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COMPARATIVE EVALUATION OF EFFICACY OF DIFFERENT COMMERCIALLY AVAILABLE REMINERALIZING AGENTS CONTAINING HYDROXYAPATITE, NOVAMIN, ARGININE ON EROSIVE LESIONS REMINERALIZATION -IN VITRO STUDY

Dentistry

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ABSTRACT

Biomimetic agents like nano-hydroxyapatite, NovaMin, and Arginine have been incorporated into dentifrices for their ability to facilitate enamel repair and protect against further erosive damage. While individual studies show promising results, comparative evaluations of their efficacy on erosive lesions remain limited. Hence this study aimed to evaluate and compare the effectiveness of nano-hydroxyapatite, NovaMin, and arginine in remineralizing artificially induced erosive lesions in vitro. Methods and Material: 45 mandibular premolars were decoronated and embedded in acrylic resin. Erosive lesions were induced by placing in 1% w/v citric acid for 6 days, followed by SEM/EDS analysis. Samples were divided into three groups (n=15): Group 1 – Nano-Hydroxyapatite (DENTE 91), Group 2 – Arginine (Colgate Total), and Group 3 – Bioactive Glass (SHY-NM) and treated for 7 days. Post-treatment, SEM/EDS analysis was conducted to assess mineral gain. The scores were subjected to statistical analysis using Wilcoxon test ($p < 0.05$). The results were statistically significant difference in gain of mineral content between Colgate Total (62.29%) to SHY-NM (55.6%), SHY-NM (55.6%) to DENTE91 (44.15%), DENTE91 (44.15%) to Colgate total (62.29%). Conclusions: All tested agents were effective in promoting mineral gain; however, the Arginine group showed significantly superior remineralization compared to the other groups.

KEYWORDS

Erosion, Remineralization, Colgate Total, Dente91, ShyNM.

INTRODUCTION

Dental erosion, caused by acidic exposure from contemporary dietary habits and lifestyle factors, affects nearly 20% of the world's population, leading to sensitivity and functional problems.[1,2]

Dentifrices with nano-hydroxyapatite, NovaMin, and arginine aid in enamel repair and erosion prevention.[3] Hydroxyapatite improves hardness and reduces sensitivity by filling microdefects.[4] NovaMin forms a hydroxyapatite-like layer that blocks dentinal tubules and supports remineralization.[5] Pro-Argin enhances calcium deposition in enamel, reducing hypersensitivity and promoting enamel repair.[6,7] Despite individual promising results, comprehensive comparisons of their effectiveness in erosive lesion remineralization are scarce. Therefore, this study aimed to evaluate and compare the effectiveness of nano-hydroxyapatite, NovaMin, and arginine in remineralizing artificially induced erosive lesions in vitro.

The null hypothesis posited that there would be no significant difference in the remineralization and mineral content gain among the three groups.

MATERIALS AND METHODS

45 mandibular premolars tooth samples which were freshly extracted for periodontic and orthodontic reasons were collected from the Department of Oral and Maxillofacial Surgery, Malla Reddy Institute of Dental Sciences, Hyderabad. The collected teeth were examined at 2.5x magnification using a microscope (Labomed Inc, USA) to rule out any fractures, cracks or craze lines, hypoplasia or white spot lesions.

Teeth with intact enamel were included. Teeth with cracks, fissures, fractures, enamel hypoplasia, craze lines, white spot lesions, reduced enamel and exposed dentin (abrasions and attrition) were excluded.

The samples were disinfected with 1% thymol (MDent, India) until further use. Each tooth was decoronated using a diamond disc (Generic) attached to a micromotor (NSK), approximately 1 mm below the cementoenamel junction. Subsequently, the tooth samples were embedded in acrylic resin molds, ensuring that the coronal portion remained exposed to demineralizing agents.[8]

The teeth samples were kept in an artificial saliva(AS) solution during the entire experimental period. This solution is recognized and validated as an effective substitute for natural saliva in in-vitro studies of remineralization. Here commercially available salivary substitute Wet mouth (ICPA, India) was used as artificial saliva (pH 7.2 was adjusted).

To induce erosive enamel lesions through demineralization, the 45 test samples (n=45) were placed in 1% W/V citric acid (Generic) solution which was freshly prepared (pH 2.3). This process was repeated six times daily for 2 minutes each time, over a period of 6 days at 37°C.[8]

Periods of remineralization in which each resin block (DPI, India) was rinsed with distilled water (IHL Medicare Pvt. Ltd. India) for 10sec and immersed in artificial saliva for 2hours. Following the final day of erosive treatment, the samples were stored overnight in artificial saliva, which was renewed daily.[9]

Scanning electron microscopy coupled with energy dispersive X-ray spectroscopy (SEM/EDX) was utilized to analyze the mineral content remaining after erosion.

To establish the demineralized mineral content (baseline), before conducting energy-dispersive X-ray spectroscopy (SEM/EDX) analysis, all specimens were coated with carbon. Readings of the samples were obtained, and elemental values for calcium, phosphorus, and fluoride were analyzed based on weight % and volume % peaks (Figure 1).

The demineralized enamel samples were divided into three groups based on the dentrifice being used. Group 1: Nano Hydroxyapatite [DENTE 91, India] (n=15), Group 2: Arginine [Colgate Total, USA] (n=15), Group 3: Bioactive glass [SHY-NM, India] (n=15) (Figure 2).

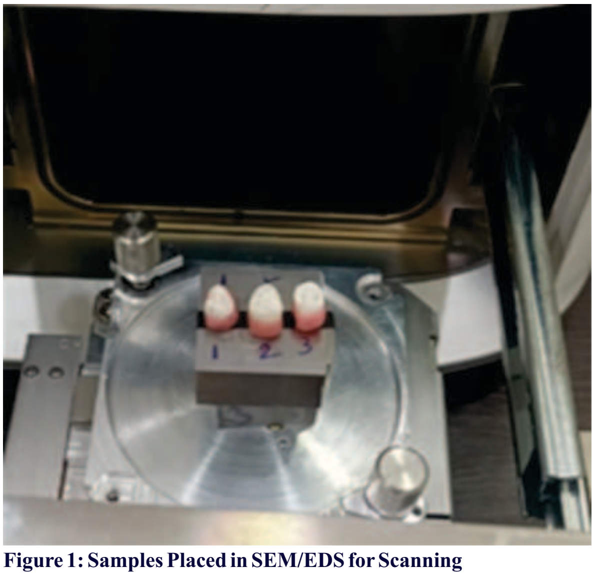


Figure 1: Samples Placed in SEM/EDS for Scanning

Figure 2: DENTE 91, Colgate Total, SHY-NM

Tooth pastes slurry was prepared by 1 part of dentrifice to three parts of artificial saliva in 1000ml of distilled water.[10] Twice daily, the treatment involved brushing the specimens with toothpaste slurries for 1 minute using a standard toothbrush manually. After brushing, the specimens underwent a 10-second rinse in water before immersion in artificial saliva. This process continued for a period of 7 days.[9]

SEM/EDX analysis was performed after applying the dentifrice to evaluate the increase in mineral content. Elemental values for calcium, phosphorus, and fluoride were obtained through peak analysis of the samples weight % and volume %.

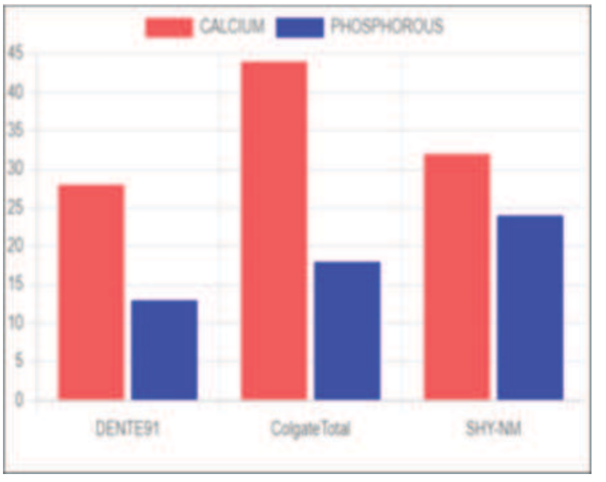
RESULTS

Data were analysed by SPSS software version 23.0. SEM/EDS analysis was employed to measure the mineral content gain before and after remineralization at the occlusal surface in three groups: Dente 91, SHY-NM, and Colgate Total using Wilcoxon test ($p < 0.05$).

A total of 45 samples were examined using SEM/EDX. For calcium mineral gain, Colgate Total, containing 1.5% arginine (44.02%) as a key ingredient, demonstrated the highest increase in mineral content, followed by SHY-NM with bioactive glass Novamin (32.37%), and then Dente91 with nano hydroxyapatite (27.74%). In terms of phosphorus mineral gain, SHY-NM (23.23%) showed the largest increase in mineral content, followed by Colgate Total with 1.5% arginine (18.27%), and then Dente91 (13.71%) (refer to Table 1 and Graph 1 for detailed results).

Table 1: Comparison of Gain of Mineral Content Between all the Three Groups

	CALCIUM GAIN % MEAN	PHOSPHOROUS GAIN % MEAN
DENTE 91	27.74	13.71
COLGATE TOTAL	44.02	18.27
SHY-NM	32.37	23.23



Graph 1: Comparison of Gain of Mineral Content Between all the Three Groups

The P ($p<0.05$) value here is less than 0.05 which shows the results are statistically significant difference in gain of mineral content between Colgate Total (62.29%) to SHY-NM (55.6%), SHY-NM (55.6%) to DENTE91 (44.15%), DENTE91 (44.15%) to Colgate total (62.29%).

DISCUSSION

Dental erosion occurs when acidic pH of the oral cavity increases. The effects of decreased pH can be subdued by precipitation of calcium and phosphate ions. Many consumables used on everyday basis with a low pH can damage the tooth surface. These include carbonated drinks, acidic beverages and fruits which overcome saliva's natural ability to buffer, resulting in the loss of tooth minerals and increasing the likelihood of tooth demineralization and caries.[11]

Demineralization refers to the loss of inorganic substances from the enamel structure, which can result in the formation of white spot lesions. Under natural conditions, demineralization begins when the pH of hydroxyapatite reaches a critical level of 5.5, indicating an oral environment where mineral ion saturation is lower compared to the mineral content like calcium phosphates of the teeth as described by Cury JA et al.[12]

According to HU W and Featherstone et al., remineralization involves replenishing calcium, phosphate, and fluoride ions that were lost within the tooth structure. These ions are incorporated into fluorapatite crystals, which are larger and more resistant to acidic dissolution compared to the original crystals. This process fills the crystal voids in demineralized enamel, resulting in net mineral gain.[13]

Fluoride is a widely recognized remineralizing agent. However, despite fluoride being considered a gold standard agent in toothpastes, caries remains prevalent. As plaque acid attacks intensify, the pH drops to around 4.5, rendering fluoride ineffective in controlling the progression of lesions as described by Pfarrer AM and Lussi A.[14]

There are few reasons to search for fluoride alternatives that were Fluoride demonstrates strong effectiveness against smooth-surface cavities, though its impact appears more restricted when dealing with occlusal areas. Adopting a high-fluoride approach is not viable due to the risks of adverse effects, such as fluorosis, which can arise from excessive fluoride exposure.

Non-fluoridated remineralizing agents work through various mechanisms: some interact directly with tooth enamel, others neutralize bacterial acidity, and some act as anti-plaque agents. The need for calcium and phosphorate ions availability in the oral environment has spurred the development of new materials designed to provide these essential elements for remineralization. Hence this study has been choosen for comparing Hydroxyapatite, NovaMin, and arginine remineralising agents that have gained significant attention recently.

The test samples were embedded in cold cure acrylic to ensure standardization and restrict exposure solely to the occlusal surfaces.

The demineralization solution used in the present study was 1%citric acid as described by srujana karumuri, Jyothi mandava et al.[15]

According to Dundar and Besinis A et al Citric acid was chosen for its ability to demineralize enamel effectively, aided by its chelating action that binds calcium-like minerals from hydroxyapatite.[16] It erodes enamel, exhibits a rougher surface texture with loss of interprismatic minerals.

Energy dispersive spectroscopy (EDS) elemental analysis has been validated as a dependable method for quantifying changes in mineral content and validating the efficacy of remineralizing agents. It is regarded as the gold standard for assessing mineral loss or gain in artificially induced initial erosive lesions. EDS utilizes micro-analytical techniques along with scanning electron microscopy (SEM) for detailed structural analysis.[17]

According to Hegde MN et al, the nanoparticles are known for their superior dispersion compared to bulk materials, allowing them to quickly penetrate, which typically have a diameter of 2–3 micrometers. The increased surface area of the crystals enhances their solubility and reactivity, which in turn accelerates their deposition on rough and demineralized surfaces.[18]

According to Huang SB at al, many invitro studies stated that remineralization rates were fastest across all treatments during the initial 6 days of the period, after which they gradually slowed down and stabilized. Therefore, a remineralization period of 7 days was chosen for assessment.[19]

In this present study, three different materials were used to compare remineralization: nano hydroxyapatite, Arginine, and bioactive glass (Novamin).

The null hypothesis was rejected as a statistically significant difference among the three groups was noticed after remineralisation.

In our current study, Colgate Total with arginine demonstrated the highest increase in mineral content compared to DENTE 91 and SHY-NM. Specifically in terms of net calcium ion gain, Colgate Total performed well, followed by SHY-NM followed by Dente-91. Regarding net phosphorus ion gain, SHY-NM showed the highest effectiveness, followed by Colgate Total followed by Dente-91.

According to Kulal et al., Poggio et al., and Yesilyurt et al., arginine demonstrates significant remineralizing efficacy.[20,21,22] Colgate Total with Pro-Argin, containing 1.5% arginine (an amino acid naturally found in saliva) and calcium carbonate (an insoluble calcium compound), was originally formulated to block dentinal tubules and alleviate sensitivity. Arginine and calcium carbonate bind to the negatively charged surfaces of enamel and dentin, creating a layer that protects them from acidic stimuli. This layer effectively covers surface imperfections and seals exposed dentinal tubules, thereby reducing sensitivity.

The enhanced mineral content gain observed with 1.5% arginine can be attributed to the presence of arginine, calcium carbonate, and sodium monofluorophosphate in its composition. According to Nanwal R et al, arginine alone may not suffice for remineralizing demineralized lesions or providing resistance against acid challenges. Therefore, the combined action of arginine and fluoride within a calcium carbonate base likely facilitated fluoride uptake, resulting in the formation of more acid-resistant enamel and promoting remineralization.[5] This was further supported by Yin W et al, Bijli MNA.[23,24]

According to recent clinical trials by X. Cheng et al., the fluoride reservoir hypothesis helps elucidate why arginine-containing toothpaste demonstrates superior anti-caries efficacy compared to conventional fluoride toothpaste.

The bond between the positively charged guanidinium group of arginine and negatively charged fluoride ions prevents fluoride from incorporating into hydroxyapatite crystals. Nevertheless, arginine-fluoride complexes could potentially function as reservoirs (arsenal reservoir) stored within enamel. These reservoirs may release fluoride when exposed to acidic conditions, potentially supporting remineralization processes.[25]

NovaMin (calcium sodium phosphosilicate) has been shown to exhibit effective remineralization properties. This inorganic compound releases calcium, sodium, and phosphate ions gradually in aqueous environments. Originally developed for bone regeneration, NovaMin also effectively occludes dentinal tubules by forming a mineral layer similar to hydroxyapatite. Upon contact with water or saliva, NovaMin first liberates sodium ions, elevating the pH to a range (7.5–8.5) conducive to hydroxyapatite formation. This is followed by the release of calcium and phosphate ions, supplementing natural saliva levels. These ions precipitate onto the tooth surface, forming calcium hydroxycarbonate apatite (HCA)as described by Diamanti I etal.[26]

HCA (calcium hydroxycarbonate apatite) possesses a chemical structure similar to enamel crystals, effectively mimicking and thereby almost reproducing the lost enamel layer.[27] Bioactive glass (BAG) deposits can serve as reservoirs for ions, which are then released to areas susceptible to demineralization. This mechanism contributes to the increased mineral content observed with NovaMin. This was supported by Wang et al., Aggarwal et al.[28,29]

According to Carvalho et al., Soares et al., and Haghgoo et al.[30,31,32] nHAP Dente-91, a fluoride-free toothpaste, has demonstrated significant remineralization effects. Hydroxyapatite (HAP) is the primary constituent of dental hard tissues, comprising 95 wt% of enamel and 75 wt% of dentin. Similar to its role in bone, HAP contributes to the mechanical properties of tooth. Poorly crystalline nanocrystals of hydroxyapatite (HA) possess excellent biological properties, such as biocompatibility, non-toxicity, and lack of inflammatory responses.

These nanocrystals under physiological conditions also exhibit bioresorption properties, a characteristic that can be modulated by controlling their crystallinity through innovative synthesis techniques that produce nanoscale crystals. Phosphate nanocrystals smaller than 100 nm enhance the bioactivity of HAP due to their increased surface area and improved wettability. These calcium phosphate nanocrystals penetrate deeply into demineralized subsurfaces, forming a reservoir-like deposit of calcium and phosphate ions.[33.34]

Limitations

Enamel remineralization in oral cavity is a complex process, with challenges in accurately replicating the biological aspects of caries and the varied intraoral conditions, including the enzymes and their role that contribute to decay. Existing solutions primarily consist of inorganic ions, overlooking the potential impacts of pellicle formation, salivary proteins and plaque on mineralization inhibition. Confounding factors include potential experimental errors and variations in the enamel microstructure among different specimens.

CONCLUSIONS

It can be concluded that all tested agents promoted a degree of enamel remineralization, as evidenced by mineral gain; however, Colgate Total showed significantly higher mineral gain compared to DENTE 91 and SHY-NM.

Clinical Significance

The combination of saliva and commercially available remineralizing agents can effectively promote remineralization and inhibit early enamel erosion.

List of Abbreviations

AS- Artificial saliva
EDS- energy dispersive Xray spectroscopy
HAP- Hydroxyapatite
nHA- Nano hydroxyapatite
pH- Potential of hydrogen
SEM/EDS – Scanning electron microscopy/ energy dispersive Xray

spectrometer
SPSS- Statistical Package for the Social Sciences
w/v- Weight /volume

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