Al-Rafidain Dental Journal

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Evaluation of Surface Microhardness of Artificial White Spot Lesion Treated with Three Different Treatment Approaches. An *in-vitro* study

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Article information

Received: 3 January 2023
Accepted: 15 February 2023
Available online:1 September 2024

Keywords
CPP-ACP, NovaMin, PH cycle, Remineralization, Third molar.

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Abstract

Aims: The purpose of the current study is to compare the impact of three different treatment approaches on the surface microhardness of the enamel of third molar teeth. **Materials and Methods**: An *in vitro* study was done on fifty extracted impacted third molars. All samples were immersed in solutions of pH cycle for 10 days (demineralizing solution for 3 hours, remineralizing solution for 20 hours, and artificial saliva for 30 minutes twice daily). Then the samples were divided randomly into 5 groups according to enamel surface treatment, group1: Colgate (containing Arginine) toothpaste, group2: GC (containing Casein phosphopeptide-amorphous calcium phosphate (CPP-ACP)-tooth mousse, group 3: Sensodyne (containing NovaMin) toothpaste group 4: distilled water and group 5: pH cycle solutions. The microhardness numbers were calculated from the length of the indentation on the enamel surface, the indentation length was determined microscopically with 70X magnification. An ANOVA was constructed (value $P \leq 0.05$) followed by Duncan's post –hoc test for comparisons of mean values. **Results**: there were significant differences among the study groups with respect to Vickers microhardness (VMH) mean values of samples. The lowest value was for the control group after the pH cycle followed by the Colgate (containing Arginine) group and the highest value was for the control group before the pH cycle followed by the Sensodyne (containing NovaMin) group. **Conclusions**: Sensodyne (containing NovaMin) toothpaste is more effective in restoring the hardness of artificial WSLs when compared with GC (containing CPP-ACP) and Colgate (containing Arginine) toothpaste

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تقييم الصلابة الدقيقة السطحية لآفة البقعة البيضاء الاصطناعية المعالجة بثلاث طرق معالجة مختلفة. دراسة في المختبر

الملخص

الأهداف: الغرض من الدراسة الحالية هو مقارنة تأثير ثلاثة مناهج علاجية مختلفة على الصلادة الدقيقة السطحية لمينا الأسنان المولية الثالثة في بيئة المختبر. **المواد وطرائق العمل**: أجريت دراسة في المختبر على 50 ضرسًا ثالثًا منحشرا تم استخراجه مؤخرًا ، لتقييم الصلادة الدقيقة السطحية لآفات البقع البيضاء الاصطناعية (WSLs) بعد العلاج بثلاثة طرق باستخدام آلة فيكرز. تم غمر جميع العينات في محاليل دورة الأس الهيدروجيني لمدة 10 أيام (محلول التنقية لمدة 3 ساعات ، محلول إعادة التمعدن لمدة 20 ساعة واللعاب الاصطناعي لمدة 30 دقيقة مرتين يوميًا) ثم تم تقسيم العينة بشكل عشوائي إلى 5 مجموعات وفقًا لمعاملة سطح المينا ، المجموعة الأولى: كولجيت (تحتوي على أرجينين) معجون أسنان ، المجموعة 2: GC (تحتوي على الكازين فوسفوببتيد - فوسفات الكالسيوم غير المتبلور (CPP-ACP)) موس الأسنان ، المجموعة 3: مجموعة معجون الأسنان سنسوداين (تحتوي على NovaMin) مجموعة 4: الماء المقطر والمجموعة 5: محاليل دورة الأس الهيدروجيني. أرقام الصلادة محسوبة من طول المسافة البادئة على سطح المينا ، تم تحديد طول المسافة البادئة مجهريًا بتكبير X70. تم اجراء اختبار ANOVA (القيمة P 0.05) متبوعًا باختبار Duncan اللاحق لمقارنات القيم المتوسطة. **النتائج**: توجد فروق ذات دلالة إحصائية بين مجموعات الدراسة فيما يتعلق بقيم فيكرز للصلادة الدقيقة (VMH). كانت أقل قيمة لمجموعة التحكم بعد دورة الأس الهيدروجيني تليها مجموعة Colgate (المحتوية على الأرجينين) وكانت أعلى قيمة لمجموعة التحكم قبل دورة الأس الهيدروجيني تليها مجموعة سنسوداين (التي تحتوي على NovaMin). **الاستنتاجات**:معجون الأسنان سنسوداين (الذي يحتوي على نوفامين) أكثر فعالية في استعادة صلادة WSLs الاصطناعية بالمقارنة مع معاجين الأسنان GC (المحتوية على CPP-ACP) وكولجيت (المحتوية على الأرجينين).

DOI: 10.33899/RDENJ.2024.137614.1183

INTRODUCTION

The most prevalent side effect of orthodontic therapy is the development of white spot lesions [1]. It is may reach to 73% of individuals receiving treatment with fixed orthodontic appliances experienced WSLs accruement. The most frequent location for WSLs is in the labio-gingival region of the lateral incisors. WSLs frequently form around brackets on the buccal surfaces of teeth, especially in the gingival region [2]. In the oral cavity, de/remineralization is a dynamic process that happens throughout time, a WSL will form on the tooth surfaces when the delicate balance between them breaks [3]. Following the removal of the orthodontic device, it is typical to see a regression in the emergence of WSLs as a result of salivary remineralization and brushing abrasion in the presence of good dental and nutritional hygiene. Depending on the severity of the lesions, this improvement usually lasts for about six months after de-bracketing, but it is insufficient and these WSLs should be treated [2].

Fluoride is a member of the halogen family. Fluorides are both organic and inorganic chemicals. Inorganic fluorides are mostly ingested by living things through food, drink and air. Initiation of carious lesions and progression are under the control of fluoride. The balance between de- and remineralization can be tipped in favor of the latter condition by fluoride [4]. When the fluoride ion is present in the saliva at the proper concentration, fluoride's primary and most significant impact is topical. Bacterial cells are impacted by fluoride ions in a number of ways, such as the direct suppression of glycolytic enzymes H+ATPases. It influences the permeability of cellular membranes and lowers cytoplasmic pH, which reduces the amount of acid produced during glycolysis [5].

Arginine is a natural component of human saliva, which is released in free form with an average concentration of 50 Mm. The histidine-rich salivary proteins contain 10 to 20 moles percent of Arginine that is abundantly present in salivary peptides and proteins and is released by the activity of proteases and peptidases [6]. Arginine is mostly processed by the arginine deiminase route (ADS) of certain oral bacteria to create ornithine, citrulline, adenosine triphosphate (ATP), CO2, and ammonia. Ammonia preserves the biofilm and aids in preventing the transition from a "healthy" to a "cariogenic" plaque by reducing the acidity of the biofilm and allowing acid-labile organisms to survive [7]. After then, the plaque's pH rises, which encourages remineralization and lessens demineralization [8].

Casein is the predominant phosphoprotein in bovine milk and accounts for approximately 80% of its total protein which is typically found as calcium phosphate-stabilized micellar complexes, CPP-ACP contains nanocomplexes of milk protein casein with ACP [9]. The ACP-CCP solution is supersaturated and provides

Ca^{2+} and $PO4^{2-}$ ions for remineralization [10]. By preserving a supersaturated condition of vital minerals, it aids in the remineralization of carious lesions and prevents cariogenic bacteria from colonizing tooth surfaces. The integration of nanocomplexes into plaque and on tooth surfaces is CPP- ACP's mechanism [11]. The casein phosphor-peptides (CPP) play a crucial function in directing the highly soluble calcium phosphate phase to the tooth surface as an ACP carrier. This localization preserves the subsurface enamel's high concentration gradients of calcium and phosphate ions, which helps with remineralization [12].

NovaMin was created and patent-protected by NovaMin Technology, Inc., which was acquired by GlaxoSmithKline in May 2010 [13]. Commonly referred to as calcium sodium phosphosilicate, is made up of bioactive glass and body-produced minerals. It is white, powdered, and extremely biocompatible. NovaMin interacts with liquids like water and saliva, releasing calcium, sodium, phosphorus, and silica into the solution to form hydroxycarbonate apatite crystals that are identical to the hydroxyapatite crystals that make up the mineral makeup of enamel [14]. The sodium ions from NovaMin quickly interchange with hydrogen cations (in the form of H3 O+) in the aqueous environment around the tooth, i.e., saliva in the oral cavity, and this causes the release of Ca^{2+} and $PO4^{2-}$ ions from the glass and momentary rise in PH. The increased calcium and phosphate ions given by NovaMin assist precipitate to create a calcium phosphate layer as a result of the pH rise. This layer crystallizes into hydroxycarbonate apatite (HCA) as these processes continue [15].

The measurement of surface microhardness (SMH) is an appropriate method for understanding the de-remineralization process. A material like enamel that has a fine microstructure, is non-homogeneous, or is prone to breaking is suited for microhardness testing. A comparatively straight forward, non-destructive, and quick approach for demineralization and remineralization research is provided by SMH indentations [16].

The present study was conducted to compare the surface treatment by Colgate (containing Arginine), GC (containing CPP-ACP), and Sensodyne (containing NovaMin) toothpastes on the surface microhardness of the enamel of third molars. The null hypotheses tested was that, no difference between enamel microhardness of demineralized WSLs after treatment by these three treatment protocols.

MATERIALS AND METHODS

Sample Collection and Preparation

After getting ethical approval from the research ethics committee in the University of Mosul / College of Dentistry (UOM.DENT/H.L.16/21), fifty extracted impaction human third molars with normal

size, undamaged enamel buccal surfaces, with no evidence of hypo- or hyper mineralization were collected. The teeth were thoroughly cleansed, rinsed with deionized water, and maintained in a 0.1% thymol solution. Teeth were cleansed, polished with non-fluoridated pumice, and the residual roots were cut using a straight diamond bur, 2mm below the level of cemento-enamel junctions, with a generous irrigation of water [17]. to obtain an enamel block with a 4x4mm window, one tooth was fastened at the labial surface in the center of the plastic ring [17]. One by one, fin-grit silicon carbide sheets (600, 800, and 2400 grit) were used to polish the rings with exposed tooth surfaces.

The Formation of Artificial Demineralized Lesion.

PH Cycle Procedure: Teeth were immersed in a demineralizing solution (PH 4.5) for three hours and a remineralizing solution (PH 7.0) for twenty hours. Between treatments, teeth were briefly rinsed with deionized water, and they were then placed in artificial saliva for 30 minutes after each cycle, which lasted for ten cycles and each lasted for 24 hours. After every treatment, the artificial saliva was replaced, and the demineralizing and remineralizing solutions were changed daily. The PH was checked using a PH meter to ensure that there would be no changes in the pH values days later [18].

The Solutions Preparation.

Demineralization Solution: consists of acetic acid (0.05 M), (2.2 mM), and NaH2 PO4 (2.2 mM), PH of 4.5, adjusted with KOH (1M), 15 ml/tooth [17].

Remineralizing solution: consists of NaHPO4 (0.9 mM), KCl (0.15 mM), CaCl2 (1.5 mM), PH of 7.0, 15 ml/tooth [18].

Artificial Saliva: components of artificial saliva are CaCL2.2H2O 0.79, NaCl 0.40, NaH2 PO4.2H2O 0.78, KCl 0.40, CO(NH2)2 Urea 0.1, NaS9.H2O 0.005, in 1000 ml distilled water, pH of 7 (concentration G \ L) [19].

Study Samples Grouping: the sample was divided into 5 groups of 10 teeth each as follows:

Group 1; Arginine and fluoride-containing toothpaste (Table1): the teeth' labial surfaces were subjected to a pH cycling procedure for ten days and then Colgate toothpaste (Colgate sensitive PRO_Relief, Poland) was applied as a thin layer of paste on each tooth specimen by fine brush for one minute, then the teeth were washed with deionized water for 30 sec. and lightly dried with absorbent papers. This procedure was repeated two times daily for 7 days [20].

Table (1): Description and composition of Colgate toothpaste

Material	Description
Colgate toothpaste	Colgate sensitive PRO__ Relief, Poland **Composition**: Sodium. Mono-fluorophosphate 1.1%W/W (1450 Ppm F), Calcium Carbonate, Aqua, Sorbitol, Arginine, Aroma, Tetrasodium Pyrophosphate, Sodium Saccharin, Cellulous Gum, Sodium Bicarbonate, Sodium Lauryl Sulfate, Benzyl Alcohol, Limonene, Xanthan Gum, Ci77891.

Group 2; (Casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) tooth mousse cream (Table 2): the teeth labial surfaces were subjected to a pH cycling procedure for ten days and then CPP-ACP tooth mousse(GC America, Reclident, Alsip, USA) was applied as thin layer of the cream on each tooth specimen by fine brush for 3minutes, then again the cream was distributed by the brush and left for 30 minutes then washed with deionized water for 30 sec. and lightly dried with absorbent papers. This procedure was repeated two times daily for 7 days [21].

Table (2): Description and composition of CPP-ACP tooth mousse

Material	Description
CPP-ACP tooth mousse cream	Topical cream with bio-available calcium and phosphate (GC America, Reclident, Alsip, USA). Composition: 10% by weight of CPP-ACP, glycerol, CMC-Na, D-sorbitol, silicon Dioxide, titanium Dioxide, propylene glycol, xylitol, Acid, flavorings, phosphoric zinc oxide, Oxide, guar gum, magnesium butyl phydroxybenzoate, propyl p-hydroxybenzoate, sodium saccharin, ethyl p-hydroxybenzoate, Pure water.

Group 3; Sensodyne toothpaste containing novamin, NUPRO, (Table 3) th**e** teeth labial surfaces were subjected to a pH cycling procedure for ten days and then 0.5 g of Sensodyne toothpaste (Prophylaxis Paste with NovaMin; Gsk, Ireland) was applied with a rubber cup to each tooth for 2 minutes in a clockwise direction. Then the teeth were immersed in deionized water for 2 minutes and then gently rinsed with deionized water for 30 Sec. This procedure was repeated two times daily for 7 days [3].

Table (3): Description and composition of Sensodyne toothpaste

Material	Description
Sensodyne toothpaste	Nova Min (containing paste) NUPRO (Prophylaxis Paste with NovaMin; Gsk, Ireland). **Composition**: Glycerin., Pumice.,15%Calcium Sodium. Sodium Silicate, Dioxide, Titanium Methyl Salicylate, Phosphosilicate (Novamin), Purified Water, Sodium Carboxymethylcellulose, Sodium Saccharin, Flavor

Group 4; (Control before PH cycle): No agent was applied, only immersed in deionized water.

Group5; (Control after PH cycle): The teeth were treated to a ten-day pH cycling technique before being submerged in deionized water.

Vickers Micro hardness Test: The Vickers microhardness machine (OTTO WOLPERT/Germany) was used to assess the mechanical characteristics of the tooth samples. The length of the depression on the enamel surface, which was measured microscopically using a 70X magnification, was used to calculate the microhardness values [22]. A fixed load of 500 grams was applied to the enamel surface sample for 15 sec. for each sample. The square indent's two diagonals were measured to establish the indent's size visually. According to the formula, the Vickers hardness number was determined [23]:

VHN= (kg \mm^2) = 1.854 × P \d^2

P= the testing. load in grams.

d= the length of the diagonal line across the indentation in microns.

Statistical Methods: Statistical analysis of the results was performed by the SPSS Statistics (version 26.0, USA). The normality of distribution was assessed by the Shapiro–Wilk test. Descriptive statistics: mean, standard deviation, minimum, and maximum values were reported. Both intragroup time points (before PH cycling, post-treatment, after PH cycling) comparisons and intergroup comparisons were performed by using ANOVA and Duncan's post-hoc tests. The statistical significance of differences between the groups was accepted at the $P \leq 0.05$ level.

RESULTS

The Shapiro-Wilk test of normality was done for VMH test data to determine the statistical tests needed to analyze the results. The results of the normality test showed that the data were parametric and normally distributed at $P \leq 0.05$ as shown in Table (4).

Table (4): Shapiro-Wilk test of normality for VMH.

Groups	Statistic	Df	Sig.*
Colgate	0.904	10	0.243
GC	0.862	10	0.080
Sensodyne	0.909	10	0.273
Control before pH cycling	0.931	10	0.459
Control after pH cycling	0.914	10	0.313

* Significant difference at $P \leq 0.05$, DF=degree of freedom.

A comparison among the five study groups was done. Table (5) shows the descriptive statistics of VMH values of the sample among the study groups.

Table (5): Descriptive statistics of VMH means values of the study groups

Groups	N	Means	Std	Minimum	Maximum
Control after pH cycling	10	118.20	21.03	92.70	152.36
Colgate	10	185.71	11.88	164.80	200.47
GC	10	263.15	9.67	251.65	276.51
Sensodyne	10	296.45	7.86	279.71	307.56
Control before PH cycling	10	346.35	33.59	285	386.08

GC=GC tooth mousse, Std= Standard Deviation; N=number of samples.

Table (6) demonstrates the comparison of mean values of VMH for samples in five groups by (ANOVA) test, and the results showed that there were statistically significant differences among groups ($P \leq 0.05$).

Table (6): ANOVA test for VMH mean values among five study groups

VHM	Sum of Squares	Df	Mean Square	F	Sig.*
Between Groups	327953.257	4	81988.314	219.623	0.000
Within Groups	16799.140	45	373.314		
Total	344752.397	49			

* Significant difference at $P \leq 0.05$, F=F-test.

Duncan's multiple analysis range test was done to further explain that there was a significant difference in VMH values among the groups that existed at $P \leq 0.05$. The highest value was for control before PH cycling and then NovaMin but the lowest value was for control after PH cycling, (Table 7).

Table (7): Duncan's Multiple Analysis Range tests for the study groups

Groups	N	Subset For Alpha = 0.05				
		1	2	3	4	5
Control After pH Cycling	10	118.20				
Colgate	10		185.71			
GC	10			263.15		
Sensodyne	10				296.45	
Control Before pH Cycling	10					346.35
Sig.*		1.000	1.000	1.000	1.000	1.000

* Significant difference at $P \leq 0.05$.

DISCUSSION

The earliest indication of dental caries is enamel decalcification, or the production of WSLs, which typically appear as chalky white spaces on the outside of a tooth [(1)]. One test that has been used to explore the processes of demineralization and remineralization is the hardness test, which is quick, inexpensive, and easy to perform in order to calculate the quantities of minerals lost and restored [(24)]. The Vickers Hardness analysis in the current study was done in order to decide the capacity of Colgate (Arginine and fluoride containing tooth paste), GC tooth mousse cream containing CPP-ACP complex and Sensodyne tooth paste containing Novamin in restoring hardness of enamel surface after the formation of artificial WSLs, our decision depended on comparison of hardness value of these three groups with hardness values of control group before PH cycle and control group after PH cycle.

According to the results based on the mean value, it had been showed that the VMH value of control group before PH cycle was the highest value because the teeth were sound and was not subjected to any acidic environment, but VMH value of control group after PH cycle was the lowest value because the teeth were subjected to acidic environment and lost mineral content from their enamel surface.

The VMH value of Sensodyne group was less than control group before the PH cycle but it had the highest value when compared with other treatment groups, the NovaMin material that have the ability to restore the enamel surface hardness after exposure to an acidic environment and demineralization. This agreed with the study of Abbasoğlu *et al.,* (2019) who stated that" while in contact with liquids like water and saliva, Novamin releases calcium and phosphate ions into the oral environment". The Sensodyne toothpaste containing NovaMin has a capacity for remineralization of enamel more than GC tooth mousse cream this agreed with the study of Mahta *et al.,* (2014) who assumed that "compared to CPP-ACP, Novamin remineralized the carious lesion more successfully, due to its amorphous structure, CPP-ACP was unable to cling to the enamel surface effectively. While NovaMin produced bigger and more angular deposits, CPP-ACP produced smaller and more amorphous deposits. CPP-ACP also showed lower hardness values as a result, but Novamin displayed greater hardness values due to its more compact attachment to the surface [(16)]. Even after careful washing and brushing, the sediments remain firmly adhered. *In-vitro* tests have demonstrated that Novamin may release ions and change into hydrycarbonate apetite for up to two weeks". But in contrast to study of Benjasuwantep *et al.,* (2017) who found that no significant difference in the remineralization effect of NovaMin compared to CPP-ACP [(9)]. Also, in contrast to Indrapriyadharshini *et al.,* (2019) who found that because CPP-ACP keeps

calcium and phosphate in saliva at a supersaturated level and helps to keep them close to the enamel lesion, it can promote remineralization. This will reduce demineralization and improve remineralization of the enamel lesion [(1)].

The hardness value of Sensodyne toothpaste was more than that of Colgate toothpaste, also Colgate toothpaste has the lowest ability in remineralization when compared with GC tooth mousse and Sensodyne toothpaste, this agreed with the study of Yu *et al.,* (2016) who stated that" The hardness, elastic modulus, and nanotribological characteristics of early enamel caries could not be fully restored to those of undamaged enamel by arginine toothpaste. The application of mineral crystals was aided by the arginine toothpaste treatment, however the original enamel structure was not preserved" [(24)]. Additionally, Bak *et al.,* (2013) assumed that" fluoride ions cannot penetrate deeply into the lesions, topical fluoride treatment, which promotes enamel remineralization, is limited in its ability to provide adequate outcomes. It only lessens the crystal's solubility" [(25)]. In contrast Li *et al.,* (2015) stated that" A semi-essential amino acid called arginine is present in several human salivary proteins and peptides. Through the arginine deiminase system, it is digested by non-pathogenic bacteria like *Streptococcus sanguinis* to create energy, ammonia, and carbon dioxide. A more alkaline environment that is unfavourable to cariogenic bacteria is promoted by the generation of ammonia, which raises the local pH, counteracts the effects of acidification from sugar metabolism, reduces the cariogenicity of oral biofilms, and aids in remineralization" [(26)].

Limitations of the Study

The current study was conducted under *in vitro* conditions which were dissimilar to the natural oral cavity where there is plaque, oral microflora, saliva, the normal process of demineralization and remineralization which occur alternatively intra-orally and the protective effect of salivary minerals, also the synergistic effect of saliva and experimental materials (NovaMin, Arginine, fluoride, and CPP-ACP) couldn't be determined. The use of artificially produced WSLs, and the short-term evaluation of enamel microhardness.

CONCLUSIONS

From this study, we can conclude that: Sensodyne (containing Novamin) toothpaste, GC (containing CPP-ACP) tooth mousse, and Colgate (containing Arginine) toothpaste have remineralizing ability reflected by increased enamel microhardness, nevertheless, Sensodyne is considered the best one for remineralization and enhancing the surface microhardness value approximately to normal and making recovery for enamel, followed by GC then Colgate which have the lowest remineralizing ability.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this manuscript.

REFERENCES

1. Indrapriyadharshini K, Madan K P D, Sharma K, Iyer KRemineralizing potential of CPP-ACP in white spot lesions – A systematic review. Indian J Dent Res. 2018; 29:487-96.
2. Khoroushi M and Kachuie M. Prevention and Treatment of White Spot Lesions in Orthodontic Patients. Contemp Clin Dent 2017;8(1):11-19.
3. Shihabi S, AlNesser S, and Comisi JC. Comparative remineralization efficacy of topical novamin and fluoride on incipient enamel lesions in primary teeth: scanning electron microscope and vickers microhardness evaluation. EurJ Dent 2020; (5):1-5.
4. Cagetti MG, Campus G, Milia E& Lingström P A systematic review on fluoridated food in caries prevention. Acta Odontologica Scandinavica.2013;71:381-7.
5. Kanduti D, Sterbenk P, and Artnik B.Fluoride: a review of use and effects on health. MSM 2016; 28(2): 133-137.
6. Cheng X, Xu P, Zhou X. Arginine promotes fluoride uptake into artificial carious lesions in vitro. Australian Dental Journal 2015;60: 104–111.
7. Wolff MS and Schenkel AB. The Anticaries Efficacy of a 1.5% Arginine and Fluoride Toothpaste. Advances in Dental Research 2018; 29 (1): 93–97.
8. Santarpia R P, Lavender S, Gittins E. A 12-week clinical study assessing the clinical effects on plaque metabolism of a dentifrice containing 1.5% arginine, an insoluble calcium compound, and 1,450 ppm fluoride. Am J Dent 2014; 27:100-105.
9. Benjasuwantep P., Rirattanapong P. and Vongsavan K. The Remineralization Effect of Bioactive Glass on Enamel Caries-Like Lesions in Primary Teeth. Southeast Asian J Trop Med Public Health. 2017; 48(5):127-137.
10. Palaniswamy UK, Prashar N, Kaushik M, Lakkam S R, Arya S and Pebbeti S. A comparative evaluation of remineralizing ability of bioactive glass and amorphous calcium phosphate casein phosphopeptide on early enamel lesion. Dent Res J 2016; 13:297-302.
11. Rajendran R, Kunjusankaran RN, Sandhya R, et al. Comparative Evaluation of Remineralizing Potential of a Paste Containing Bioactive Glass and A Topical Cream Containing Casein Phosphopeptide-Amorphous Calcium Phosphate: An In Vitro Study. APESB 2019;1-10.
12. Al-Batayneh OB. The clinical applications of tooth moussetm and other cpp-acp products in caries prevention: evidence-based recommendations. Smile Dental Journa.l 2009; 4 (1):8-12.
13. Khijmatgar S, Reddy U, John S, Badavannavar NA and Souza T D. Is there evidence for Novamin application in remineralization? A Systematic review.Jobcr 2020; 10:87–92.
14. Abbasoğlu Z, Bıçak DA, Dergin DÖ, Kural D and Tanboğa I. Is novamin toothpaste effective on enamel remineralization? an in-vitro study. cumudj 2019; 22(1):22-30.

15. Gluzman R, Katz R V, Frey B J & Mc-Gowanm R. Prevention of root caries: A literature review of primary and secondary agents. Spec Care Dent. 2013; 33: 133-140.
16. Mehta AB, Kumari V, Jose R and Izadikhah V. Remineralization potential of bioactive glass and casein phosphopeptide-amorphous calcium phosphate on initial carious lesion: An in-vitro pH-cycling study. JCD. 2014; 17(1):3-7.
17. Mohammad N & Farahmand Far M H. Effect of fluoridated varnish and silver diamine fluoride on enamel demineralization resistance in primary dentition. J Indian Soc Pedod Prev Dent. 2018; 36(3): 257–261.
18. Prabhu A, Prasanna BG, Sakeenabhi B, Prashanth G M, Subramaniam R& Ragher M. Effect of Fluoride Varnish and Dentifrices and Its Combination on Deciduous Enamel Demineralization: An Invitro Study. J Pharm Bioallied Sci. 2017; 9(1): 112–116.
19. Taqa A, Sulieman R & Al-Sarraf HA. Artificial Saliva Sorption for Three Different Types of Dental Composite Resin (An In Vitro Study). EC Dental Science 2019; 18(10): 2339−2344.
20. Santarpia R P, Lavender S, Gittins E, et al. A 12-week clinical study assessing the clinical effects on plaque metabolism of a dentifrice containing 1.5% arginine, an insoluble calcium compound and 1,450 ppm fluoride. Am J Dent. 2014; 27:100-5.
21. Chaudhary I, Tripathi AM, Yadav G, SahaSEffect of Casein Phosphopeptide–amorphous Calcium Phosphate and Calcium Sodium Phosphosilicate on Artificial Carious Lesions: An in vitro Study. Int J Clin Pediatr Dent. 2017; 10(3):261-266.
22. Mushashe AM, Coelho BS. Effect of different bleaching protocols on whitening efficiency and enamel superficial microhardness. J Clin Exp Dent 2018; 10(8): 772–775.
23. Hegazy R & Mubarak R. Is Whitening Pre-Brush Rinse a Double-Edged Weapon? Evaluation of Listerine Effect on Enamel Microhardness and Surface Morphology. J Am Sci. 2012; 8 (3):126-132.
24. Yu P, Arola D D, Min J. Investigation on the remineralization effect of arginine toothpaste for early enamel caries: nanotribological and nanomechanical properties. J. Phys. D: Appl. Phys. 2016; 49 (435401): 1-9.
25. Bak SY, Kim YJ and Hyun HK. Color Change of White Spot Lesions After Resin Infiltration. COLOR research and application 2014; 39 (5): 506-510.
26. Li J, Huang Z, Mei L, Li G and Li H. Anti-Caries Effect of Arginine-Containing Formulations in vivo: A Systematic Review and Meta-Analysis. Caries Res. 2015; 49: 606–617.