

## The effect of a novel toothpaste in children with white spot lesions

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### Abstract

**Objective:** To investigate the effect of a novel mineral containing toothpaste in comparison to a fluoride toothpaste in children with white spot lesions.

**Method:** The clinical study was conducted from 2016 to 2018 at Marmara University Department of Pediatric Dentistry Clinic after approval from the ethics review committee of Yeditepe University, Istanbul, Turkey and comprised children of either gender aged 4-5 years having white spot lesions. They were randomly allocated into two groups. The FT (Fluoridated Toothpaste) group was given a 500ppm fluoridated toothpaste, while the Mineral Containing Toothpaste (MCT) group was given toothpaste containing calcium glycerophosphate, magnesium chloride, and 12% xylitol. The white spot lesions were examined using Laser Fluorescence (LF) at baseline and after a month of usage. The two readings were compared. Stimulated saliva was collected for measuring the salivary potential of hydrogen, buffering capacity, and streptococcus mutans. Data was analysed using SPSS 19.

**Results:** Of the 26 children, 10(38%) were girls and 16(62%) were boys. The overall mean age was 4.77±0.54 years. There were 13(50%) subjects in each of the two groups. Of the 381 measurements done, 198(52%) were in the MCT group and 183(48%) in the FT group. LF scores decreased in both the groups ( $p=0.001$ ). The remineralising potential was not significantly different ( $p=0.866$ ), while salivary buffering capacity and potential of hydrogen increased in both the groups but the change was not significant ( $p>0.05$ ). The number of children positive for streptococcus mutans decreased in both the groups ( $p>0.05$ ).

**Conclusion:** The toothpaste containing calcium glycerophosphate, magnesium chloride and 12% xylitol had the remineralization properties needed for the prevention of white spot lesions in children.

**Keywords:** Remineralization, Calcium glycerophosphate, Fluoride, Saliva buffer, Saliva pH. (JPMA 71: 2170; 2021)

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### Introduction

In general, enamel demineralization and remineralization develop in a balance throughout the day, and disruption of this balance triggers the development of dental caries.<sup>1</sup> The accumulation of acidogenic biofilms on tooth surfaces causes the dissolution of the enamel, a process known as demineralization, which, if maintained for prolonged periods, may lead to the development of dental caries.<sup>2</sup> *Streptococcus (S.)* mutans have properties, such as acidogenicity, resistance to acidic environments, and the capacity to synthesize extracellular polysaccharides, that contribute to the initiation of bacterial colonization on the surface of enamel and the development of initial dental caries.<sup>3</sup> Saliva is a protective liquid for oral tissues. It reduces the development of caries via saliva flow rate, antimicrobial capacity, and buffering feature, and its washing effect in removing foods from the mouth provides prevention against tooth decay.<sup>4</sup>

Evidence-based literature reports that having calcium

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cation ( $Ca^{++}$ ) and phosphate ( $PO_4^{3-}$ ) ions in a bioavailable form and containing different proteins in saliva has multiple effects in providing hard tissue integrity.<sup>5</sup> This supersaturation at the physiological potential of hydrogen (pH) keeps these ions bioavailable to diffuse demineralization areas of the hard tissue.<sup>6</sup>

Fluoridated toothpaste reduces the prevalence and incidence of dental caries which has been extensively documented worldwide.<sup>7</sup>

Although fluoride prevents caries development and remineralization of initial caries lesions, dental caries is a condition seen in individuals of all ages.<sup>8</sup>

There are limitations to the use of fluoride alone in the prevention of dental caries.<sup>8</sup> These limitations may be associated with the fact that fluoride becomes less effective below a pH of about 4.5,<sup>9</sup> fluoride still needs  $Ca^{++}$  and  $PO_4^{3-}$  ions in a bioavailable form in saliva and other sources to be effective.

Recently, organic or inorganic polyphosphates have been included into toothpaste to improve their remineralization properties.<sup>10</sup> Among these compounds, calcium glycerophosphate (CaGP), that is used medically as a source

of calcium and phosphate, has represented anticariogenic features.<sup>11,12</sup>

CaGP is an organic phosphate that is adsorbed on the surface of the tooth,<sup>13</sup> essential to the release of calcium (Ca) ions, which activates the remineralization process. The results of demineralization studies confirm that it provides a powerful protective effect on the enamel surface. This effect had no relationship with the action of fluoride. Thus, the use of fluoride as a prophylactic agent in toothpastes or gels does not prohibit the addition of CaGP.<sup>14</sup>

The addition of CaGP to sodium monofluorophosphate (MFP) improved the protection of enamel against acid attacks. It is attributed to the increased uptake of fluoride.<sup>15</sup> The cariostatic properties of CaGP have been demonstrated in various in vivo and in vitro studies and several mechanisms have been proposed, including plaque-pH buffering, increased levels of calcium and phosphate in plaque and direct interaction with dental mineral.<sup>14,16-18</sup>

However, the formulation should be evaluated regarding the effect on caries' prevention.

The current study was planned to investigate the effect of a novel mineral-containing toothpaste in comparison to a fluoride toothpaste in children with white spot lesions (WSLs).

## Material and Method

This study was reviewed and approved by The Human Research Ethics Committee of Yeditepe University, School of Medicine (protocol number of 392) and performed from 2016 to 2018 at Marmara University Department of Pediatric Dentistry Clinic.

The minimum number of subjects required for the expectation of a lesion density difference of  $11 \pm 7.03$  between the groups to be found statistically significant<sup>19</sup> was determined as 9 in each group ( $\alpha=0.05$ ,  $-\beta=0.80$ ). It is recommended to increase this number by 10% due to possible dropouts. Therefore 13 patients were included in both groups. The analysis is done in Gpower3.1 version.

☆ The sample comprised healthy children without any systemic disease, with primary dentition, having one or more WSLs, having no previous preventive or restorative treatment on the affected teeth, and residing in the same fluoridated area (between 0.10-0.20mgF/L). Those excluded were children with systemic medical conditions, children with a history of prolonged use of antibiotics or medication, which might affect the quality of saliva or may have caused developmental defects in dentition, those with

previous use of fluoride compounds in the preceding two months or previous restorations or caries on the affected teeth, uncooperative, and periodontal disease or other oral diseases. All consent from parents or guardians, medical and dental history of each subject was taken along with oral examination that included visual inspection with smooth-surfaced standard mouth mirror and tactile inspection with standard dental probe.

The subjects were randomised into two groups. Each eligible child was allocated a number at the time of recruitment. It generated a random allocation sequence using simple computer-generated random allocation application. The researcher was blinded to the identity of the children during the randomisation process.

The FT group was given a 500ppm fluoridated toothpaste (100mg tube of Colgate® Kids, Colgate-Palmolive Central Asia & Russia, Moscow, Russia), while the MCT group was given toothpaste containing calcium glycerophosphate (CaGP), magnesium chloride (MgCl<sub>2</sub>) and 12% xylitol (45mg tube of R.O.C.S® Kids Toothpaste, DRC Group, Moscow, Russia).

The parents were provided with oral health related instructions and dietary advice.

The two products were weighed before being provided to the parents. They were advised to use the toothpaste samples they were given to brush their children's teeth for one minute two times a day for 4 weeks.

The parents were requested to bring the tubes of the product with them on their follow-up appointment. The tubes were then re-weighed to assess the amount used in the 4-week period, and suggestions regarding compliance were given if needed.

The clinical evaluation was examined by two independent paediatric dentists allowing a blinded study for both participants and evaluators. One observer made the first measurements and distributed toothpastes among the participants of the two research groups, while the other observer, unaware of the groups, took the second measurements in the control session. Following evaluation and analysis, the coding was revealed.

Oral examination was performed under the standard dental unit light. The surfaces of teeth were cleaned and dried with air-water syringe. Visual examination was performed to diagnose the WSLs according to the International Caries Detection and Assessment system (ICDAS II; grades 0–3).<sup>20</sup>

The teeth were quantitatively examined by a portable laser

fluorescence (LF) system (DIAGNOdent pen, KaVo, Biberach, Germany). LF is based on the fluorescence emitted from various surfaces when they are irradiated by a laser beam with a wavelength of 655nm. Standard LF recordings were taken at this stage as per the manufacturer's instructions. The LF device was calibrated before every use on a ceramic mount provided by the manufacturer. The buccal surface of tooth, which was diagnosed WSLs, was cleaned and dried. The tip of the DIAGNOdent pen was placed to the smooth surface of the tooth. All measurements were repeated 3 times by the same examiner.

Baseline and 1-month follow-up readings on the pen for the status of WSLs were recorded for each tooth and tabulated numerically and the changes in the amount of the values were recorded. Depth of demineralization were compared with LF threshold for initial enamel lesion which was set between 7 and 20.<sup>21</sup>

Saliva samples were used to evaluate buffering capacity utilising the Saliva-Check Buffer™ test kit (GC Corporation, Tokyo; Japan). Saliva was stimulated by paraffin wax. Children were supposed to spit any pooled saliva into the collection cup. After this procedure, an enclosed potential of hydrogen (pH) strip was placed into the sample of collected saliva for 10 seconds. Colour change on the pH strip was checked while the paper was still moist. The pH reading was noted and results were recorded as 5.0-5.8 (high acidic); 6.0-6.6 (moderately acidic) and 6.8-7.8 (healthy saliva). For assessing the buffering capacity, 5-minute stimulated saliva was used and the test pad's colour changing was evaluated as green 4; green/blue 3; blue 2; Red/Blue 1 and Red 0 as per the manufacturer's instructions. The salivary samples were also checked for S. mutans count using a test kit (GC Corporation, Tokyo, Japan).

Stimulated saliva, obtained after the child was instructed to chew on a piece of paraffin wax supplied for 30s, was tested to measure S. mutans levels at baseline. Guidelines were followed according to the manufacturer's instructions. A positive result was obtained if a thin red line appeared in the T window. The sample collection and testing were repeated at the end of the 1-month experimental period to check the result of intervention.

Data was analysed using SPSS 19. Categorical variables were expressed as frequencies and percentages (%). Data normality was tested using Shapiro Wilk test. To compare baseline and post-intervention LF values, paired t-test was

used since data was found to be normally distributed. Categorical dependent variables were tested using the McNemar test. Level of significance was set at  $p < 0.05$ .

### Results

Of the 26 children, 10(38%) were girls and 16(62%) were boys. The overall mean age was  $4.77 \pm 0.54$  years. There were 13(50%) subjects in each of the two groups. Of the 127 WSLs, 66(52%) were in the FT group, while 61(48%) were in the MCT group. A total of 198(52%) measurements for FT group and 183(48%) measurements for MCT group were included from 127 primary incisors/ canines or molars.

LF scores decreased in both the groups ( $p = 0.001$ ). The remineralising potential was not significantly different ( $p = 0.866$ ) (Table 1).

Salivary buffering capacity and pH increased in both the groups, but the change was not significant in the FT group (Table 2).

The number of children positive for S. mutans decreased in both the groups, but the change was not statistically significant ( $p > 0.05$ ) (Table 3).

**Table-1:** Laser fluorescence values before and after using mineral containing toothpaste and fluoride toothpaste.

LF values	Fluoridated Toothpaste Group (n= 198) Mean±SE	Mineral Containing Toothpaste Group (n= 183) Mean±SE
baseline	15.16±1.00	20.71±1.50
one-month	12.09±0.79	17.00±1.27
p-value	0.001	0.001

Paired test was used ( $p < 0.05$ ); SE: Standard Error

**Table-2:** Saliva buffer and potential of hydrogen (pH) before and after using mineral containing toothpaste and fluoride toothpaste (n=13).

	Fluoridated Toothpaste Group			Mineral Containing Toothpaste Group		
	baseline	Mean±SE one-month	p-value	baseline	Mean±SE one-month	p-value
Saliva pH	6.94±0.1	7.11±0.15	0.934	7.08±0.10	7.22±0.12	0.222
Saliva buffer	7.85±0.83	8.00±0.68	0.856	7.08±0.61	9.46±0.62	0.003

Paired test was used ( $p < 0.05$ ); SE: Standard Error.

**Table-3:** The frequency of streptococcus (S.) Mutans in the two groups before and after interventions.

	Fluoridated Toothpaste Group (n=13) n (%)	Mineral Containing Toothpaste Group (n=13) n (%)
baseline	11 (84.62)	8 (61.54)
one-month	8 (61.54)	5 (38.46)
p-value	0.082	0.082

Salivary S. mutans level:  $> 5 \times 10^5$  CFU/m; Not significant difference ( $p > 0.05$ )

## Discussion

The current study is the first to investigate the efficacy of CaGP+xylitol on WSLs by using LF. Some studies have reported that LF method's sensitivity, reliability and efficacy in detecting caries are higher than the other diagnostic methods<sup>22,23</sup> Especially in the diagnosis and evaluation of initial enamel lesions, the use of DIAGNOdent™ has increased in recent years and many studies have been done on this.<sup>24-26</sup>

In this study, the higher LF scores recorded in early caries lesion indicated a lower mineral content at baseline. The decreased LF readings suggest increased mineral content post-intervention.

In vitro studies have shown the remineralising capacity of fluoride and other remineralising agents, including CaGP in human and bovine teeth. The polyphosphate takes attention in new approaches to improve the antimicrobial properties of biomaterials.<sup>27</sup>

Increasing of calcium and phosphate levels in dental plaque, direct interaction with dental minerals and thus plaque-pH buffering are the main anti-cariogenic properties of CaGP.<sup>23,28,29</sup> However, there are limitations to achieving effectiveness. Consequently, evaluating the effect of calcium-containing toothpastes is valuable research, especially in WSLs seen in very young children. A comprehensive literature review done recently showed very little information on published peer-reviewed papers on the efficacy of non-fluoride containing remineralising toothpastes.<sup>29</sup> An in-situ study<sup>30</sup> showed a toothpaste with a low fluoride concentration (500ppm, sodium fluoride [NAF] or sodium monofluorophosphate [SMFP]) combined with 0.25% CaGP, which has similar remineralization potential to 1100ppm fluoride toothpaste. The study suggested that the CaGP-containing toothpaste had anti-caries properties comparable to commercial toothpastes with fluoride concentration of 1100ppm, but with added benefit of providing a much lower risk of excessive fluoride intake by the young. It concluded that the developed toothpaste prevented caries as effectively as the fluoridated one (500ppm) and was safe for any age group.<sup>30</sup> In the current study, the CaGP-containing toothpaste was found to be effective in reducing the factors that lead to dental caries in WSL.

In fluoride toothpastes containing CaGP, there is a supersaturation of Ca and phosphorus (P) ions in the biofilm layer on enamel surface.<sup>30</sup> Tenuta LM et al. suggested that calcium monophosphide (CaP) was not effective in the inhibition of the enamel demineralization.<sup>31</sup>

CaGP is a source of calcium and phosphate, and has

demonstrated significant anti-cariogenic properties. An in vitro study showed that the addition of 0.25% of CaGP to low-fluoride toothpastes (500ppm; NaF) achieved the same anti-caries efficacy as 1100ppm fluoride toothpastes.<sup>32</sup>

Edgar WM et al. showed that CaGP interacted directly with the outer layers of the hydroxyapatite (HA) in a rat study.<sup>33</sup> Having 0.13% CaGP with fluoride >500ppm, fluoride might be effective for preventing demineralization.<sup>34</sup>

No specific mechanism, increasing the plaque-pH buffering capacity and elevation of plaque calcium and phosphate levels by CaGP, cause decreasing demineralization.<sup>28,35</sup>

The current study has some limitations, like a limited sample size, a short follow-up post-intervention, and the non-inclusion of groups containing only CaGP and only xylitol. In addition, it was not possible to know for sure that the patients were using the products correctly at home due to the in-vivo study. The oral cavity is a dynamic environment where many factors, such as saliva or diet, can contribute to progression or regression of WSLs.

Adverse effects should be measured and reported via in vitro and in vivo studies and long-term assessment should be done. Considering the effects of the novel toothpaste, future research could provide a realistic and meaningful estimate of the caries prevention effect.

## Conclusions

The toothpaste containing CaGP, MgCl<sub>2</sub> and xylitol, provided improvement with respect to WSLs.

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**Conflicts of interest:** None.

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