Al-Azhar Journal of Dentistry

Manuscript 1587

The Effect of Poly Amido Amine Dendrimer, Nano-hydroxyapatite and Their Combination on Microhardness of Demineralized Enamel

Asmaa A. Khater

wael E. Jamil

Nevin A. Gad

ORIGINAL STUDY

The Effect of Polyamidoamine Dendrimer, Nano-hydroxyapatite, and Their Combination on Microhardness of Demineralized Enamel

Asmaa A. Khater [a,*], Wael E. Jamil [b], Nevin A. Gad [b]

[a] Operative Dentistry, Faculty of Dental Medicine, Menofia University, Menofia, Egypt
[b] Operative Dentistry, Faculty of Dental Medicine for Girls, Al-Azhar University, Cairo, Egypt

Abstract

Purpose: This study was designed to evaluate the effect of polyamidoamine dendrimer (PAMAM), nano-hydroxyapatite (nHA), and their combination (PAMAM-nHA) on the microhardness of demineralized enamel. Patients and methods: A total of 30 freshly extracted premolar human teeth were used in this study. Individual specimens were prepared and demineralized in a 37 % phosphoric acid gel (H_3 PO_4) for 30 s before being divided into three groups based on the materials used for the treatment of demineralized enamel. In the first group, PAMAM dendrimer was applied (A1). In the second group, nHA was applied (A2), in the third group; a combination of PAMAM dendrimer and nHA were applied (A3). The specimens were subdivided into three subgroups groups (T) according to assessment time. At baseline (T0), after 4 weeks (T1) and after 12 weeks (T2). Each treated group was placed in a separate container of artificial saliva, which was replenished every 24 h. All the specimens were subjected to microhardness assessment before demineralization (baseline), after demineralization, and 4 and 12 weeks after the application of treatment materials using a Digital Display Vickers Microhardness Tester. Results: At 4 and 12 weeks, the highest mean value was recorded for the PAMAM-nHA group followed by the nHA group, while the PAMAM group recorded the lowest mean value. Group A3 was significantly the highest, while there was an insignificant difference between groups A1 and A2. Conclusion: All the treatment materials used in the study were effective in the microhardness recovery of enamel.

Keywords: Demineralized enamel, Nano-hydroxyapatite, Polyamidoamine dendrimer

1. Introduction

Because it is the most prevalent chronic disease in both children and adults around the world, dental caries continues to be the main problem in dentistry [1]. Dental caries is a dynamic, non-communicable disease that is triggered by diet and biofilms that cause mineral loss from hard tooth tissues [2]. The current understanding of the development of caries is based on the recurrent cycles of demineralization and remineralization phases brought on by acid-producing bacteria in the oral microenvironment [3,4]. The dissolution of mineral ions like calcium and phosphate, which are responsible for generating the hydroxyapatite crystals in enamel, is brought on by the bacterial metabolism of fermentable carbohydrates, which results in acids [5]. Because of the fluid flow in the dentinal tubules and the development of caries disease, enamel demineralization can expose the dentine and cause dentinal hypersensitivity [6]. However, if the demineralized enamel prism is subjected to oral conditions that promote remineralization, it can revert to its embryonic state [7].

Moreover, early tooth decay is often treatable and preventable. There are two strategies to inhibit the demineralization of enamel and dentin: by employing salivary protective chemicals and by preventing the growth of biofilms. The primary objective of caries research in recent years has been the development of methods for the noninvasive management of early caries lesions through remineralization to preserve the tooth structure [8]. Remineralization can occur biologically as a result of

Received 29 October 2022.
Available online 2 February 2024

* Corresponding author at: Operative Dentistry, Faculty of Dental Medicine, Menofia University, Menofia, Egypt.
E-mail address: asmaakhater881@gmail.com (A.A. Khater).

https://doi.org/10.58675/2974-4164.1587

remineralizing substances or naturally as a result of saliva's buffering mechanism [9].

Fluoride is highly effective at preventing caries and remineralizing early carious lesions, but its use has several drawbacks [10]. Fluoride loses effectiveness when the pH of the oral cavity falls below 4.5, and it also needs the right amounts of Ca^{2+} and PO_4^{3-} to be effective. Besides, only the topmost layer of enamel is impacted by the remineralizing process during the resurfacing procedure, leaving the lesion's center unaffected [11]. However, overcoming the safety dosages, exposure to the risk of fluorosis (in the case of children), and toxicity is the most important drawback connected with fluoride use. These factors have necessitated the development of new chemicals to get around fluoride restrictions. To move from enamel remineralization to enamel regeneration, one of the most current technologies is represented by biomimetic materials [12].

Dendrimers made of polyamidoamine (PAMAM) are synthetic proteins with several reactive end groups, internal cavities, a specific size, form, etc. These amelogenin-inspired dendrimers have been referred to as 'artificial proteins' because they may mimic the functions of organic matrices in regulating the biomineralization of tooth enamel. PAMAM dendrimers with carboxyl and phosphate terminations both show a strong propensity to self-assemble into hierarchical enamel crystal structures, according to numerous in vitro investigations. PAMAM organic templates produce new crystals that nearly resemble the original prism-shaped enamel crystals in terms of their structure, orientation, and mineral phase [13,14]. The crystal size of nano-hydroxyapatite (nHA) crystals ranges from 50 to 1000 nm. It was discovered that nHA has characteristics with biological apatite. The nanoparticle's size significantly enhances the bonding surface area, giving the nHA its distinctive bondability. This allows calcium or phosphate ions that are readily available to bind to the surface of enamel and fill the porosities of carious lesions [15]. In the precipitation process, nHA crystals penetrate the enamel rods and serve as a template, supporting crystal integrity and growth [16].

Amphiphilic, carboxyl-terminated, and phosphate-terminated PAMAM dendrimers showed a strong propensity to self-assemble into hierarchical enamel crystal structures, according to several in vitro tests. The new crystals created by the PAMAM organic templates have the same structure, orientation, and mineral phase as the enamel, and the hydroxyapatite (HA) nanorods are oriented parallel to the original prisms [13,14].

The crystal size of nHA crystals ranges from 50 to 1000 nm. It was discovered that nHA has characteristics with biological apatite. The nanoparticle's size significantly enhances the bonding surface area, giving the nHA its distinctive bondability. This allows calcium or phosphate ions that are readily available to bind to the surface of enamel and fill the porosities of carious lesions [15]. In the precipitation process, nHA crystals serve as a template, entering the enamel pores and fostering the integrity and growth of crystals [16].

Therefore, the purpose of this study was to investigate the effect of PAMAM, nHA, and their combination PAMAM + nHA on the microhardness of demineralized enamel.

2. Patients and methods

2.1. Trial design and sample size calculation

To test the null hypothesis, which states that there is no difference between the effects of PAMAM dendrimer, nHA, and their combination on the microhardness and micromorphology of demineralized enamel, a power analysis was created. Elzankalouny, Shaimaa M., and Wegdan M. Abdelfattah's findings suggest [17]. Assuming an effect size (f) of (1.18), a power of 80 % and an alpha (a) level of 0.05 (5 %), the estimated sample size (n) was a total of 15 specimens or 5 for each group.

2.2. Selection of teeth

A total of 30 freshly extracted premolar human teeth were used in this study. Teeth were extracted from patients for orthodontic purposes, and the patients were informed about and consented to the use of their teeth following approval of the Ethics Committee of the Faculty of Oral and Dental Medicine for Girls', Al-Azhar University (approval code: REC-OP-019-02). Teeth were cleaned by a scalpel to remove attached soft tissues, and a low-speed handpiece with pumice paste was used to remove the remaining debris, and then were stored in distilled water for a maximum period of 1 month till use. The teeth used for this investigation had buccal enamel surfaces that had not been impacted by any chemical pretreatment agents, were free of white spot lesions or caries, and did not have hypoplastic enamel [18].

In all, 30 premolar human teeth were used to create specimens. The roots of the teeth were removed using a high-speed diamond rotary bur and were cut at the intersection of the enamel and the cementum. The specimens were inserted in the specially designed acrylic block with the buccal surface directed upward and exposed after the self-

cured acrylic resin was poured inside the custom-made plastic cylinder molds (Fig. 1), and then the enamel surfaces were flattened and smoothed using carborundum disks (1200 (Germany) and polished using diamond paste (15 mm diamond paste, Germany) [18].

2.3. Demineralization of enamel specimens

The buccal surface of each sample was demineralized with 37 % H_3PO_4 gel for 30 s and then rinsed with sufficient deionized water [19], and then the specimens were divided into three groups.

2.4. Sample grouping

The specimens were separated into three groups after demineralization based on the materials used for treatment (A). In the first group, PAMAM was used to treat the demineralized enamel (A1). The demineralized enamel (A2) in the second group was treated with nHA, while the demineralized enamel (A2) in the third group was treated with PAMAM + nHA (A3). According to the evaluation time, the specimens were separated into three subgroups: baseline (T0), after 4 weeks (T1), and after 12 weeks (T2).

2.5. Application of treatment agents

The treatment agents in each group were applied to the demineralized enamel specimens one time. An insulin syringe (1 ml) was used to standardize the quantity applied on the enamel surface; the treatment agents were brushed using a swiping motion with a micro brush (Flowthru, Microbrush Products, Dungarvan, Ireland) for 20 s, left for 10 min [20], and then rinsed with distilled water. In the third group, the PAMAM solution was applied on the exposed surfaces of the demineralized enamel sample for 10 min and then the tooth was rinsed with deionized water and the nHA slurry was applied to the dental surface for another 10 min, and then rinsed with deionized water. After treatment, the specimens were stored in artificial saliva.

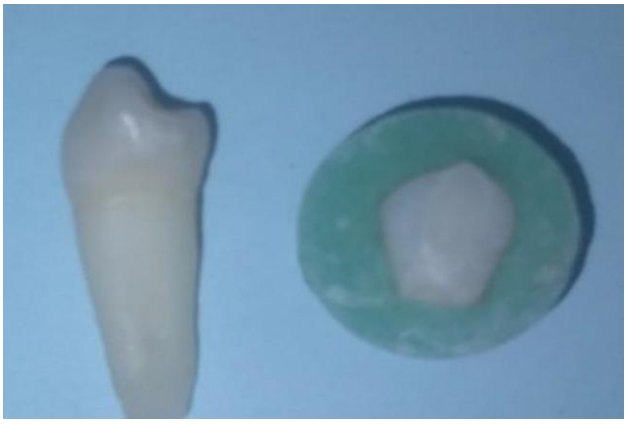

Fig. 1. Specimen embedded in the acrylic resin block.

2.6. Storage of specimens

Each treated group was placed in a separate container of artificial saliva at room temperature and the artificial saliva was replenished every 24 h [21].

2.7. Surface microhardness assessment (SMH)

All the specimens were subjected to microhardness assessment before demineralization (baseline), after demineralization, and 4 and 12 weeks after application of treatment materials. Vickers A microhardness tester with digital display was used to determine the surface microhardness of the specimens. Equation [22] was used to calculate microhardness: $HV = 1.854\ P/d^2$, where P is the load in Kgf; d is the length of the diagonals in mm; and Kgf is the Vickers hardness in Kgf/mm^2.

2.8. Statistical analysis

All the information was gathered, collated, and examined. The mean, standard deviation (SD), and confidence intervals for the data were reported. The KolmogoroveSmirnov test results showed that the data were normally distributed (parametric data); hence, a repetitive one-way ANOVA was used to compare the various stages of each group. Tukey's post hoc test was then used for multiple comparisons. Microsoft Excel 2016 was used for statistical analysis, along with SPSS 20 and GraphPad Prism.

3. Results

3.1. The effect of different treatment materials on microhardness of demineralized enamel after 4 and 12 weeks

Table 1 represents the percentage change of mean values of remineralized enamel with different groups after 4 and 12 weeks. The results at 4 weeks showed that the highest mean value was recorded for the PAMAM-nHA group (9.12 %) followed by the nHA group (6.55 %), while the PAMAM group recorded the lowest mean value (5.80 %). Group A3 was significantly the highest, while there was an

Table 1. Percentage change of mean value of remineralized enamel after 4 and 12 weeks.

Treatment materials	Percentage change of mean value after 4 weeks		Percentage change of mean value after 12 weeks	
	M	SD	M	SD
A1 (PAMAM)	5.80[a]	2.68	6.09[a]	2.82
A2 (nHA)	6.55[a]	2.39	8.59[b]	2.86
A3 (PAMAM-nHA)	9.12[b]	3.01	9.90[b]	3.88
P value	<0.0001*			

P: probability level which is significant at $P \leq 0.05$; means with the same superscript letters within the same column were insignificantly different ($P > 0.05$); and means with different superscript letters within the same column were significantly different ($P \leq 0.05$).

insignificant difference between groups A1 and A2. After 12 weeks, the results showed that the highest mean value was recorded for the PAMAM-nHA group (9.90 %) followed by the nHA group (8.59 %), while PAMAM group recorded the lowest mean value (6.09 %). After 12 weeks, group A1 was significantly the lowest, while there was an insignificant difference between groups A2 and A3.

3.2. The effect of time on the microhardness of each group

Table 2 represents the change of mean value of demineralized enamel at 4 and 12 weeks. The change of mean values of the remineralized enamel with PAMAM dendrimer at 4 and 12 weeks: microhardness of the sound enamel was 287.21 ± 23.59, demineralized enamel was 257.67 ± 13.14, after 4 weeks of remineralization it was 272.60 ± 24.19, while after 12 weeks of remineralization it was 273.35 ± 15.60. Demineralization was significantly the lowest, with insignificant differences between other intervals.

The change of mean values of remineralized enamel with nHA at 4 and 12 weeks: microhardness of the sound enamel was 278.21 ± 4.70, demineralized enamel was 244.71 ± 15.32, remineralized enamel at 4 weeks it was 260.75 ± 19.58, while at 12 weeks it was 265.73 ± 12.89. Demineralization and remineralization after 4 weeks were significantly the lowest with insignificant difference between them, while the sound enamel and remineralization after 12 weeks were significantly the highest with insignificant difference between them.

The change of mean values of remineralized enamel with PAMAM dendrimer and nano-hydroxyapatite combination at 4 and 12 weeks; microhardness of sound enamel was 270.55 ± 6.41, demineralized enamel was 240.63 ± 9.79, after 4 weeks of remineralization it was 262.57 ± 16.08, while after 12 weeks of remineralization it was (264.45 ± 9.85). Demineralization was significantly the lowest, with insignificant differences between other intervals.

Means with the same superscript letters were insignificantly different ($P > 0.05$) and means with different superscript letters were significantly different ($P < 0.05$).

4. Discussion

The enamel structure shields it from outside threats, yet it is susceptible to alterations or irreparable harm from things like an acidic environment brought on by bacterial activity. Demineralization of the tooth occurs as a result of the acid that bacteria create spreading across the tooth surface and dissolving the mineral content of carbonated hydroxyapatite. However, the demineralization process is reversible, and dissolved apatite crystals can form once again if the pH returns to neutral, and there are sufficient concentrations of calcium and phosphate ions in the surrounding environment. To give the enamel time to remineralize and heal, enamel surface lesions should be detected as soon as feasible. Modern dentistry strives to prevent cavitation and maintain the integrity of healthy enamel by treating non-cavitated carious lesions without surgery [23].

Table 2. Mean and standard deviation of sound, demineralized, and remineralized enamel after 4 and 12 weeks in different treatment groups.

	A1 (PAMAM dendrimer)		A2 (nano-hydroxyapatite):		A3 (PAMAM dendrimer + nano-hydroxyapatite)	
	SD	M	SD	M	SD	M
Sound enamel	287.21[a]	23.59	278.21[a]	4.70	270.55[a]	6.41
Demineralized enamel	257.67 [b]	13.14	244.71 [b]	15.32	240.63 [b]	9.79
Remineralized enamel after 4 weeks	272.60[a]	24.19	260.75 [b]	19.58	262.57[a]	16.08
Remineralized enamel after 12 weeks	273.35[a]	15.60	265.73[a]	12.89	264.45[a]	9.85
P value	<0.0001*					

M, mean; SD, standard deviation.
P: probability level which is significant at *P* less than or equal to 0.05.

This work was conducted to investigate how nHA, PAMAM, and their blend impacted the microhardness of demineralized enamel. PAMAM dendrimer was picked due to its protein-like design. These exceptionally spread polymers have inside cavities and outside terminal gatherings, with the interior holes being used for medication or particle organization and the outer terminal gatherings being used for specific capabilities or associations. It was found that in a watery arrangement, PAMAM dendrimers self-collect into an order of designs, beginning with nanospheres, advancing to nanochains, microfibers, and finally macroscopic aggregates. PAMAM dendrimers can mirror the capability of amelogenin, which is urgent for the crystallization of hydroxyapatite because of it self-get-together way of behaving and primary closeness. As the most common protein in enamel development, amelogenin makes up more than 90 % of the extracellular natural network that impacts hydroxyapatite arrangement. PAMAM dendrimers are not set in stone to be promising helpful materials for hard tissues as they work as atomic layouts and have previously exhibited the ability to be outstanding on remineralization [13].

This study's decision to choose nHA depended on areas of strength for its affinity for proteins and parts of dental plaque and microorganisms. This is because of the nanoparticles' size, shape, and bigger surface region for protein restriction. As they are hydrophilic, the nHA particles can hydrate the surface. It has been guaranteed that the nHA particles have the ability of enamel remineralization as when they are applied to the tooth surface, they make major areas of strength for a covering on the lacquer surface that sticks to the tooth structure. Moreover, in view of the minuscule molecule size of nHA, it goes about as a filler to fill the porosities on the outer layer of the enamel [24].

A total of 30 freshly extracted premolar human teeth were used in this study. Specimens prepared from human teeth were preferred because they allow for testing of the study hypothesis in a more clinically relevant substrate. As premolar teeth are more available than other teeth due to their extraction for orthodontic treatment, they were enrolled in this study [17]. Thirty enamel specimens were prepared and used [18]. The specimens were demineralized individually with 37 % H_3PO_4 gel for 30 s as it was shown to be a reliable method to produce enamel demineralization [19]. Each treated group was placed in a separate container of artificial saliva at room temperature and the artificial saliva was replenished every 24 h to simulate as possible, the conditions that are found in the oral cavity, and it has been reported that the artificial saliva could act as a chemical reservoir for calcium and phosphate ions promoting the remineralization process [21].

Surface microhardness assessment (SMH) of the specimens was assessed before demineralization (baseline), after demineralization, and 4 and 12 weeks after the application of treatment materials. This assessment method provides a simple, nondestructive, and rapid method for determining the mechanical properties of enamel. Also, it allows hardness determination in the same sample before and after the treatments, which decreases the experimental error [25]. The PAMAM-nHA group in the current study had the highest mean value, followed by nHA, and the PAMAM group had the lowest mean value, according to the results of the percentage change of mean values of remineralized enamel with different groups at 4 and 12 weeks. The best score was in group A3, which had a considerable advantage over groups A1 and A2.

Regarding the results of microhardness recovery of enamel, at 4 weeks' the enamel group treated with PAMAM dendrimer and nanohydroxyapatite combination showed the highest percentage of microhardness recovery followed by PAMAM dendrimer while the nanohydroxyapatite group recorded the least value. At 12 weeks′, the enamel group treated with the PAMAM dendrimer and nanohydroxyapatite combination showed the highest percentage of recovery followed by nanohydroxyapatite, while the PAMAM dendrimer group recorded the least value. Comparison between different groups was performed and revealed insignificant differences, while comparison between different intervals also revealed an insignificant difference in all groups.

Following are some possible explanations for why demineralized enamel's microhardness increased with PAMAM dendrimer: The PAMAM dendrimer has a lot of amine groups on the outside and a lot of amide groups in the branches. The ability of these reactive groups to attract phosphate ions was crucial to the remineralization process. Furthermore, the liquid nature of PAMAM dendrimer and its capacity to be retained on the enamel surface due to its monodispersed molecular weight allow it to interact with negatively charged sites of hydroxyapatite crystals. These elements work together to enable the positive charge of the PAMAM dendrimer formation as a whole [26]. The PAMAM gathering's discoveries are reliable with a review that investigated lacquer remineralization utilizing PAMAM and glue sap containing calcium phosphate nanoparticles [14] and found that this procedure is promising for use after tooth depression readiness or as a covering on

polish with white spot injuries (WSLs) for counteraction, to decrease optional caries, stop caries movement, and protect tooth structures.

The consequence of the PAMAM bunch likewise correspond with other reviews utilizing a PAMAM dendrimer with various terminal gatherings examining the remineralizing impact on fake early lacquer carious injury [13] and found that all PAMAM gatherings could prompt remineralization of polish, with amine-terminated PAMAM dendrimer (PAMAM-NH_2) being the most noticeable remineralizing impact, trailed by PAMAM-COOH with PAMAM-Goodness having the most un-remineralizing impact.

It was found that 4.5G PAMAM-COOH goes about as the natural plate on the outer layer of lacquer, and in the remineralization answer for control the site of nucleation and recently framed gems morphology to shape the biomimetic design of normal veneer, which might be a promising strategy for fixing harmed finish. The outcomes are additionally steady with different investigations using various ages of PAMAM dendrimer to assess its impact on biomimetic polish remineralization [19].

Following are a few potential clarifications for the expansion in microhardness of demineralized lacquer with nHA: A few scientists argued that nHA biomimetic capability upholds remineralization by making an engineered veneer layer on the tooth or by saving finish apatite nanoparticles in polish imperfections, albeit the specific technique by which it does so is hazy [15]. Others, notwithstanding, it has been confirmed that nHA goes about as a calcium phosphate repository, forestalling demineralization and advancing remineralization while protecting a supersaturated condition for finish minerals [16].

The findings of the nHA group are consistent with a study that compared the ability of the nHA toothpaste to remineralize fake carious lesions to those of tricalcium phosphate and fluoride toothpaste [15] and was found that nHA can act as a remineralization product for treating early carious lesions. The increase in microhardness of the demineralized enamel with PAMAM dendrimer and nHA combination has not been previously investigated; however, this result was confirmed due to the combination of the two remineralizing materials.

4.1. Conclusion

All the treatment materials used in the study; PAMAM dendrimer, nHA, and their combination increased the microhardness of the demineralized enamel; however, the combination of PAMAM + nHA was the most effective after 4 and 12 weeks.

Funding

Public, private, or nonprofit funding organizations did not provide any grants for this research. This is with a conflict of interest.

Conflicts of interest

The authors have no proprietary, financial, or other personal interest of any nature.

Acknowledgements

The author acknowledge Dr. E M A, Professor of Physical Chemistry, Faculty of Science, Al-Azhar University for Girls' for her assistance with the preparation of the material.

References

[1] Rathee M, Sapra A. Dental caries. In: StatPearls. Treasure Island, FL, USA: StatPearls Publishing; 2022.
[2] Pitts NB, Zero DT, Marsh PD, Ekstrand K, Weintraub JA, Ramos-Gomez F, et al. Dental caries. Nat Rev Dis Prim 2017; 3:17030.
[3] Farooq I, Bugshan A. The role of salivary contents and modern technologies in the remineralization of dental enamel: a Narrative Review 2020;9:171.
[4] Pinelli MM, Catelan A, de Resende LFM, Soares LES, Aguiar FHB, Liporoni PCS. Chemical composition and roughness of enamel and composite after bleaching, acidic beverages and toothbrushing. J Clin Exp Dent 2019;11: 1175e80.
[5] Uthman US. Impact of fluoride varnishes on enamel surface microhardness of primary teeth: an in vitro study. World J Dent 2022;13:469e72.
[6] Muhammad SA, Ahmed BM. Experimental studies on the pH levels that affect demineralization and remineralization of human tooth enamel. Erbil dent Jour (EDJ) 2022;5:57e66.
[7] Kim MJ, Lee MJ, Kim KM, Yang SY, Seo JY, Choi SH, et al. Enamel demineralization resistance and remineralization by various fluoride-releasing dental restorative materials. Materials 2021;14:4554.
[8] Orsini G, Tosco V, Monterubbianesi R, Orilisi G, Putignano A. The first outstanding 50 years of 'Universita` Politecnica Delle Marche'. A New Era in restorative dentistry. Cham, Switzerland: Springer; 2020. p. 19e34.
[9] Zhang F, Cheng Z, Ding C, Li J. Functional biomedical materials derived from proteins in the acquired salivary pellicle. JMater Chem B 2021;9:6507e20.
[10] Zampetti P, Scribante A. Historical and bibliometric notes on the use of fluoride in caries prevention. Eur J Paediatr Dent 2020;21:152.
[11] Amaechi BT, AbdulAzees PA, Alshareif DO, Shehata MA, Abdollahi A. Comparative efficacy of hydroxyapatite and fluoride toothpaste for prevention and remineralization of dental caries in children. Brit dent jour Open 2019;5:1e9.
[12] Philip N. State-of-the-art enamel remineralization systes: the next frontier in caries management. Caries Res 2019;53: 284e95.
[13] Fan M, Zhang M, Xu H, Tao S, Yu Z, Yang J, et al. Remineralization effectiveness of the PAMAM dendrimer with different terminal groups on artificial initial enamel caries in vitro. Dent Mater 2020;36:210e20.
[14] Gao Y, Liang K, Weir M, Gao J, Imazato S, Tay F, et al. Enamel remineralization via poly (amido amine) and

adhesive resin containing calcium phosphate nanoparticles. Jour dent 2020;92:103262.
[15] Juntavee A, Juntavee N, Sinagpulo AN. Nano-Hydroxyapatite gel and its effects on remineralization of artificial carious lesions. Int J Dent 2021.
[16] Thimmaiah C, Shetty P, Shetty SB, Natarajan S, Thomas NA. Comparative analysis of the remineralization potential of CPP-ACP with fluoride, tri-Calcium phosphate, and nano-hydroxyapatite using SEM/EDX-an in vitro study. J Clin Exp Dent 2019;11:1120e6.
[17] Shaimaa ME, Wegdan MAEF, Sonia MES. Penetration depth and enamel microhardness of resin infiltrant and additional techniques for treatment of artificial enamel lesions. Alex Dent J 2016:20e5.
[18] Vyavhare S, Sharma DS, Kulkarni VK. Effect of three different pastes on remineralization of initial enamel lesion: an in vitro study. Clin Pediatr Dent jour 2015;39:149e60.
[19] Chen L, Yuan H, Tang B, Liang K, Li J. Biomimetic remineralization of human enamel in the presence of poly amido amine dendrimers in vitro. Caries Res 2015;49:282e90.
[20] Gomes YSBL, Alexandrino LD, Alencar CDM, Alves EB, Faial KCF, Silva CM. In situ effect of nanohydroxyapatite paste in enamel teeth bleaching. J Contemp Dent Pract 2017; 18:996e1003.
[21] Chen M, Yang J, Li J, Liang K, He L, Lin Z, et al. Modulated regeneration of acid-etched human tooth enamel by a functionalized dendrimer that is an analog of amelogenin. Acta Biomater 2014;10:37e46.
[22] Pallepati A, Yavagal CP. Enamel remineralization efficacy of three widely used remineralizing toothpaste: an in-vitro study. IJADS 2020;6:392e6.
[23] Ahmed SAA, Raya JAN. Biomimetic enamel remineralization: a comparative in vitro study of self-assembling peptide, fluoride varnish, and their combination at different times by surface microhardness test. Al-Rafidain Dent J 2022;22:245e54.
[24] Scribante A, Dermenaki Farahani MR, Marino G, Matera C, Rodriguez Y, Baena R, et al. Biomimetic effect of nano-hydroxyapatite in demineralized enamel before orthodontic bonding of brackets and attachments: visual, adhesion strength, and hardness in vitro tests. BioMed Res Int 2020.
[25] Fernandes NLS, Meira IA, Alves VF, Sampaio FC, Oliveira AFBD. Tara Gum as a controlled delivery system of fluoride in toothpaste: in vitro enamel remineralization study. Pesqui Bras em Odontopediatria Clínica Integr 2021: 21e46.
[26] Yang X, Shang H, Ding C, Li J. Recent developments and applications of bioinspired dendritic polymers. Polym Chem 2015;6:668e80.