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IMPACT OF MEDICINAL PLANTS EXTRACTS ON MI VARNISH REMINERALIZING ABILITY ON PRIMARY TEETH: IN VITRO STUDY

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ABSTRACT

Aim: This study aimed to assess the effect of methanolic plant extracts on the remineralization ability of MI varnish on extracted primary teeth.

Methods: An in vitro study was conducted on the crowns of 45 extracted primary teeth. A methanolic extraction was done for both clove and cinnamon and the treatment solution was obtained by using dimethyl sulfoxide solvent. The Vickers microhardness assessment was used to assess the hardness in different intervals. The teeth underwent demineralization to develop caries-like lesions and were then treated with MI varnish. The teeth were randomly divided into three equal groups Group A: MI varnish only, Group B: MI varnish + clove and cinnamon methanolic extract + solvent, and Group C: MI varnish + solvent. In the pH cycling the treatment was repeated each day for 10 days. Each group had a different treatment.

Results: The intragroup comparison revealed that group A had the highest remineralization value (269.54±28.54), and group B had the lowest (263.82±15.73). There was a statistically significant difference between the MI varnish control group and the intervention group treated with methanolic plant extract (p=0.049).

Conclusion: MI varnish alone was effective in increasing the microhardness. Adding the treatment with Clove and cinnamon methanolic extract diminishes the MI varnish remineralization potential.

KEYWORDS: Prevention, early childhood caries, medicinal plants, MI varnish, microhardness.

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INTRODUCTION

Dental caries, a prevalent and multifactorial oral disease, remains a significant public health concern globally. The demineralization of tooth enamel is primarily due to acids produced by the fermentation of dietary sugars by oral bacteria[1,2]. Traditional preventive measures, including mechanical cleaning, fluoride use, and dietary modifications, have significantly reduced the incidence of caries [3]. However, pathogenic microorganisms' increasing resistance to conventional antimicrobial agents necessitates searching for alternative preventive strategies.

In recent years, medicinal plants and plant-based compounds have garnered attention as safe and beneficial materials for treating oral health issues, including halitosis, bleeding gums, mouth ulcers, and dental caries. Herbal medicines have the added benefit of having few adverse effects and being free of alcohol and sugar. [4]

Clove (*Syzygium aromaticum*) is a dried flower bud commonly used in Ayurvedic medicine in India. In dental emergencies, clove essential oil is often applied as a pain reliever. A review of existing studies indicates that clove oil and its various extracts possess significant antimicrobial properties, effectively targeting a range of bacteria and fungi [5,6]. Clove oil exhibits antibacterial, antifungal, insecticidal, and antioxidant effects, and may even have the potential as an anti-cariogenic agent [7]. Both water and methanol extracts of clove have been shown to have anti-cariogenic effects, as they help reduce bacterial adhesion and lower the hydrophobicity of bacterial cell surfaces [8].

Cinnamon (*Cinnamomum verum*) has been used in traditional medicine for several years for its antiemetic, anti-diarrheal, anti-flatulent, antioxidant, anti-inflammatory, coagulant, stimulant, antibacterial, antifungal, and insecticidal properties[9,10]. It is used to treat toothache and bad breath and as an antibacterial agent against Streptococcus mutans [11].

The effect of fluoride varnishes combined with casein phosphopeptide amorphous calcium phosphate (CPP-ACP) is well-recognized [12,13]. MI varnish (CPP- ACP with 5 % sodium fluoride GC) is a bioavailable varnish treatment that contains calcium, phosphate, and fluoride. CPP-ACP complex acts as a reservoir that stores calcium and phosphate ions leading to better remineralizing ability [14].

A study assessed the anti-cariogenic effects of five medicinal plants and their combination with MI varnish. The findings revealed that Cinnamon and Clove extracts exhibited the strongest anti-cariogenic effects among the plants tested. When Cinnamon and Clove extracts were incorporated into MI varnish, the resulting mixture demonstrated enhanced antibacterial activity. This combination showed a more significant effect on the suppression of *S. mutans* and *L. acidophilus* compared with commercial varnish only. [15]

Studies on the effect of medicinal plants on tooth hardness are scarce. Therefore, the present study was conducted to evaluate the effect of the clove and cinnamon extract on the remineralizing potential of MI varnish versus the MI varnish alone.

MATERIALS AND METHODS

PICO Question: In extracted primary teeth (P), does the treatment with MI varnish with a mix of clove and cinnamon plant extract (I), compared to treatment with MI varnish (C), have the same remineralizing ability (O)?

Type of study: An in vitro study was conducted to investigate the effect of plant extracts on MI varnish remineralizing potential on extracted primary teeth.

Ethical approval: The Cairo University, Faculty of Dentistry's, Research Ethics Committee (REC) obtained ethical approval for the protocol on 29/3/2022. The approval number was (7-3-22).

MATERIALS

Teeth

a) Teeth selection

Forty-five extracted primary anterior and posterior teeth were collected from the clinics of the Pediatric Dentistry Department, Faculty of Dentistry, Cairo University.

b) Eligibility criteria

Inclusion Criteria:

The teeth were evaluated visually and only selected if there were no cracks, abrasions, or hypoplasia and with no cavity or restoration.

Exclusion criteria:

Any tooth that has signs of attrition and hypo-mineralization was excluded. Also, any carious or restored teeth were excluded.

c) Samples preparation

The teeth were washed and scrubbed carefully using a hand scaler (DENTSPLY Ash instruments, Surrey, UK) to remove any hard deposits or blood remnants. The enamel of the teeth was polished using a polishing paste and brush to remove any stains.(16) Any root parts were cut using a straight handpiece and a diamond disc at a private dental laboratory in Cairo. Then, the teeth were immersed in 10% formalin and maintained at room temperature for one week as the formalin is a suitable media for research purposes and an effective post-extraction sterilization media. At intervention time the teeth were mounted in acrylic blocks (Figure 1). [17]

Demineralizing solution

The demineralizing solution was prepared with 2.2 mM $CaCl_2$ (Calcium chloride), 50 mM of (1% conc) acetic acid, and 2.2 mM NaH_2PO_4 (Sodium dihydrogen phosphate). The solution was adjusted to pH 4.5. [18]

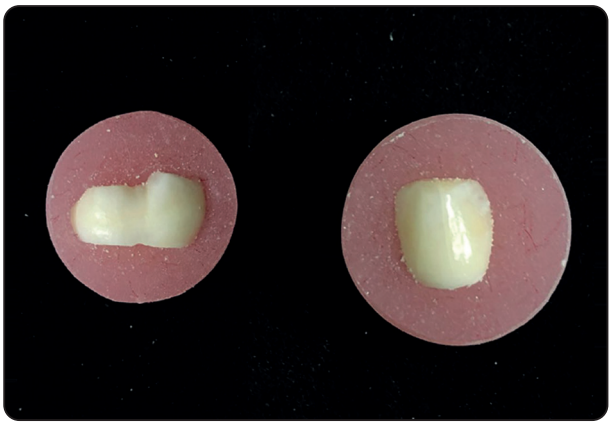

Fig. (1) Teeth samples mounted in acrylic blocks

Remineralizing solution

The composition of the remineralizing solution used was 0.90 mM NaH_2PO_4 (Sodium dihydrogen phosphate), 0.15 mM KCL (Potassium chloride), 1.5 mM, and $CaCl_2$ (Calcium chloride) with the pH adjusted to 7.2. [19]

Artificial saliva

The pH was adjusted to 7.2. The content of artificial saliva used was 3.90 mM Na_3PO_4 (Trisodium phosphate), 4.29 mM NaCl (Sodium chloride), 17.98 mM KCL (Potassium chloride), 1.10 mM $CaCl_2$ (Calcium chloride), 0.08 Mm $MgCl_2$ (Magnesium chloride),0 0.50mM H_2SO_4 (Sulfuric acid), 3.27 mM $NaHCO_3$ (Sodium bicarbonate). [18]

MI varnish

The varnish was obtained from the DentaCarts dental store in Cairo, Egypt. MI varnish (GC America, GC Corporation, Tokyo, Japan) contains 5% NaF and 2% CPP-ACP.

Plants extract

Ceylon cinnamon (bark) and clove (flower buds) were purchased from (Haj Arafa) store in Cairo, Egypt, and were ground to powders. A mixture of 100 grams of clove and cinnamon powders in a 1:1 ratio was macerated in methanol at room temperature

with occasional stirring for 48 hours until fully extract the bioactive compounds. The extract was then filtered through Whatman (no. 1) filter paper to remove any particulate matter, and the filtrate was concentrated using a Buchi® R-210 Rotavapor® Evaporator manufactured in Switzerland, under reduced pressure and controlled temperature (45°C) (Figure 2). The resulting extract was stored in an airtight container at 2-8°C in the refrigerator until further use. [15,20]

Fig. (2) The extract concentration procedure using Rotavapor

Treatment solution

The extract stock solution was prepared as the first step in getting the extract in a liquid homogenous form. The stock solution was prepared by weighing 1600 mg of the extract and dissolving it in 16ml of 99% dimethyl sulfoxide (DMSO) solvent (Figure 3).

The DMSO solvent was used because the extract could not dissolve in water. it was diluted to 3% concentration to avoid cell toxicity. Then, the treatment solution with a concentration of 15.6ml was obtained by using 15.6ml of the concentrated stock solution and diluting it up to 100ml volume with diluted DMSO. (Figure 4) [8,15,21]

Fig. (3) Stock solution

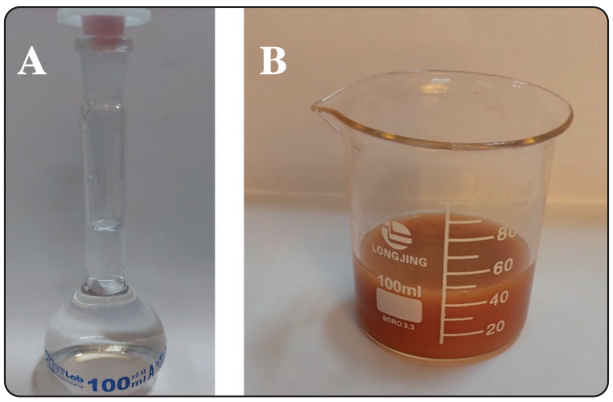

Fig. (4) (A) diluted DMSO 3%, (B) treatment solution 15.6%

Intervention The intervention was done as shown in the procedural flow chart (Figure 5).

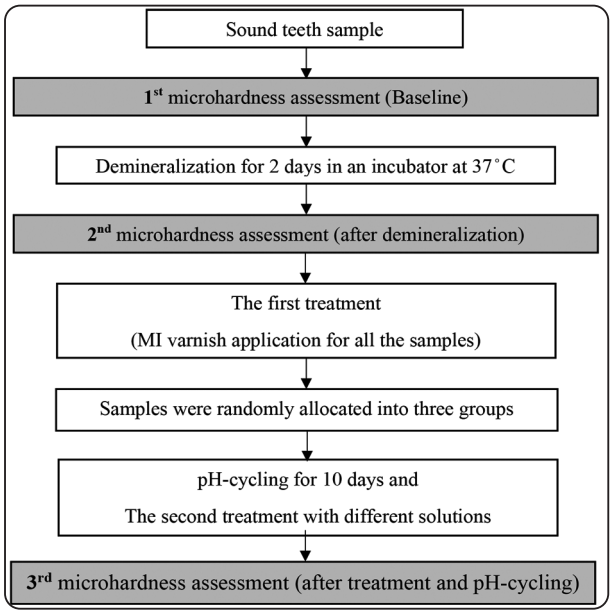

Fig. (5) Flow chart of the experimental design of the study

Demineralization

The teeth samples were immersed in the demineralizing solution for 48 hours at 37°C. The solution was renewed daily to avoid precipitate accumulation. After that, the samples were washed with distilled water. [22]

First surface treatment

After the second microhardness assessment, a thin layer of MI varnish was applied to all the samples using a soft-bristled applicator tip provided by the manufacturer. To mimic the oral environment, the samples were immersed in artificial saliva for 24 hours and incubated at 37˚C. Then, the varnish was carefully removed from the teeth samples. The blocks were then washed with distilled water for 1 min. [22]

- Randomization: Teeth were then allocated into three groups using randomization. (Table 1)

TABLE (1) Group names and treatment assigned

Group A	MI varnish alone
Group B	MI varnish + (extract + DMSO)
Group C	MI varnish + (DMSO)

pH cycling

All the teeth samples were subjected to pH cycling to simulate the oral environment. During each 24-h period, the samples were immersed in the remineralization solution for 23 h and then in the demineralization solution for 1 h. The blocks were rinsed with pure water between solutions to prevent contamination. (Figure 6) [19]

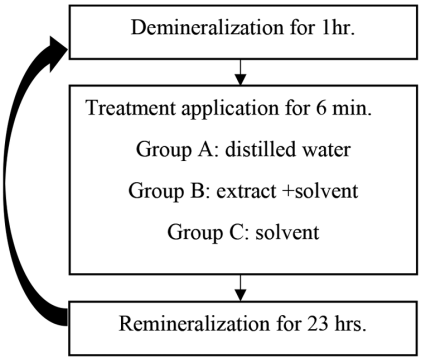

Fig. (6) pH cycle for each day

The samples were treated with the treatment solutions during pH cycling. Treatments were conducted once daily (after demineralization and before remineralization). During each treatment, the samples were immersed in the treatment solution - each group according to the assigned treatment- and kept at 37°C for 6 min, followed by rinsing with pure water for 1 min. (Figure 7)

Fig. (7) Treatment cycle with a different solution for each group

Surface microhardness assessment:

Microhardness of the samples was assessed before immersion in demineralized solution (baseline), after demineralization, and after pH and treatment cycling. Vicker's micro hardness testing machine (Wilson hardness tester model TUKON 1102 Germany) was used. The load was 100 grams (HV 0.1) and was applied for 10 seconds. After the load was removed, the indentation was focused with the magnifying eyepiece, and the two impression diagonals were measured, usually to the nearest 0.1-μm with a micrometer, and averaged [23] . At each testing interval, three indentations were made on each sample's smooth surface, and the mean value of these three readings represents the hardness of the tooth at this point (Figure 8)

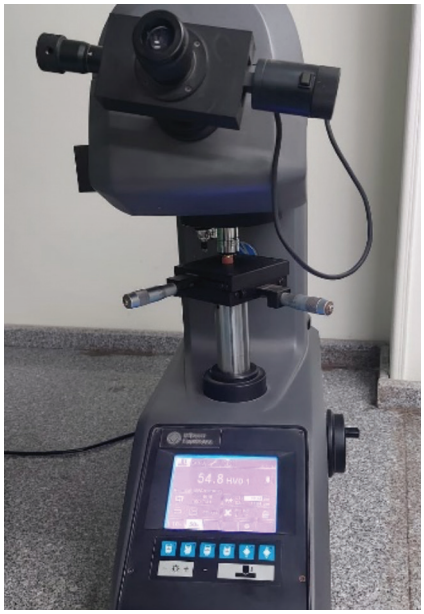

Fig. (8) Vickers microhardness Testing Machine

Statistical analysis:

The mean and standard deviation values were checked for normality and variance homogeneity using Shapiro-Wilk's and Levene's tests. Microhardness data showed parametric distribution but the homogeneity assumption was violated so they were analyzed using Welch one-way ANOVA followed by the Games-Howell test. Percentage change data were non-parametric and were analyzed using the Kruskal-Wallis test followed by Dunn's post hoc test with Bonferroni correction. The significance level was set at $p \leq 0.05$ within all tests. Statistical analysis was performed with R statistical analysis software version 4.2.3 for Windows.

RESULTS

The intragroup comparison of the mean and standard deviation values of microhardness in different intervals are presented in Table (2) and Figure (9). In the three groups, there was a significant difference between values measured at baseline, demineralized, and after treatment ($p<0.001$). The highest values in the three groups were found at the baseline. In group A (MI varnish only) and group C (MI varnish + solvent) the lowest value was found after demineralization, while in group B, which had treatment with plant extract, the lowest value was found after pH and treatment cycle.

There was no significant difference between different groups ($p=0.213$) after pH and Treatment cycle. The highest value was found in Group C: MI varnish + solvent (271.47±3.05), followed by Group A: MI varnish only (269.54±28.54), while the lowest value was found in Group B: MI varnish + extract + solvent (263.82±15.73). The mean and standard deviation (SD) values of the micro-hardness percentage change after the treatment and pH cycle are presented in Table (3) and Figure (10). There was a significant difference between different groups ($p=0.049$). The highest value was found in Group A: MI varnish only (5.37±8.71), followed by Group C: MI varnish + solvent (0.28±12.29), while the lowest value was found in Group B: MI varnish + extract + solvent (- 2.10±6.82).

TABLE (2) Intragroup comparisons, mean and standard deviation (SD) values of the micro-hardness

Group \ Interval	Micro-hardness (Mean ± SD)			p-value
	Baseline	After demineralization	After remineralization	
Group A: MI varnish only	292.45±20.12^{A}	255.91±19.19^{B}	269.54±28.54^{B}	<0.001*
Group B: MI varnish + extract + solvent	306.85±6.83^{A}	270.30±19.28^{B}	263.82±15.73^{B}	<0.001*
Group C: MI varnish + solvent	310.74±3.85^{A}	270.54±9.33^{B}	271.47±3.05^{B}	<0.001*

Means with different superscript letters within the same horizontal row are significantly different *; significant (p ≤ 0.05) ns; non-significant (p>0.05)

TABLE (3) Intergroup comparisons, mean and standard deviation (SD) values of the micro-hardness percentage change (%)

Group / Interval	Micro-hardness percentage change (%) (Mean ± SD)			p-value
	Group A: MI varnish only	Group B: MI varnish + extract + solvent	Group C: MI varnish + solvent	
Baseline-demin.	12.43±4.32^{A}	9.59±4.91^{A}	13.09±3.23^{A}	0.072ns
Remin.-demi	5.37±8.71^{A}	-2.10±6.82^{B}	0.28±12.29^{AB}	0.049*
Baseline-remain.	7.62±9.86^{A}	11.56±7.07^{A}	13.11±8.58^{A}	0.102ns

Means with different superscript letters within the same horizontal row are significantly different *; significant (p ≤ 0.05) ns; non-significant (p>0.05)

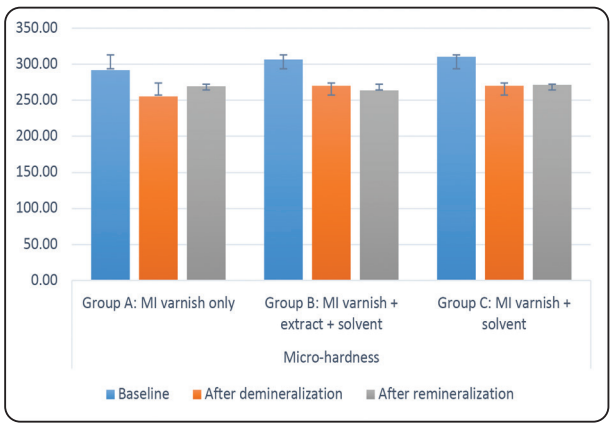

Fig. (9) Bar chart showing mean and standard deviation (error bars) values for micro-hardness in different intervals

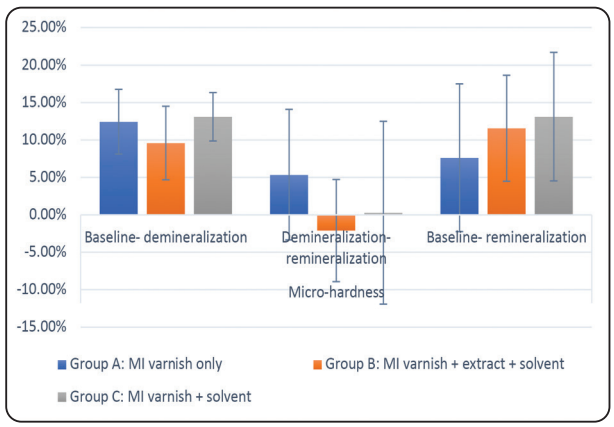

Fig. (10) Bar chart showing mean and standard deviation (error bars) values for micro-hardness percentage change (%) in different groups.

DISCUSSION

The most popular noninvasive methods for preventing dental caries are improving tooth resilience, creating an oral hygiene regimen, and modifying diet [3]. Increasing tooth resistance decreases the acid solubility of enamel and enhances the capacity for remineralization of demineralized enamel [24]. Natural bioactive components found in medicinal plants like clove and cinnamon promote health and do not have the unfavorable side effects of synthetic chemicals [25]. Clove and cinnamon extract have an antibacterial effect against cariogenic bacteria. [8,11]

This study showed a decrease in the microhardness in all the samples after immersion in the demineralizing solution. This indicated a demineralization of the enamel surface. This result coincides with other studies that reported that the primary enamel caries without cavitation showed a lower mineral content and microhardness than the intact enamel surfaces. [22,26]

After the pH cycle, the hardness of the samples in each group was measured representing the remineralization that occurred with different treatment solutions. According to the statistical analysis, there was a significant difference between groups with p value= 0.049. The highest value of remineralization was found in the control group A which had MI varnish only, and the lowest remineralization value was found in the intervention group B which contained MI varnish, plant extract, and the solvent. The difference between groups A and B was significant with a p-value lower than 0.001.

MI varnish was used in Group A as a control group as it is efficient as a remineralizing and an anti-cariogenic agent [12,13]. DMSO solvent was used in group C as a second control as it is a chemical solvent that could affect the results of the intervention group.

The findings of Group B are inconsistent with a previous study that reported an increase in microhardness when teeth were treated with a combination of Mi paste, clove, and cinnamon extract [27]. On the contrary, the findings align with a prior study that concluded clove extract is not a dependable remineralizing agent [28]. Clove and cinnamon extracts contain various compounds, with phenolics being one of the primary components. These phenolics are acidic and possess potent antioxidant and antimicrobial propertie[s] [29]. The acidity of the phenolic acids could explain the reduction in enamel microhardness observed in the extract-treated group. Also, It was demonstrated that the clove extract contains various components besides calcium, such as manganese, which may replace the calcium ion in hydroxyapatite crystals, lowering the Ca/P ratio. [28]

The study had limitations in simulating human-body interactions as it is an in vitro study. Also, the use of the solvent may increase the inhibition in the remineralization. So, Further research is needed to study each plant's chemical content with the amounts of active ingredients that would affect their effect on the remineralization of enamel. Color change of enamel caused by the different extracts should be considered in the studies. The safety of any extract has to be studied as extracts may affect gingival tissues negatively.

CONCLUSION

MI varnish effectively enhances remineralization and increases the teeth' microhardness. Clove and cinnamon methanolic extracts diminish the remineralizing ability of MI varnish.

List of abbreviations

Abbreviation	Full Term
CPP-ACP	Casein phosphopeptide-amorphous calcium phosphate
DMSO	Dimethyl sulfoxide
NaF	Sodium fluoride
$CaCl_2$	Calcium chloride
NaH_2PO_4	Sodium dihydrogen phosphate
KCL	Potassium chloride
Na_3PO_4	Trisodium phosphate
NaCl	Sodium chloride
$MgCl_2$	Magnesium chloride
H_2SO_4	Sulfuric acid
$NaHCO_3$	Sodium bicarbonate
pH	Potential of Hydrogen

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