Nanosilver Fluoride on Remineralization of Artificial Enamel Caries in Primary Teeth: An *In Vitro* Study

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Abstract

Dental caries is a prevalent chronic disease affecting children. An alternative remineralizing formulation has been developed as a new anti-caries agent. This study aimed to investigate the remineralization effects of self-prepared nanosilver fluoride (NSF) on artificial enamel caries in primary teeth. Early caries-like lesions were created on the specimens obtained from sound primary incisors. Then, the specimens were assigned to two groups: the treatment group (self-prepared NSF) and the control group (no treatment). The treatment agent was applied, following the pH cycling model for 7 days. The surface mineral density of each specimen was measured before and after treatment using micro-CT to assess changes and remineralization percentage. The data were analyzed using a paired *t*-test and an independent *t*-test.

The results revealed no significant difference in baseline mineral density between groups (p=0.206). After treatment and pH-cycling, the mineral density was significantly decreased in the control group (p<0.001). Conversely, the post-treatment mineral density significantly increased in the test group (p<0.001). The mean remineralization percentages for the test and control groups were 9.43 ± 2.18 and -18.25 ± 4.01, respectively. In comparing the groups, the test group showed a significantly higher remineralization percentage than the control group (p<0.001). In conclusion, NSF demonstrated an effect on the remineralization of artificial enamel caries in primary teeth. Nanosilver fluoride could be a promising alternative to promote the remineralization of early enamel caries in children. Moreover, additional studies are suggested to evaluate enamel remineralization using a microbial model and *in vivo* conditions.

Keywords: *Nanosilver Fluoride, Remineralization, Artificial Caries, Primary Teeth*

1. Introduction

Dental caries stands as a prevalent chronic disease affecting children globally (Kazeminia et al., 2020). It can significantly influence the oral health-related quality of life for both children and their parents (Martins-Júnior et al., 2013). In current caries management, the focus is on a minimally invasive strategy to prevent or delay caries progression (Wong, Subar, & Young, 2017). Fluoride is commonly employed to prevent and arrest caries by inhibiting demineralization and supporting remineralization (Amaechi, & van Loveren, 2013; Paiva et al., 2017). According to the recommendations of the American Academy of Pediatric Dentistry, the application of 5% sodium fluoride (NaF) is suggested for the effective reduction of enamel caries (American Academy of Pediatric Dentistry, 2023). It is generally applied as the primary professional fluoride therapy for preschool children because of its safety and ease of application by healthcare providers (Marinho et al., 2013).

Due to its notable antibacterial properties, silver was integrated into medical applications as an alternative metal ion agent, leading to the development of silver diamine fluoride (SDF) as one of the topical fluoride chemotherapeutic agents (Peng et al., 2012). The evidence based practice supported using 38% SDF for the purpose of arresting cavitated carious lesions in primary teeth (Crystal, Marghalani, & Ureles, 2017). However, a major drawback of SDF application is the black staining caused by the oxidation of silver ions on treated carious lesions, impacting the aesthetic aspect (Chu, Lo, & Lin, 2002; Mei et al., 2013).

With the advancement of nanoparticles, silver nanoparticles (AgNPs) have been introduced. The minimized particle size contributes to a remarkable antibacterial effect due to the increased surface area to volume ratio (Burgess, & Vaghela, 2018; Yin et al., 2019). Employing the combined actions of AgNPs and fluoride, nanosilver fluoride (NSF) has been developed as an innovative anti-caries agent. An *in vitro* study revealed that NSF's antimicrobial effectiveness against *Streptococcus mutans* (*S. mutans*) was comparable to SDF. Additionally, NSF showed lower cytotoxicity levels and did not result in staining on treated teeth (Targino et al., 2014). However, the availability of NSF was limited, and it was developed as an experimental formulation. By overcoming the limitation of SDF, we are also in the process of formulating our self-prepared NSF as a caries-arresting agent without causing tooth discoloration. Regarding remineralizing ability, the mechanism of NSF remains unclear.

2. Objectives

To assess the remineralization effect of self-prepared nanosilver fluoride on artificial enamel caries lesions in primary teeth

3. Materials and Methods

Nanosilver fluoride in this study was prepared by combining a solution of silver nanoparticles (~240 ⌠g/mL) with sodium fluoride (22,600 ppm of fluoride), carboxymethyl cellulose, and ethanol. The aqueous solution of silver nanoparticles was synthesized at 300 ⌠g/mL, based on the minimum eradication concentration from our previous study (Asanahsak, Rirattanapong, & Ruangsawasdi, 2023). It was kept at -80°C until used. The synthesis was carried out by chemical reduction in a laboratory at the Pharmacology Department, Faculty of Dentistry, Mahidol University, Thailand.

This *in vitro* investigation was approved by the Ethical Institutional Review Board at Faculty of Dentistry, Mahidol University, Thailand. The minimal sample size was calculated based on pilot study using G*power 3.1. A total sample of 20 specimens was required based on a 5% alpha error. Twenty sound primary incisors without a carious lesions, crack lines, fluorosis, or any enamel defect were obtained and stored a normal saline solution for no longer than six months.

All teeth were cleaned from blood and debris and then the roots were cut off 1 mm below a cementoenamel junction. The specimens were coated with two layers of nail varnish (Revlon nail enamel™); expect ~~for~~ a square-shaped space (2x2mm^2) in the middle third of the labial surface. Subsequently, utility wax and silicone kinetic mount positioning were prepared for micro-CT measurement.

The artificial enamel caries were induced by immersing all specimens in demineralizing solution 1 (D1 solution) and incubating at 37°C for 4 days to achieve a depth of 90-110 ⌠m of carious lesions (Rirattanapong et al., 2017). The D1 solution was renewed daily. After that, all specimens were cleaned in deionized water using an ultrasonic cleaner (Vibraclean 30, MDT Co., USA) for 1 minute. Following the caries formation and cleaning, they were repositioned on prepared mounts and scanned by micro-CT, evaluating the baseline or pre-treatment mineral density.

After measuring baseline mineral density, all specimens were randomly assigned to two groups of 10 teeth each: NSF group (self-prepared nanosilver fluoride) and the control group (no treatment). In the NSF group, 5 ⌠L of the agent was applied to the specimen surfaces using a micro-pipette, left for 3 minutes, and then ultrasonically removed in deionized water for 1 minute.

Following the treatment, the pH cycling process in Figure 1 was employed to imitate pH changes in the oral environment. Specimens were immersed in demineralizing solution 2 (D2 solution) and remineralizing solution (R solution) in cycles for 7 days (Rirattanapong et al., 2017). Each cycle comprised 3 hours of demineralization (D2 solution) twice daily and 2 hours of remineralization (R solution) daily in between. Subsequently, the specimens were immersed in R solution overnight at 37 °C. The specimens were ultrasonically cleaned in deionized water during each immersion, and the solutions were renewed daily.

Table 1 Formula of solutions

Solution	Formula
Demineralizing solution 1 (D1 solution)	2.2mM $CaCl_2$, 2.2mM NaH_2PO_4, 0.05 M acetic acid, deionized water, pH was adjusted to 4.4 with 1M KOH
Demineralizing solution 2 (D2 solution)	2.2mM $CaCl_2$, 2.2mM NaH_2PO_4, 0.05 M acetic acid, deionized water, pH was adjusted to 4.7 with 1M KOH
Remineralizing solution (R solution)	1.5 mM $CaCl_2$, 0.9 mM NaH_2PO_4, 0.15 M KCl, deionized water, pH was adjusted to 7 with 1M KOH

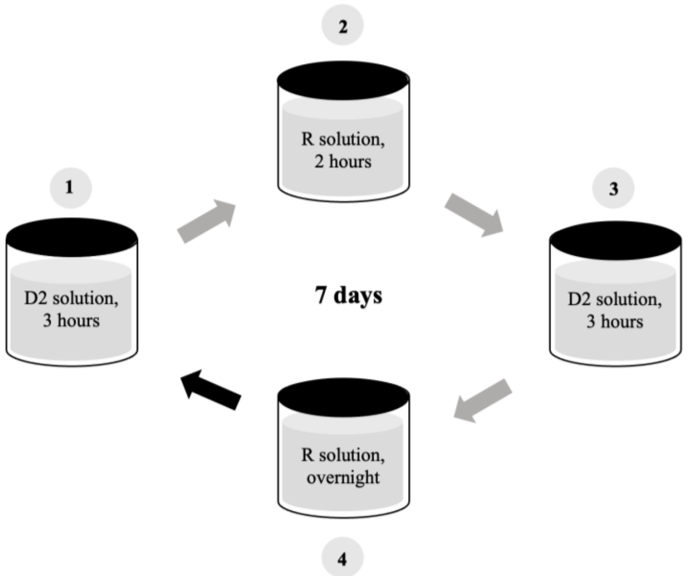

Figure 1 Each cycle of pH cycling process

After the pH cycling, the mineral density (MD) was measured again using micro-CT as the post-treatment mineral density. The mean MD of each group was evaluated, and the mineral density gain was calculated by subtracting pre-treatment MD. From post-treatment MD: (MD gain = post-treatment MD - pre-treatment MD). The remineralization percentage was indicated as the proportion of mineral density gain to the mineral density of the original lesion. [%Remineralization = (MD gain/ pre-treatment MD) x 100] (Punyanirun et al., 2018).

The data were evaluated using the Shapiro-Wilk test for normality. ($p>0.05$) The pair *t*-test was used to compare the mineral density between pre- and post-treatment values within the group. The remineralization percentage between the NSF and control groups was compared by an independent *t*-test. All analyzes were performed using IBM SPSS Statistic Version Grad Pack 28.0 (SPSS Inc., IBM Corporation, New York, USA), with a significant level set at 0.05.

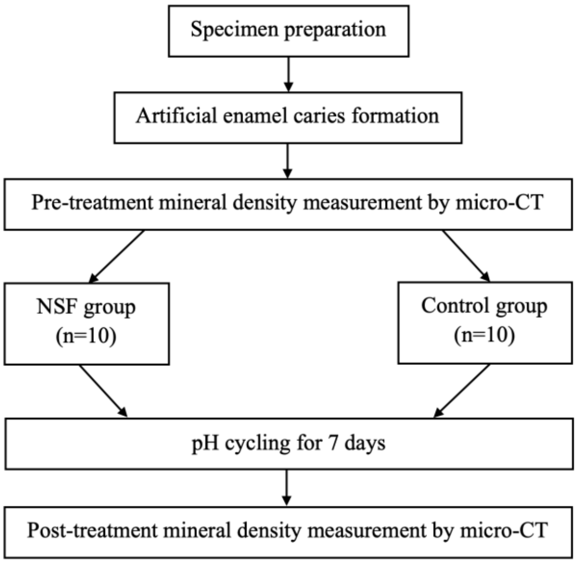

Figure 2 Schematic of the experimental procedure

4. Results and Discussion

4.1 Results

Before treatment, the assessment of baseline mineral density at the surface was performed using micro-CT. The results indicated no statistical differences in mineral density between samples at pre-treatment (p=0.206); see Table 2.

Table 2 Mean mineral density at the surface of the groups at pre- and post-treatment

Groups	n	Mean mineral density (g/cm^3) ± SD		Within-group *p*-value
		Pre-treatment	Post-treatment	
NSF	10	0.983 ± 0.147[a]	1.077 ± 0.165[b]	<0.001*
Control (no treatment)	10	1.066 ± 0.134[a]	0.870 ± 0.102[c]	<0.001*

The different superscript letters indicate a significant difference between groups in each column (p<0.05)
* Significant difference within each group (p<0.001)

Following treatment and pH cycling, there was a significant difference in mineral density between baseline and post-treatment mineral density in both the control and NSF groups. The control group with no treatment showed a significant reduction in post-treatment mineral density (p<0.001). Conversely, the post-treatment mineral density significantly increased in the test group (p<0.001), see Table 2.

Table 3 Mean remineralization percentage (%Remineralization) at the surface between NSF group and control group

Groups	n	Mean %Remineralization ± SD	Between-group *p*-value
NSF	10	9.433 ± 2.183	<0.001*
Control (no treatment)	10	-18.250 ± 4.016	

* Significant difference between 2 groups (p<0.001)

In addition, the effectiveness of remineralization was investigated by calculating the remineralization percentage (%Remineralization). The comparison between the control and test groups revealed a significantly higher remineralization percentage in the NSF group than the control group (mean± SD = 9.433 ± 2.183 and -18.250 ± 4.016, p<0.001, respectively), see Table 3.

4.2 Discussion

Minimally invasive dentistry is recognized as the contemporary principle in dental practice, with a focus on arresting active caries through non-operative interventions and preserving tooth structure as much as possible (Frencken et al., 2012). Professionally applied fluoride has been employed with the extended purpose of remineralizing early enamel caries and arresting the progression of dentinal caries. The novel approach involving NSF has been developed as a caries - arresting agent that possesses both antibacterial and remineralizing properties. Our new formulation of self-prepared NSF was investigated in this study for its remineralization potential on enamel caries-like ~~in~~ primary teeth. The findings showed that our self-prepared NSF influenced the remineralization of artificial enamel caries in primary teeth.

Considering the evaluation of mineral changes in *in vitro* studies, TMR is considered as the conventional gold standard method. However, this technique is destructive and unsuitable for the longitudinal assessment of mineral changes (Lo, Zhi, & Itthagarun, 2010). Thus, micro-CT was employed to evaluate remineralization efficacy in this study due to its advantages, including specimen preservation and the ability to analyze internal structures. Accordingly, comparing mineral density between pre- and post- treatment can be determined without a destruction procedure by using micro-CT (Farooq et al., 2021; Nakata et al., 2012).

After creating artificial caries, the baseline (pre-treatment) mineral density among specimens showed no significant differences. This implies that the level of demineralization was comparable in both groups. Consequently, the standardized enamel caries lesions were achieved. Following the treatment and pH cycling, the control group with no treatment demonstrated a significant decrease in post-treatment mineral density. Therefore, the pH cycling process was suggested to cause ~~the~~ demineralization. In contrast, the test group revealed a significant increase in post-treatment mineral density. The comparison of remineralization effects was assessed using the mean percentage of remineralization. The difference in remineralization percentage between the NSF and control groups was observed, indicating a higher remineralization in the NSF group. These findings were in accordance with previous *in vitro* studies focusing on the remineralizing potential of various NSF formulations (Akyildiz, & Sönmez, 2019; Favaro et al., 2022; Nozari et al., 2017). The proposed mechanism of NSF on enamel remineralization was similar to that of SDF, involving silver precipitation on the tooth surface (Favaro et al., 2022; Yu et al., 2018). Previous *in vitro* studies on the remineralization effect also found that silver ions increased the mineral density of demineralized enamel, but the synergistic effects of fluoride and silver ions were relatively low (Alcorn et al., 2022; Aldhaian et al., 2021; Zhi, Lo, & Kwok, 2013).

Most previous *in vitro* studies evaluating the NSF's enamel remineralization impact used surface microhardness measurements in comparison with other fluoride agents. Fluoride varnish, or 5% NaF, was regarded as a commercially topical fluoride with proven safety and effectiveness in the remineralization of enamel caries (American Academy of Pediatric Dentistry, 2023). A previous *in vitro* study by Nozari et al. investigated the NSF formulation with 22,600 ppm of fluoride, in which the fluoride concentration was similar to our formulation. The study demonstrated that the surface remineralizing potential of NSF was greater than that of fluoride varnish for treating enamel caries in primary incisors (Nozari et al., 2017). Our preliminary findings represented the positive impact of our NSF formulation on enamel remineralization compared to the control group. Considering the amount of fluoride concentration, the remineralization effect of our NSF formulation might be comparable to or greater than that of 5% NaF. Despite the effectiveness of 38% SDF in arresting dentinal caries, there were a few comparative *in vitro* studies investigating ~~on~~ its impact on enamel remineralization compared to NSF. Favaro *et al.* reported that enamel remineralization treated with the combination of AgNPs and 9,000 ppm of fluoride was comparable to that obtained with 30% SDF (Favaro et al., 2022). On the contrary, the study by Akyildiz indicated that the post-treatment microhardness values of NSF containing 10,147 ppm of fluoride in third molars were lower than those of 5% NaF and 38% SDF (Akyildiz, & Sönmez, 2019). This difference could relate to variations in NSF formulation and study design, including fluoride concentration, degree of artificial caries formation, type of enamel, and treatment contact time. The experimental NSF formulations in previous studies included different concentrations of both silver nanoparticles and fluoride. Considering the remineralizing potential, fluoride concentration is one of the crucial factors. Higher fluoride concentrations may result in the formation of a calcium fluoride layer on the enamel surface, serving as a fluoride reservoir and consequently enhancing the remineralization potential (Hellwig et al., 2010). Regarding the artificial caries formation, variations in demineralization protocols among studies could also affect the degree of the caries lesion, resulting in a greater magnitude of the remineralization effect (Aldhaian et al., 2021). Furthermore, the type of enamel specimens with different compositions and structures contributed to the caries-like formation, in which the caries progression in primary teeth is faster than in permanent teeth (Wang et al., 2006). In addition, the NSF and SDF had a short treatment contact time of only two to three minutes, while NaF was left on the tooth surface for 24 hours, following its manufacturer's instructions.

The limitations of this study should be considered. The artificial caries model in this study was to create initial caries, so the results cannot be inferred from the effects on dentinal caries. Furthermore, the pH cycling model was applied to mimic complex clinical conditions but did not account for oral function, biofilm, or the dynamics of human saliva. Further investigations are suggested to examine enamel remineralization involving a microbial model and *in vivo* settings. Additionally, comparative studies are required to assess our NSF formulation's efficacy compared to other anticaries, such as 5% NaF and 38% SDF, and to evaluate its antimicrobial effect as well as cytotoxicity.

5. Conclusion

Self-prepared nanosilver fluoride had an effect on the remineralization of artificial enamel caries in primary teeth. Based on the results, NSF could be a potential alternative for remineralizing early enamel caries in children. Further investigations are suggested to examine enamel remineralization involving a microbial model and accounting for oral factors.

6. References

Akyildiz, M., & Sönmez, I. S. (2019). Comparison of remineralising potential of nano silver fluoride, silver diamine fluoride and sodium fluoride varnish on artificial caries: an in vitro study. *Oral Health & Preventive Dentistry*, *17*(5), 469-477. https://doi.org/10.3290/j.ohpd.a42739

Alcorn, A., Al Dehailan, L., Cook, N. B., Tang, Q., & Lippert, F. (2022). Longitudinal in vitro effects of silver diamine fluoride on early enamel caries lesions. *Operative Dentistry*, *47*(3), 309-319. https://doi.org/10.2341/20-237-l

Aldhaian, B. A., Balhaddad, A. A., Alfaifi, A. A., Levon, J. A., Eckert, G. J., Hara, A. T., & Lippert, F. (2021). In vitro demineralization prevention by fluoride and silver nanoparticles when applied to sound enamel and enamel caries-like lesions of varying severities. *Journal of Dentistry*, *104*, 103536. https://doi.org/10.1016/j.jdent.2020.103536

Amaechi, B. T., & van Loveren, C. (2013). Fluorides and non-fluoride remineralization systems. *Monographs in Oral Science*, *23*, 15-26. https://doi.org/10.1159/000350458

American Academy of Pediatric Dentistry. (2023). Fluoride therapy. In *The Reference Manual of Pediatric Dentistry* (pp. 352-358). American Academy of Pediatric Dentistry.

Asanahsak, S., Rirattanapong, P., & Ruangsawasdi, N. (2023). Antibiofilm activities of the self-prepared silver solution against *Streptococcus Mutans* biofilm: *In Vitro*. Proceeding in RSU International Research Conference 2023, Pathum Thani, Thailand.

Burgess, J. O., & Vaghela, P. M. (2018). Silver diamine fluoride: a successful anticarious solution with limits. *Advances in Dental Research*, *29*(1), 131-134. https://doi.org/10.1177/0022034517740123

Chu, C. H., Lo, E. C. M., & Lin, H. C. (2002). Effectiveness of silver diamine fluoride and sodium fluoride varnish in arresting dentin caries in Chinese pre-school children. *Journal of Dental Research*, *81*(11), 767-770. https://doi.org/10.1177/0810767

Crystal, Y. O., Marghalani, A. A., & Ureles, S. D., et al. (2017). Use of silver diamine fluoride for dental caries management in children and adolescents, including those with special health care needs. *Pediatric Dentistry*, *39*(5), 135-145.

Farooq, I., Ali, S., Farooqi, F. A., AlHumaid, J., Binhasan, M., Shabib, S., Vohra, F., & Abduljabbar, T. (2021). Enamel remineralization competence of a novel fluoride-incorporated bioactive glass toothpaste-a surface micro-hardness, profilometric, and micro-computed tomographic analysis. *Tomography*, *7*(4), 752-766. https://doi.org/10.3390/tomography7040063

Favaro, J. C., Detomini, T. R., Maia, L. P., Poli, R. C., Guiraldo, R. D., Lopes, M. B., & Berger, S. B. (2022). Anticaries agent based on silver nanoparticles and fluoride: characterization and biological and remineralizing effects-an in vitro study. *International Journal of Dentistry*, *2022*, 9483589. https://doi.org/10.1155/2022/9483589

Frencken, J. E., Peters, M. C., Manton, D. J., Leal, S. C., Gordan, V. V., & Eden, E. (2012). Minimal intervention dentistry for managing dental caries - a review: report of a FDI task group. *International Dental Journal*, *62*(5), 223-243. https://doi.org/10.1111/idj.12007

Hellwig, E., Polydorou, O., Lussi, A., Kielbassa, A. M., & Altenburger, M. J. (2010). The influence of saliva on the dissolution of calcium fluoride after application of different fluoride gels in vitro. *Quintessence International*, *41*(9), 773-777.

Kazeminia, M., Abdi, A., Shohaimi, S., Jalali, R., Vaisi-Raygani, A., Salari, N., & Mohammadi, M. (2020). Dental caries in primary and permanent teeth in children's worldwide, 1995 to 2019: a systematic review and meta-analysis. *Head & Face Medicine*, *16*(1), 22. https://doi.org/10.1186/s13005-020-00237-z

Lo, E. C. M., Zhi, Q. H., & Itthagarun, A. (2010). Comparing two quantitative methods for studying remineralization of artificial caries. *Journal of Dentistry*, *38*(4), 352-359. https://doi.org/10.1016/j.jdent.2010.01.001

Marinho, V. C., Worthington, H. V., Walsh, T., & Clarkson, J. E. (2013). Fluoride varnishes for preventing dental caries in children and adolescents. *Cochrane Database of Systematic Reviews*, (7), Cd002279. https://doi.org/10.1002/14651858.CD002279.pub2

Martins-Júnior, P. A., Vieira-Andrade, R. G., Corrêa-Faria, P., Oliveira-Ferreira, F., Marques, L. S., & Ramos-Jorge, M. L. (2013). Impact of early childhood caries on the oral health-related quality of life of preschool children and their parents. *Caries Research*, *47*(3), 211-218. https://doi.org/10.1159/000345534

Mei, M. L., Ito, L., Cao, Y., Li, Q. L., Lo, E. C., & Chu, C. H. (2013). Inhibitory effect of silver diamine fluoride on dentine demineralisation and collagen degradation. *Journal of Dentistry*, *41*(9), 809-817. https://doi.org/10.1016/j.jdent.2013.06.009

Nakata, K., Nikaido, T., Nakashima, S., Nango, N., & Tagami, J. (2012). An approach to normalizing micro-CT depth profiles of mineral density for monitoring enamel remineralization progress. *Dental Materials Journal*, *31*(4), 533-540. https://doi.org/10.4012/dmj.2011-228

Nozari, A., Ajami, S., Rafiei, A., & Niazi, E. (2017). Impact of nano hydroxyapatite, nano silver fluoride and sodium fluoride varnish on primary teeth enamel remineralization: an in vitro study. *Journal of Clinical and Diagnostic Research*, *11*(9), Zc97-zc100. https://doi.org/10.7860/jcdr/2017/30108.10694

Paiva, M. F., Delbem, A. C. B., Danelon, M., Nagata, M. E., Moraes, F. R. N., Coclete, G. E. G., Cunha, R. F., Buzalaf, M. A. R., & Pessan, J. P. (2017). Fluoride concentration and amount of dentifrice influence enamel demineralization in situ. *Journal of Dentistry*, *66*, 18-22. https://doi.org/10.1016/j.jdent.2017.09.004

Peng, J. J., Botelho, M. G., & Matinlinna, J. P. (2012). Silver compounds used in dentistry for caries management: a review. *Journal of Dentistry*, *40*(7), 531-541. https://doi.org/10.1016/j.jdent.2012.03.009

Punyanirun, K., Yospiboonwong, T., Kunapinun, T., Thanyasrisung, P., & Trairatvorakul, C. (2018). Silver diamine fluoride remineralized artificial incipient caries in permanent teeth after bacterial pH-cycling in-vitro. *Journal of Dentistry*, *69*, 55-59. https://doi.org/10.1016/j.jdent.2017.09.005

Rirattanapong, P., Vongsavan, K., Saengsirinavin, C., & Waidee, S. (2017). Enhancing remineralization of primary enamel lesions with fluoride dentifrice containing tricalcium phosphate. *The Southeast Asian Journal of Tropical Medicine and Public Health*, *48*(2), 494-500.

Targino, A. G., Flores, M. A., Santos, V. E., Jr., de Godoy Bené Bezerra, F., de Luna Freire, H., Galembeck, A., & Rosenblatt, A. (2014). An innovative approach to treating dental decay in children. A new anti-caries agent. *Journal of Materials Science: Materials in Medicine*, *25*(8), 2041-2047. https://doi.org/10.1007/s10856-014-5221-5

Wang, L. J., Tang, R., Bonstein, T., Bush, P., & Nancollas, G. H. (2006). Enamel demineralization in primary and permanent teeth. *Journal of Dental Research*, *85*(4), 359-363. https://doi.org/10.1177/154405910608500415

Wong, A., Subar, P. E., & Young, D. A. (2017). Dental caries: an update on dental trends and therapy. *Advances in Pediatrics*, *64*(1), 307-330. https://doi.org/10.1016/j.yapd.2017.03.011

Yin, I. X., Yu, O. Y., Zhao, I. S., Mei, M. L., Li, Q.-L., Tang, J., & Chu, C.-H. (2019). Developing biocompatible silver nanoparticles using epigallocatechin gallate for dental use. *Archives of Oral Biology*, *102*, 106-112. https://doi.org/https://doi.org/10.1016/j.archoralbio.2019.03.022

Yu, O. Y., Mei, M. L., Zhao, I. S., Li, Q. L., Lo, E. C. M., & Chu, C. H. (2018). Remineralisation of enamel with silver diamine fluoride and sodium fluoride. *Dental Materials*, *34*(12), e344-e352. https://doi.org/10.1016/j.dental.2018.10.007

Zhi, Q. H., Lo, E. C. M., & Kwok, A. (2013). An in vitro study of silver and fluoride ions on remineralization of demineralized enamel and dentine. *Australian Dental Journal*, *58*, 50-56. https://doi.org/10.1111/adj.12033