partially accepted.

Regarding the remineralization technique**,** early enamel lesions could be remineralized with n-HAP, CPP-ACP, and BAG pastes. The results revealed that all groups' demineralized enamel surfaces had significantly decreased microhardness, which is a sign of mineral loss. This could be explained by the fact that all samples were demineralized using the same process and duration in order to standardize the results. Also confirmed the ability of n-HAP, CPP-ACP & BAG to aid in remineralizing enamel.

In the present study n-HAP provided the highest microhardness value as the presence of Ca/PO4 that triggers the precipitation of apatite by the creation of subsurface high mineral content and accelerates the remineralization process can be used to explain the greater microhardness value of the n-HA group [24].

These results agreed with **Surmeneva et al., in 2015**[25], they discovered that full remineralization is not possible and that n-HAP promotes preferential remineralization of enamel outer layer caries lesions. This shows that n-HAP exhibits a treatment for the remineralization of early enamel defects[26]. The ability of n-HAP to gradually remineralize through mineral precipitation and nucleation in the dark zone of demineralization, culminating in the complete regeneration of lost crystallites, is what accounts for the significant improvement in surface microhardness in the n-HAP groups on softened enamel [27].

Another proposed explanation by **Huang et al. in 2009** [28] determined that varying concentrations of n-HAP may remineralize enamel, and that the ideal concentration of n-HAP for this purpose was 10% in this investigation. Similarly, **Kim et al. in 2007**(29) observed that a longer treatment period and a higher concentration (10%) of n-HAP had a stronger remineralization effect. **Manchery et al. in 2019**(30) found that n-HAP enhances remineralization better than fluoride and BAG. This was confirmed by results obtained by **Geeta et al., in 2020** (31) found that n-HAP shows higher surface microhardness than CPP-ACP.

This study's findings are conflicting with **Salinovic et al. in 2021** (32) found that CPP-ACP has the highest microhardness rating because it securely adheres to the enamel surface and stops fluoride ions, retaining them near the enamel. This finding is consistent with those studies, as CPP-ACP had a higher microhardness mean value than n-HAP (32,33).

This is in disagreement with **Palaniswamy et al., in 2016** (34) found that BAG reduces lesion depth more than n-HAP as particles classified as non-resorbable material and show less degradation and solubility. This might be because calcium and phosphate (PO_4^{3-}) ions are released from the glass as a result of sodium ions from the BAG particles rapidly exchanging with hydrogen cations (in the form of H_3O^+). Sodium release creates a localized, transitory elevation in pH during the material's initial interaction with water. As the processes proceed, this layer crystallizes as hydroxycarbonate apatite (HCA) (35).

Those findings could be related to differences in regimes, microhardness assessment methods, different ingredients of the pastes, and differences in the tooth structures in these studies.

The results of this study, demonstrated that there was a statistically significant variation in mean microhardness values between (W2&W5). Regardless of the applied surface treatment, the W5 revealed the highest microhardness value and the least one was W2 in all tested groups. This could be related to the time factor; as time passes, the frequency and volume of hydroxyapatite precipitation rises, accompanied by the deposition of considerable amounts of Ca^{2+} and PO_4^{3-}, so greatly boosting the remineralization effect. This was in agreement with **Huang S et al., in 2009**(28) and **Kim et al., in 2007**(29) They demonstrated that as the concentration of nano-hydroxyapatite grew over time, demineralized enamel's surface hardness increased as well.

Also, these in agreement with **Hedge et al., in 2014** (36) who found that remineralization was dependent and increase with an increase the time.

Regarding the electrophoresis remineralization technique**,** the results of this study, showed that there was a statistically significant difference in mean microhardness values. As n-HAP is a highly conductive material while BAG is a low conductive material, the influx of remineralizing ions into the deepest part of the subsurface caries lesion has maybe been increased by iontophoresis. This produces an environment that encourages lesion remineralization, which further matures to offer optimum hardness and mineral density to the repaired lesion (37).

The surface charge varies with grain borders' nanoscale positions as well, and because various regions of the same grain have statistically distinct surface charges, it is most likely related to an exposed crystal plane. Extra PO_4^{3-} groups at the surfaces cause all surfaces to have a negative charge and variance is most likely due to different arrangements on each crystal plane of the additionally charged ions making up the HAP lattice. Surface charge is predicted to have a significant impact on inorganic and organic deposition processes as well as structural evolution(38). Ionic flux from the glass matrix and crystallization have been significantly impacted by changes in the BAG component with cation addition (39).

CONCLUSIONS

The following findings could be stated in light of the investigation's circumstances:

1. Application of remineralizing agents has a favorable impact on the microhardness of enamel.
2. Various remineralizing agent compositions have different effects on the enamel surface.
3. 3. Extended time produces an additive effect in the remineralization process.
4. The effects of remineralizing agents can be hastened by electrophoresis, which can help strengthen and re-harden demineralized enamel.

RECOMMENDATION

1. More investigation is required to determine how other materials interact with the electrophoresis technique.
2. More research is required to determine the impact of various remineralization times, electric volts, or repeated application of materials using the electrophoresis technique.
3. BAG should not be used because it has a little impact with the electrophoresis technique.

REFERENCES

1. Chen H, Tang Z, Liu J, Sun K, Chang S, Peters M, et al. Acellular synthesis of a human enamel-like microstructure. Adv Mater. 2006; 18(14):1846-51.
2. Fincham A, Moradian-Oldak J, Simmer J. The structural biology of the developing dental enamel matrix. J Struct Biol. 1999;126(3):270- 99.
3. Elkassas D, Arafa A. Remineralizing efficacy of different calcium phosphate and fluoride-based delivery vehicles on artificial caries like enamel lesions. J Dent. 2014; 42(4):466-74.
4. Reynolds C, Cai F, Cochrane J, Shen P, Walker G, Morgan M. Fluoride, and casein phosphopeptide-amorphous calcium phosphate. J Dent Res, 2008; 87:344-8.
5. Ten Cate J. New agents for caries prevention: introduction to ICNARA 2. Adv in Dent Res 2012; 24:53-7.
6. Reynolds E. Remineralization of enamel subsurface lesions by casein phosphopeptide-stabilized calcium phosphate solutions. J Dent Res,1997; 76:1587-95.
7. Zhang L, Li Z, Dong Y. Experimental study of phosphopeptide in promoting tooth remineralization. Chin J Dent Res, 2000; 3:27-30.
8. Featherstone J. Remineralization, the natural caries repair processes the need for new approaches. Adv in dent Res. 2009; 21(1):4-7.
9. Zhou Y, Cao Y, Liu W, Chu C, Li Q. Polydopamine-induced tooth remineralization. ACS Appl Mater Interfaces. 2012; 4(12):6901-10.
10. Li L, Pan H, Tao J, Xu X, Mao C, Gu X, et al. Repair of enamel by using hydroxyapatite nanoparticles as the building blocks. J Mater Chem. 2008; 18:4079–84.
11. LaTorre G, Greenspan D. The role of ionic release from novamin (calcium sodium phosphosilicate) in tubule occlusion: an exploratory in vitro study using radio-labeled isotopes. J Clin Dent. 2010; 21(3):72-6.
12. Golpayegani M, Sohrabi A, Biria M, Ansari G. Remineralization effect of topical novamin versus sodium fluoride (1.1%) on caries like lesions in permanent teeth. J Dent. 2012; 9(1):68-75.
13. Tay F, Pashley D. J Biomater 2008; 29: 1127-37.
14. Qian C, Huang H, Chen L, Li X, Ge Z, Chen T, et al. Dielectrophoresis for bioparticle manipulation. Int J Mol Sci, 2014; 15(10):18281-309.
15. Katsuda S, Waki H, Nagayama T, Yamasaki M, Ishi H, Katahira K, et al. Time-dependent change in baroreflex control capacity of arterial pressure by pentobarbital anesthesia in rabbits. Exp Anim J. 2000; 49(2):111-8.
16. Fenwick N, Danielson P, Griffin G. Survey of Canadian animal-based researchers' views on the Three Rs: replacement, reduction and refinement. PloS One J. 2011; 6(8): e22478.
17. Wakwak M. Biomimetic Remineralization with nano-hydroxyapatite treatment of enamel erosion (in vitro study). AJDS. 2021;24(2):125-31.
18. Tschoppe P, Zandim D, Martus P, Kielbassa A. Enamel and dentine remineralization by nano-hydroxyapatite toothpastes.2011;39(6):430-7.
19. Balakrishnan A, Jonathan R, Benin P, Kumar A. Evaluation to determine the caries remineralization potential of three dentifrices: An in vitro study. J. Conserv. Dent. 2013;16(4):375–79.

20. Zhang Y, Wong H, McGrath C, Li Q. In vitro and in vivo evaluation of electrophoresis-aided casein phosphopeptide-amorphous calcium phosphate remineralization system on pH-cycling and acid-etching demineralized enamel. Sci Rep, 2018; 8(1): 8904:1-9.
21. SHAKILA N, ALI A, and ZAIDI S. Micro hardness of dental tissues influenced by administration of aspirin during pregnancy. Int. J. Morphol., 2015;33(2):586-93.
22. Braga R, Habelitz S. Current Developments on Enamel and Dentin Remineralization. Curr Oral Health Rep, 2019;(6) 257–63.
23. Gangwar A, Jha K, Thakur J, Nath M. In Vitro evaluation of remineralization potential of novamin on artificially induced carious lesions in primary teeth using a scanning electron microscope and Vickers hardness. Indian J Dent Res. 2019;30(4):590-4.
24. Carrouel F, Viennot S, Ottolenghi L, Gaillard C, Bourgeois D. Nanoparticles as anti-microbial, anti-inflammatory, and remineralizing agents in oral care cosmetics: a review of the current situation. Nanomaterials 2020;10(1):1–32.
25. Surmeneva M, Mukhametkaliyev T, Tyurin A. Effect of silicate doping on the structure and mechanical properties of thin nanostructured RF magnetron sputter-deposited hydroxyapatite films. Surf Coat Tech 2015; 275:176–84.
26. Onwubu S, Mdluli P, Singh S, Bharuth V, Makgobole M. Evaluation of the occluding characteristics of nanosized eggshell/ titanium dioxide with or without saliva. Eur J Dent 2019;13(4):547–55.
27. Walsh L. Contemporary technologies for remineralization therapies: a review. Inter Dent SA, 2009; 11:6-16.
28. Huang S, Gao S. Effect of Nano-hydroxyapatite concentration on remineralization of initial enamel lesion in vitro. Biomed Mater, 2009; 75:428-34.
29. Kim M, Kwon H, Choi C, Kim B. Combined effects of nano-hydroxyapatite and NaF on remineralization of early caries lesion. Key Engineering Materials. 2007:1347–50.
30. Manchery N, John J, Nagappan N, Subbiah GK, Premnath P. Remineralization potential of dentifrice containing nanohydroxyapatite on artificial carious lesions of enamel: A comparative *in vitro* study. Dent Res J (Isfahan). 2019;16(5):310-7
31. Geeta R, Vallabhaneni S, Fatima K. Comparative evaluation of remineralization potential of nanohydroxyapatite crystals, bioactive glass, casein phosphopeptide-amorphous calcium phosphate, and fluoride on initial enamel lesion (scanning electron microscope analysis) - An *in vitro* study. J Conserv Dent. 2020;23(3):275-9.
32. Salinovic I, Schauperl Z, Marcius M, Miletic I. The Effects of Three Remineralizing Agents on the Microhardness and Chemical Composition of Demineralized Enamel. Materials (Basel). 2021;14(20):6051.
33. Comar L, Souza B, Gracindo L, Buzalaf M, Magalhaes A. Impact of experimental nano-HAP pastes on bovine enamel and dentin submitted to a pH cycling model. Braz Dent J, 2013; 24:273-8.
34. Palaniswamy U, Prashar N, Kaushik M, Lakkam S, Arya S, Pebbeti S. A comparative evaluation of a remineralizing ability of bioactive glass and amorphous calcium phosphate casein phosphopeptide on early enamel lesion. Dent Res J (Isfahan). 2016;13(4):297-302.
35. Suryani H, Geholt P, Manjunath M. Evaluation of the remineralization potential of bioactive glass, nanohydroxyapatite and casein phosphopeptide-amorphous calcium phosphate fluoride-based toothpaste on enamel erosion lesion- an ex vivo study. Indian J. Dent. Res, 2020, 31, 670-7.
36. Hedge N, Reddy V, Chandreshekar B, Koushik H, Aravind S. Evaluation of remineralizing agent on enamel around orthodontic brackets – An in vitro study. J Ind Orthod Soc. 2014; 48:313–8.
37. Pitts N, Wright J. Reminova and EAER: Keeping Enamel Whole through Caries Remineralization. Adv Dent Res. 2018;29(1):48-54.
38. VANDIVER, Jennifer M. Nanoscale influences on bioactivity: ultrastructure and nanomechanics of model bioactive hydroxyapatite-based biomaterials. 2006. Ph.D. Thesis. Massachusetts Institute of Technology.
39. Ramadoss R, Padmanaban R, Subramanian B. Role of bioglass in enamel remineralization: Existing strategies and future prospects-A narrative review. J Biomed Mater Res B Appl Biomater. 2022; 110(1):45-66.