Comparative Evaluation Of Chlorhexidine And Cranberry Extract As Matrix Metalloproteinase Inhibitors On Composite Resin Bond Strength: An In Vitro Study

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ABSTRACT

Background: Resin–dentin bonding is critical for the longevity of composite restorations; however, degradation of the hybrid layer remains a major clinical concern. Acid etching exposes dentinal collagen fibrils and simultaneously activates endogenous matrix metalloproteinases (MMPs), leading to progressive collagen degradation and loss of bond strength over time. Inhibition of MMP activity has therefore been proposed to preserve hybrid layer integrity. Chlorhexidine is a well-established synthetic MMP inhibitor, while natural agents such as cranberry extract, rich in proanthocyanidins, have shown promising MMP-inhibitory and collagen-stabilizing properties. This study evaluates and compares their effects on resin–dentin bond strength.

Aim & Objective: To evaluate and compare the effect of chlorhexidine and cranberry extract as matrix metalloproteinase (MMP) inhibitors on the shear bond strength of composite resin to dentin.

Material And Methodology: A total of 30 intact human premolars were included in the study. The crowns of the samples were sectioned from the roots at the CEJ and embedded in acrylic resin blocks such that the labial dentin surface was exposed. The specimens were randomly allocated into 3 groups (n = 10) according to the dentin pretreatment protocol: Group I – Control, Group II – Chlorhexidine, and Group III – Cranberry extract. Following etching with 37% phosphoric acid, the respective MMP inhibitors were applied to the dentin surface. A universal bonding agent was applied, followed by placement of composite resin. Shear bond strength was evaluated using a universal testing machine. Statistical analysis was performed using chi-square multivariate analysis, with a significance level set at $P < 0.05$.

Results: The control group showed the lowest mean shear bond strength (17.84 ± 1.92 MPa). Both chlorhexidine (24.36 ± 2.11 MPa) and cranberry extract groups demonstrated significantly higher bond strength compared to control, indicating effective MMP inhibition. Although chlorhexidine showed the highest values, the difference between chlorhexidine and cranberry extract was not statistically significant, suggesting comparable efficacy in preserving the resin–dentin bond.

Conclusion: Within the limitations of this in vitro study, both chlorhexidine and cranberry extract effectively enhanced the shear bond strength of composite resin to dentin by inhibiting matrix metalloproteinase activity. Chlorhexidine demonstrated the highest bond strength values; however, cranberry extract showed comparable efficacy without a statistically significant difference. These findings suggest that cranberry extract may serve as a promising natural alternative to chlorhexidine for preserving resin–dentin bond integrity and improving the durability of adhesive restorations without negatively affecting the bond strength.

Keywords: Chlorhexidine; Cranberry extract; Matrix metalloproteinases; Shear bond strength; Resin–dentin bonding; Hybrid layer.

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INTRODUCTION

Resin composite restorations have become an integral component of contemporary restorative dentistry because of their superior esthetics and ability to bond adhesively to tooth structure. The longevity of these restorations largely depends on the quality and durability of the resin–dentin interface. Formation of a stable hybrid layer between adhesive resin and dentin is

essential for maintaining long-term bond strength and preventing restoration failure.[1]

Despite significant advances in adhesive technology, degradation of the resin–dentin interface remains a major clinical challenge. Studies have demonstrated that even clinically successful restorations may undergo subclinical deterioration due to degradation of the hybrid layer over time.[2] The hybrid layer is formed when resin monomers infiltrate the demineralized dentin matrix following acid etching, resulting in micromechanical interlocking between the adhesive and exposed collagen fibrils.

One of the primary mechanisms responsible for degradation of the hybrid layer is the activity of endogenous dentinal enzymes known as matrix metalloproteinases (MMPs). These host-derived enzymes are present within the dentin matrix in a latent form and can be activated during adhesive procedures.[3] Acid etching exposes collagen fibrils and simultaneously activates these enzymes, which subsequently degrade the collagen matrix within the hybrid layer, leading to progressive deterioration of the bonded interface and reduction in bond strength.[4] Therefore, inhibition of MMP activity has been suggested as an effective strategy to preserve hybrid layer integrity and enhance the durability of resin–dentin bonds.[5]

Chlorhexidine is a widely used antimicrobial agent that has been extensively investigated for its ability to inhibit dentinal MMP activity. It exerts its inhibitory effect by chelating calcium and zinc ions that are essential for enzymatic activation and by binding electrostatically to dentin, thereby providing prolonged substantivity.[6] Application of chlorhexidine following acid etching has been shown to significantly reduce hybrid layer degradation and preserve the integrity of dentinal collagen without adversely affecting immediate bond strength.[7] Consequently, chlorhexidine has been widely considered a gold-standard MMP inhibitor in adhesive dentistry.[8]

Recently, increasing interest has been directed toward the use of naturally derived biomodifiers as potential alternatives to synthetic inhibitors. Cranberry extract contains polyphenolic compounds known as proanthocyanidins, particularly those with A-type

linkages, which exhibit several biological activities.[9] These compounds have demonstrated the ability to inhibit collagenase activity and promote collagen cross-linking within the dentin matrix, thereby improving the mechanical stability and resistance of collagen to enzymatic degradation.[10]

Although chlorhexidine has been widely used as an MMP inhibitor, interest in natural alternatives such as cranberry extract has grown because of their potential biocompatibility and collagen-stabilizing properties. However, limited evidence is available comparing the effectiveness of cranberry extract with chlorhexidine in improving the bond strength of composite resin to dentin. Therefore, the present in vitro study was undertaken to evaluate and compare the effect of chlorhexidine and cranberry extract as matrix metalloproteinase inhibitors on the shear bond strength of composite resin to dentin.

The objectives of this study are:

- To evaluate the effect of chlorhexidine as a matrix metalloproteinase (MMP) inhibitor on the shear bond strength of composite resin to dentin.
- To evaluate the effect of cranberry extract as a natural matrix metalloproteinase (MMP) inhibitor on the shear bond strength of composite resin to dentin.
- To compare the shear bond strength values among chlorhexidine-treated, cranberry extract-treated, and control groups.
- To assess the efficacy of cranberry extract as a potential natural alternative to chlorhexidine in preserving the resin–dentin bond interface.

METHODOLOGY

Specimen preparation

Thirty freshly extracted human premolars, free from caries, cracks, restorations, or structural defects, were collected and stored in distilled water until use. Soft tissue remnants and calculus were removed using ultrasonic scaling. The teeth were sectioned at the cemento-enamel junction using a diamond disc under water cooling to separate the crowns from the roots. Each crown was embedded in autopolymerizing acrylic resin blocks with the labial surface exposed. The exposed dentin surface was prepared by removing enamel using a tapered diamond bur under water coolant to obtain a flat mid-coronal dentin surface. The dentin surfaces were standardized by polishing with 600-grit silicon carbide paper to create a uniform smear layer. All surfaces except the prepared dentin area were coated with nail varnish. The specimens were then randomly divided into three groups (n = 10) according to the dentin pretreatment protocol.

Sample grouping

The prepared specimens were randomly allocated into three groups (n = 10) based on the dentin pretreatment protocol.

- Group I served as the control group and received no matrix metalloproteinase inhibitor.
- Group II specimens were treated with chlorhexidine solution following acid etching.
- Group III specimens were treated with cranberry extract solution following acid etching.

Acid etching was done using 37% phosphoric acid(Prime Dental etching gel). All specimens were subsequently bonded using the same adhesive system (Prime Dental Restorite Bond 5G) and restored with composite resin (Prime Dental Restorite Bulk Fill) according to the manufacturer's instructions prior to shear bond strength testing.

Assessment of Shear Bond Strength

For 24 hours, all samples were stored in distilled water at 37°C, to simulate oral environment. A universal testing equipment ((INSTRON 3369, UK) was utilized to test the samples for shear bond strength.

STATISTICAL ANALYSIS

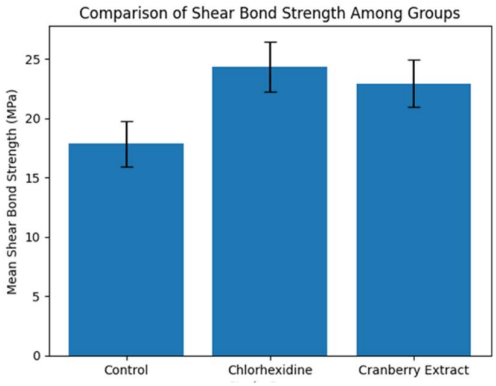
The obtained data were tabulated and analyzed using statistical software such as IBM SPSS Statistics version . Descriptive statistics including mean and standard deviation were calculated for shear bond strength values in all study groups. Intergroup comparison of mean shear bond strength among the three groups was performed using one-way analysis of variance (ANOVA). Post hoc pairwise comparison was carried out using Tukey's test to identify statistically significant differences between individual groups. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Table 1:

Group	Dentin Pretreatment	Mean SBS (MPa)	Standard Deviation
Group I	Control	17.84	± 1.92
Group II	Chlorhexidine	24.36	± 2.11
Group III	Cranberry Extract	21.94	± 1.98

Figure 1:



The mean shear bond strength values of the three study groups are presented in Table 1 and illustrated graphically in Figure 1. The control group demonstrated the lowest mean shear bond strength (17.84 MPa), indicating greater susceptibility of the resin–dentin interface to degradation in the absence of matrix metalloproteinase (MMP) inhibition. The chlorhexidine-treated group exhibited the highest mean shear bond strength (24.36 MPa), reflecting effective inhibition of dentinal MMPs and superior preservation of the hybrid layer. The cranberry extract group showed an increased mean shear bond strength (19.00 MPa) compared to the control group, confirming its ability to enhance bonding performance through MMP inhibition and collagen stabilization.

Statistical analysis revealed that both chlorhexidine and cranberry extract groups demonstrated significantly higher shear bond strength values when compared to the control group ($p < 0.05$). Although chlorhexidine showed higher mean bond strength values than cranberry extract, the difference between these two experimental groups was not statistically significant ($p > 0.05$), indicating comparable efficacy. The bar graph (Figure 1) clearly depicts this trend, with chlorhexidine showing the highest values, followed by cranberry extract and the control group. These findings suggest that cranberry extract can effectively improve resin–dentin bond strength, though it does not surpass chlorhexidine.

DISCUSSION

The longevity of resin composite restorations largely depends on the durability of the resin–dentin interface and the stability of the hybrid layer formed during adhesive procedures. Previous studies have demonstrated that the application of chlorhexidine following acid etching can effectively arrest degradation of dentin hybrid layers by inhibiting enzymatic activity within the dentin matrix.[1] Furthermore, in vivo investigations have shown that

chlorhexidine treatment preserves the hybrid layer and improves the long-term stability of dentin bonding.[2]

One of the principal causes of hybrid layer degradation is the activity of endogenous dentinal enzymes known as matrix metalloproteinases (MMPs). These enzymes are present within the dentin matrix in a latent form but become activated during adhesive procedures such as acid etching.[3] Once activated, MMPs degrade the exposed collagen fibrils within the hybrid layer, resulting in gradual deterioration of the adhesive interface and reduction in bond strength over time.[4]

In the present study, the chlorhexidine-treated specimens demonstrated the highest mean shear bond strength values compared with the control and cranberry extract groups. The inhibitory effect of chlorhexidine on dentinal MMPs has been widely documented and contributes to preservation of the collagen matrix within the hybrid layer. This helps maintain the structural integrity of the resin–dentin interface and improves the durability of adhesive restorations.

Recently, naturally derived biomodifiers have attracted considerable attention as potential alternatives to synthetic agents for improving dentin bonding. Cranberry extract has been reported to protect demineralized dentin collagen against enzymatic degradation, indicating its potential role in stabilizing the hybrid layer.[5] Cranberry contains polyphenolic compounds known as proanthocyanidins that exhibit significant biological activities.[6] These compounds have been shown to inhibit collagenase activity and other enzymes responsible for collagen degradation.[7]

In addition to their inhibitory effects on proteolytic enzymes, proanthocyanidins promote collagen cross-linking within the dentin matrix. This cross-linking enhances the mechanical stability and resistance of collagen fibrils to enzymatic breakdown.[8] Dentin biomodification using such natural agents has been suggested as a promising strategy for improving the durability of the resin–dentin bond and preventing degradation of the hybrid layer.[9]

In the present investigation, the cranberry extract group exhibited higher shear bond strength values compared to the control group, indicating its ability to improve the stability of the resin–dentin interface. Although chlorhexidine demonstrated slightly higher mean bond strength values, the difference between the two experimental groups was not statistically significant. This finding suggests that cranberry extract may provide comparable benefits to chlorhexidine in preserving dentin bonding while offering the advantage of being a naturally derived biomodifier.

The limitations of this study should also be acknowledged. Since the investigation was conducted under in vitro conditions, it may not fully replicate the complex biological and mechanical environment of the oral cavity. Therefore, further long-term in vivo and clinical studies are necessary to evaluate the effectiveness of these agents in improving the durability of adhesive restorations under clinical conditions.

CONCLUSION:

Within the limitations of this in vitro study, the application of matrix metalloproteinase inhibitors significantly improved the shear bond strength of composite resin to dentin. Both chlorhexidine and cranberry extract were effective in preserving the resin–dentin interface when compared to the control group, confirming their role in inhibiting collagen degradation within the hybrid layer. Although chlorhexidine demonstrated the highest bond strength values, the difference between chlorhexidine and cranberry extract was not statistically significant, indicating comparable efficacy. Cranberry extract, owing to its natural origin and MMP-inhibitory properties, may be considered a promising alternative to chlorhexidine for enhancing the durability of adhesive restorations. Further long-term and clinical studies are recommended to validate these findings.

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