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Comparative evaluation of remineralizing efficacy of calcium sodium phosphosilicate, ginger, turmeric, and fluoride

Amir Shayegan, Sara Arab, Victor Manyong Makanz, Nicka Safavi

Dentistry Department, Children's Hospital of Queen Fabiola (HUDERF), Free University of Brussels (ULB), Brussels, Belgium

ABSTRACT

Background: White lesions, also known as white spots, are the earliest signs of tooth decay. At this stage, noninvasive preventive treatments, such as fluoride application, can help to slow down or even reverse the progression of white lesions. For decades, fluoride has held the spotlight as the go-to agent in oral preventive care, demonstrating significant remineralizing power. Recent scientific literature reveals a growing interest in alternative products as natural substances that demonstrate potential remineralizing effects on tooth enamel. This *in vitro* study aimed to evaluate the potential remineralizing effect of calcium sodium phosphosilicate (CSP), ginger, and turmeric.
Materials and Methods: This *in vitro* study was designed to evaluate the remineralizing effects of various materials on the enamel of extracted human teeth. The aim was to compare the effectiveness of these different substances in promoting enamel remineralization. Enamel blocks were prepared and were divided into seven experimental groups: CSP, fluoride toothpaste, nonfluoride toothpaste, turmeric, ginger, fluoride varnish, and distilled water. In this study, sample mineralization is assessed through the quantitative photo-induced fluorescence test before demineralization, after demineralization, and after remineralization. Statistical analysis of the data was conducted using a one-factor analysis of variance test. The significance level was set at $P < 0.05$.
Results: The best results were obtained by groups treated with turmeric ($P < 0.0001$), Enamelast fluoride varnish ($P < 0.0001$), and NovaMin ($P < 0.01$), as compared to other remineralizing treatments.
Conclusion: While fluoride has undeniably revolutionized oral preventive care, the exploration of alternative products as natural substances and innovative compounds in recent scientific literature signals a shift in focus toward safer and potentially more diverse options.

Key Words: Curcuma, fluorides, tooth remineralization, *Zingiber officinale*

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Address for correspondence:
Dr. Amir Shayegan, Children's Hospital of Queen Fabiola (HUDERF), Free University of Brussels (ULB), 15, Avenue Jean-Joseph Crocq, Brussels 1020, Belgium.
E-mail: Amir.shayegan@hubruxelles.be

INTRODUCTION

Dental caries is a common chronic infectious disease and dynamic process caused by the demineralization of dental enamel due to the acid produced by cariogenic bacteria. Poor oral hygiene, as well as a diet high in sugars and acidic drinks,[1] can increase the risk of dental caries. The dental enamel is mainly composed of calcium hydroxyapatite crystals, which can be demineralized when the intraoral pH falls below 5.5 due to acid production by cariogenic bacteria.[2,3] White lesions, also known as white spots, are the

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earliest signs of tooth decay and are characterized by the loss of minerals in the enamel. At this stage, the decay has not yet progressed to the dentin, the layer beneath the enamel, and is, therefore, reversible.[3,4] Noninvasive preventive treatments, such as fluoride application, can help to slow down or even reverse the progression of white lesions.[5] It is essential to detect and treat white lesions early to prevent them from developing into more severe cavities.

For decades, fluoride has held the spotlight as the go-to agent in oral preventive care, demonstrating significant remineralizing power, and becoming a cornerstone in the fight against tooth decay. Its integration into various preventive products, from toothpaste to mouthwash and beyond, has contributed to its widespread use since the 1940s.[3,4] Fluoride's mechanism of action involves inhibiting demineralization by bonding with hydroxyapatite crystals within the tooth, forming durable fluorapatite crystals that resist the corrosive effects of an acidic environment.[5,6] However, as with any powerful tool, there are limits to its application, and excessive doses can lead to toxic effects, resulting in fluorosis and necessitating a cautious approach to its use.

The recent scientific literature reveals a growing interest in alternative products that demonstrate potential remineralizing effects on tooth enamel. Natural substances such as cocoa and grape seed and widely recognized spices such as ginger and turmeric are among these alternatives.

Cocoa and grape seeds, rich in polyphenols, have been studied for their antioxidant properties and ability to promote remineralization. [7,8] These natural components offer a tantalizing prospect for oral health enthusiasts seeking alternatives to fluoride-based products. Similarly, ginger and turmeric, known for their anti-inflammatory and antibacterial properties, present a promising avenue for researchers exploring novel ways to enhance oral care.[9]

In oral care, advances in materials science have paved the way for innovative solutions that go beyond traditional approaches. One such groundbreaking material is calcium sodium phosphosilicate (CSP), more commonly recognized as NovaMin or 45S5 bioactive glass, distinguished by its substantial silicon content of 45%. Originally conceived in the 1970s, this synthetic, inorganic compound is a composite of sodium, calcium, phosphorus, and silica. Its introduction into the medical field marked a turning point, harnessing biomimetic and biocompatible properties alongside an exceptional capacity for bone regeneration.[10] CSP, a compound garnering attention in recent studies, is hailed for its potential to remineralize enamel while avoiding the pitfalls associated with high fluoride doses. Its unique composition and mode of action make it an intriguing candidate in the quest for safer and more effective oral care options.

The last decade has seen a significant paradigm shift in the use of NovaMin, particularly in oral care. Dental health, a cornerstone of overall well-being, has benefited from the incorporation of this bioactive glass into various topical products.[11-15]

Recently, there has been a notable surge in interest among patients alike in the use of natural herbal products, favoring them over their chemical counterparts. This inclination toward herbal remedies is not without merit, especially considering the wealth of benefits associated with these natural substances. Traditional Indian medicine, with its rich history, provides compelling evidence that herbs and spices could be considered alternative solutions against a wide array of microorganisms.

A staple of traditional Indian medicine, ginger, has gained attention for its multiple health benefits, particularly in dentistry. Known for its antibacterial, antifungal, and antioxidant properties, ginger has already found its place in oral care practices in India. The medicinal properties of ginger extend beyond its culinary uses, showcasing a promising potential for enhancing oral health.[16]

Similarly, turmeric, another herb deeply rooted in traditional medicine, shares a remarkable overlap in medicinal properties with ginger. While both exhibit antibacterial and antioxidant qualities, turmeric is predominantly recognized for its potent anti-inflammatory effects in the medical traditions of China and India.[17] This versatility allows turmeric to play a dual role, addressing oral health concerns and broader systemic inflammation.

Notably, several *in vitro* studies have shed light on ginger's and turmeric's remarkable remineralizing effects.[18,19] This evidence underscores the potential of these natural remedies not only in preventing oral diseases but also in promoting the restoration of dental health.

This *in vitro* study aimed to evaluate the potential remineralizing effect of CSP, ginger, and turmeric.

The null hypothesis is that these materials have no difference in remineralizing effect.

MATERIALS AND METHODS

Study design

This *in vitro* study was designed to evaluate the remineralizing effects of various materials on the enamel of extracted human teeth. The aim was to compare the effectiveness of these different substances in promoting enamel remineralization. The study was approved by the Ethics Committee of the Children's Hospital of Queen Fabiola, Free University of Brussels (CEH 62/15).

Materials

The materials selected and employed for this study include CSP, fluoride toothpaste, nonfluoride toothpaste, turmeric, ginger, fluoride varnish, and distilled water as the control solution, as illustrated in Table 1.

Sample preparation

In this study, we performed a meticulous examination of 35 extracted permanent molar human teeth, which were carefully selected to ensure the absence of carious lesions, white spots, fractures, or surface irregularities.

The crowns of each tooth were methodically separated from the roots using a cylindrical diamond bur on a turbine and 70 dentin and enamel blocks were prepared, fixed on a dentin side, on a solid support using light-curing fluid resin. The samples were divided into seven experimental groups [Table 1].

The enamel at the center of each sample, with a surface area of 3 mm × 3 mm, is highlighted by a pencil line and left free to undergo the respective demineralization and remineralization treatments. Meanwhile, the enamel at the periphery is coated with varnish. This procedure aims to achieve partial demineralization of the tooth enamel and to facilitate better monitoring of the data obtained from the photo-induced quantitative fluorescence test.

The samples were stored in distilled water until they were ready for use.

Samples are immersed for 7 days at 37°C in a demineralization solution that includes 2.2 mmol/L Na2HPO4, 2.2 mmol/L CaCl2, and 0.05M HCl (hydrochloric acid). The pH of the solution is carefully maintained at 4.4 using NaOH. Following immersion, samples are thoroughly rinsed and subsequently stored in distilled water.

Each group of samples then undergoes a 10-day remineralization treatment. The remineralization products are applied twice daily to the tooth surface using a micro brush for 2 min. After each treatment session, the teeth are rinsed and stored in distilled water at room temperature.

Quantitative photo-induced fluorescence (QLF) test

This study uses the quantitative photo-induced fluorescence test to evaluate sample mineralization. The demineralization and remineralization detection system (QLF, Inspektor Research Systems BV, Amsterdam, Netherlands) harnesses tooth fluorescence to capture images, subsequently analyzed to glean insights into lesion area (measured in mm^2) and lesion depth indicated by the percentage of fluorescence loss (ΔF in %). The assessment evaluates lesion depth, expressed as fluorescence loss (ΔF in %), where a more negative percentage signifies a greater degree of demineralization.

Sample mineralization is evaluated at three time points:

1. Before demineralization: PD (t = 0)
2. Postdemineralization: DEM (t = 1)
3. Postremineralization: REM (t = 2).

Table 1: The commercial name and composition of the materials used in this study

Group	Material	Brand name	Composition
1	CSP toothpaste	Sensodyne Repair & Protect (NovaMin)	Active ingredients: CSP 5%, sodium fluoride (1450 ppm)
2	Fluoride toothpaste	Sensodyne Fluoride	Active ingredient: Sodium fluoride (1450 ppm)
3	Vegan toothpaste	Jack N' Jill Natural Certified Toothpaste	Water, vegetable glycerin, xanthan gum, silica, potassium sorbate, citric acid
4	Turmeric powder	Turmeric	Turmeric powder suspended in distilled water (10 mg/mL)
5	Ginger powder	Ginger	Ginger powder suspended with distilled water (10 mg/mL)
6	Fluoride varnish	Enamelast	Sodium fluoride 5% (22.500 ppm), Xylotol
7	Control solution	Distilled water	dH2O

CSP: Calcium sodium phosphosilicate

Statistical analysis

The results were presented as mean values ± standard deviation, calculated from the collected samples. Statistical analysis of the data was conducted using a one-factor analysis of variance test. The significance level was set at $P < 0.05$. Tukey's *post hoc* comparison test was performed to identify differences between groups. All statistical analyses were carried out using GraphPad Prism 9.4.1 (GraphPad Software Inc., La Jolla, CA, USA).

RESULTS

The best results were obtained by groups treated with turmeric ($P < 0.0001$), Enamelast fluoride varnish ($P < 0.0001$), and NovaMin ($P < 0.01$), as compared to other remineralizing treatments [Figure 1].

DISCUSSION

Addressing issues at the early stages, such as white spot lesions, underscores the significance of preventive care. Dental practitioners emphasize educating patients about effective oral hygiene practices to prevent or even reverse the progression of initial carious lesions. This includes promoting regular dental checkups, proper brushing and flossing techniques, and a balanced diet to maintain oral health.

In addition to preventive measures, advancements in dental research have led to the development of new products and technologies aimed to remineralize enamel. Remineralization is the process of restoring minerals to the tooth structure, enhancing its strength and resistance to decay. Products such as fluoride toothpaste, varnishes, and remineralizing agents are part of the therapeutic arsenal to manage early carious lesions without resorting to invasive procedures.

Modern dentistry aims to provide comprehensive, patient-centered care by combining preventive strategies with targeted interventions such as enamel remineralization. This approach aligns with "minimal intervention dentistry," which aims to preserve natural tooth structure and promote overall oral health. The ultimate aim is to enable individuals to play an active role in maintaining their oral health and to intervene conservatively and tailored to meet each patient's specific needs.

Fluoride is widely recognized as the best-known remineralizing agent and is often referred to as the "gold standard" in numerous literature reviews.[14] This designation allows us to benchmark and compare the remineralization potential of other materials. In this study, samples treated with Enamelast fluoride varnish containing 5% sodium fluoride (22,600 ppm) serve as the positive control group. Enamelast fluoride varnish is commonly used clinically to address dental sensitivities and prevent caries.

Throughout the experimental procedure, our samples were immersed in distilled water. This choice was based on our observation that immersing them in an artificial saliva solution, prepared in the laboratory, led to a significant increase in the QLF mineralization value of most enamel surfaces. This increase might indicate partial remineralization. Using distilled water allows us to study the effects of remineralizing products without the influence of factors promoting this effect.

In the study's experimental groups, Group 1 samples treated with toothpaste containing CSP at a concentration of 5% exhibited greater remineralization compared to Group 2 (fluoride toothpaste) and Group 3 (vegan toothpaste), aligning with the observed results. It is noteworthy, however, that both Group 1 and Group 2 toothpaste contain an equal amount of fluoride (1450 ppm).

Notably, the difference in enamel tissue mineralization between Groups 2 and 3 before and after treatment did not reach statistical significance. This implies that CSP, combined with fluoride, plays a more crucial role in the remineralization process than isolated fluoride alone.

The study conducted by Hsu *et al.*[6] on the remineralizing effect of a specific material compares Sensodyne Repair and Protect with another fluoridated and vegan toothpaste on hydroxyapatite discs using a scanning electron microscope. The results indicate that the crystal layer formed by the toothpaste containing bioactive glass is thicker and wider than that formed by the fluoride toothpaste. Notably, no crystal layer was formed with the vegan toothpaste. These findings suggest a synergistic effect between NovaMin (the bioactive glass) and fluoride. Importantly, our study aligns with these results.

It is worth noting that the authors[6] initially aimed to investigate the effect of isolated CSP on hydroxyapatite without the interaction of fluoride. However, they encountered a challenge as powdered CSP precipitated in distilled water instead of

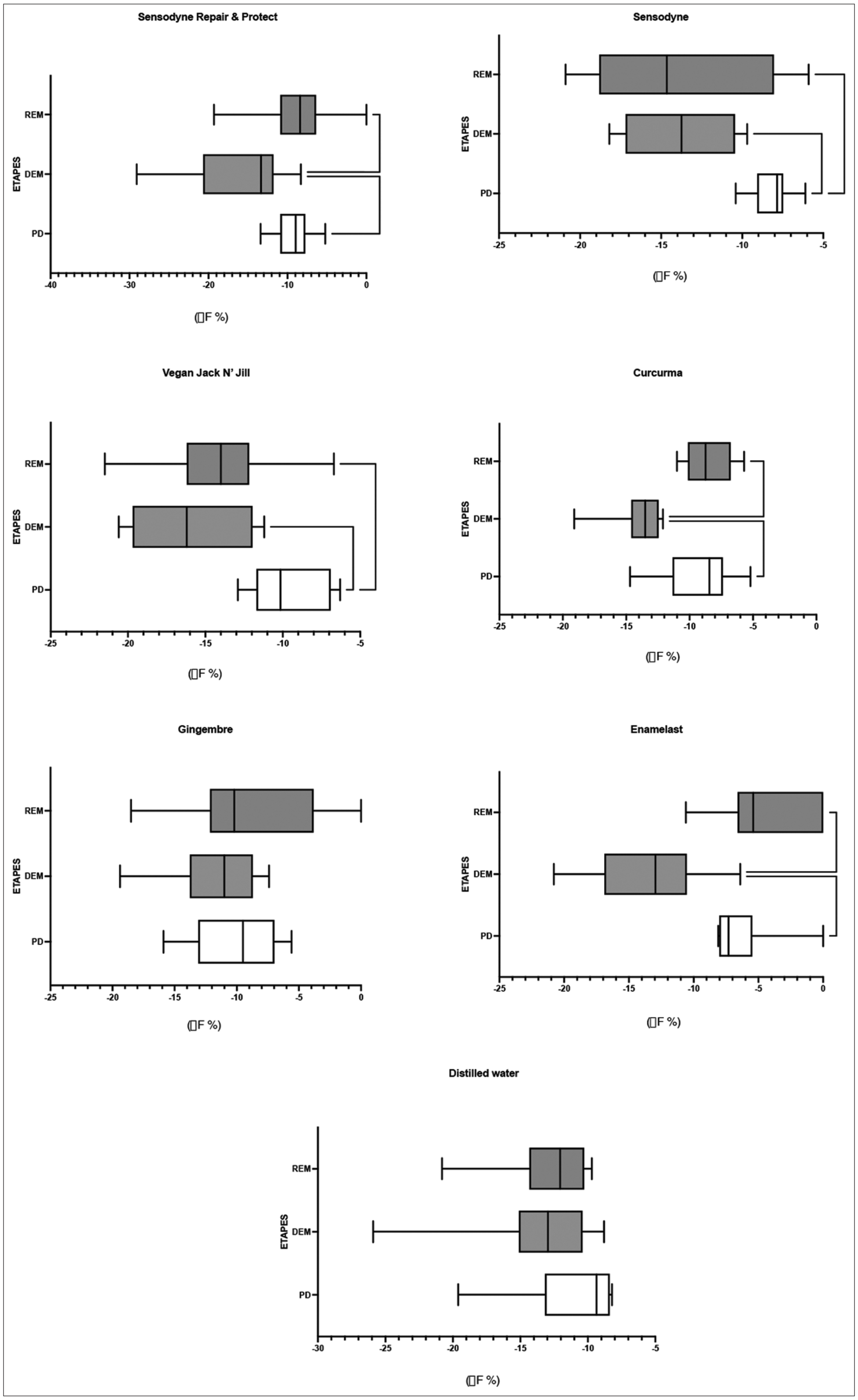

Figure 1: The results were presented for each group before demineralization (PD), after demineralization (DEM) and after remineralization (REM).

dissolving. Due to this issue, Sensodyne Repair and Protect, which contains 5% CSP and is readily available in Europe, was chosen for our study.

Shihabi *et al.*[14] conducted a study to compare the remineralizing effects of two dental prophylactic pastes manufactured in the USA on demineralized enamel of permanent teeth. One paste contained fluoride, while the other contained CSP combined with fluoride. The products were applied twice a day for 2 min for 10 days. The tooth surface was analyzed using the Vickers nanohardness test. The study's results show that the CSP-treated samples have a broad and regular material deposit, while the fluoride polishing paste shows an irregular deposit. These findings are consistent with the study's results.

In a related study, Hsu *et al.*[6] elucidate the mechanism of action of CSP. Upon contact with saliva, CSP dissociates, releasing calcium, phosphorus, and sodium ions into the oral cavity. Calcium and phosphorus ions then infiltrate the demineralization zone of the enamel, forming a calcium-phosphorus layer that subsequently crystallizes. Sodium binds with hydrogen, raising intraoral pH and inhibiting bacterial growth, demonstrating a parallel antibacterial effect.

In the case of samples from Group 4, treated with turmeric, statistically significant remineralization of demineralized enamel was observed compared to the positive group (Enamelast) and the control group (distilled water). Sari *et al.*[19] explored the remineralizing potential of turmeric combined with nanohydroxyapatite particles, revealing positive results regarding sample remineralization. Similarly, Zaleh *et al.*[20] demonstrated the remineralizing potential of turmeric on bovine teeth when combined with fluoride and propolis.

Notably, our study focused on the isolated effect of turmeric, suspended in distilled water, without association with any substance that would stimulate remineralization. While this aspect strengthens our study, the limitation lies in our inability, at this stage, to explain the molecular mechanisms involved. Further studies are warranted to comprehensively investigate enamel structure through additional and complementary tests.

Samples from group 5, treated with ginger, exhibited no remineralizing effect. Like turmeric, ginger was used in isolation, suspended in distilled water, without remineralizing substances.

In contrast, Kade *et al.*[18] conducted an *in vitro* study. They compared the effectiveness of a paste made of a ginger–honey mixture, commonly used in Indian dentistry to address gum problems, with that of fluoridated toothpaste. The products were applied to extracted permanent teeth, and the enamel samples were analyzed using the Vickers test. Remarkably, the study observed remineralization after 21 days.

In a separate study conducted by Celik *et al.*,[21] a homogeneous mixture of ginger and honey (8 mg/ml) was also used. In their experimental setup, enamel samples underwent a 7-day pH cycle involving immersion for 6 h in a demineralization solution and 18 h in a remineralization solution, with the studied products applied for 1 min daily. The analyses were conducted using a scanning electron microscope, which revealed significant remineralization in contrast to the findings in our research. This discrepancy might stem from variations in the timing of our study or the use of isolated ginger in our case.

Notably, in the aforementioned studies, ginger was combined with honey, and this combination was reported to exhibit a synergistic effect.[18,21] However, it is essential to acknowledge that honey is associated with promoting "baby bottle tooth decay" in newborns.[22] Hence, further exploring this combination in subsequent studies would be intriguing.

The inherent therapeutic properties of ginger and turmeric, coupled with their ability to contribute to enamel remineralization, position them as valuable assets in the pursuit of comprehensive oral care.

As the trend toward natural and herbal alternatives continues to gain momentum, integrating ginger and turmeric into oral health practices presents a compelling avenue for practitioners and patients. Embracing the wisdom of traditional medicine and harnessing the power of these natural wonders may pave the way for a holistic approach to oral care that addresses immediate concerns and promotes long-term dental well-being.

CONCLUSION

While fluoride has undeniably revolutionized oral preventive care, exploring alternative products in recent scientific literature signals a shift in focus toward safer and potentially more diverse options. As researchers delve into the multifaceted realm of natural substances and innovative compounds, the future of oral health may witness a broader spectrum of preventive products, each offering unique advantages without compromising safety. The ongoing pursuit of alternative remineralizing agents underscores the dynamic nature of scientific inquiry, pushing the boundaries of oral care beyond the confines of traditional fluoride-based approaches.

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Conflicts of interest
The authors of this manuscript declare that they have no conflicts of interest, real or perceived, financial or nonfinancial in this article.

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