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INFLUENCE OF DENTIN COLLAGEN BIOMODIFICATION USING PROANTHOCYANIDIN, RIBOFLAVIN/UV PHOTOCROSSLINKING, AND CARBODIIMIDE ON THE AGED MICROTENSILE BOND STRENGTH OF SELF-ADHESIVE RESIN CEMENTS

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ABSTRACT

Background: Degradation of the resin–dentin interface remains a major challenge affecting the longevity of adhesive restorations. Dentin collagen biomodification using cross-linking agents has been proposed as a strategy to enhance collagen stability and improve long-term bond durability.

Aim: To evaluate the influence of dentin collagen biomodification using proanthocyanidin, riboflavin/UV photo cross linking, and carbodiimide on the aged microtensile bond strength of self-adhesive resin cements.

Materials and Methods: A total of 100 extracted human permanent molars were randomly allocated into five groups (n=20): Control, Proanthocyanidin, Riboflavin/UV Photocrosslinking, Carbodiimide, and Combined Biomodification. Following dentin pretreatment, composite resin blocks were cemented using a self-adhesive resin cement. Each group was further subdivided into immediate and aged subgroups (n=10). Aging was performed using 10,000 thermocycles and six months of water storage. Microtensile bond strength testing was conducted using a universal testing machine, and failure modes were evaluated under stereomicroscopy. Statistical analysis was performed using one-way ANOVA and Student's t-test with a significance level of $p<0.05$.

Results: Significant differences in microtensile bond strength were observed among the groups ($p<0.001$). The Combined Biomodification Group demonstrated the highest immediate (33.14 ± 2.48 MPa) and aged (30.52 ± 2.29 MPa) bond strength values, followed by the Proanthocyanidin, Carbodiimide, and Riboflavin/UV groups. The Control Group exhibited the lowest bond strength and the greatest reduction after aging. Biomodification groups showed significantly improved bond durability and a higher frequency of mixed failures compared with the control group.

Conclusion: Dentin collagen biomodification significantly enhanced the aged microtensile bond strength of self-adhesive resin cements. The combined use of proanthocyanidin and carbodiimide provided the greatest improvement in bond durability and resistance to degradation. Biomodification strategies may represent an effective approach for improving the longevity of resin–dentin bonds and adhesive restorations.

Keywords: Dentin Collagen Biomodification; Proanthocyanidin; Riboflavin; Carbodiimide; Microtensile Bond Strength.

INTRODUCTION

The Long-term success of adhesive restorative procedures depends largely on the integrity and durability of the resin–dentin interface [1]. Despite significant advances in adhesive dentistry, degradation of the hybrid layer remains one of the principal causes of restoration failure [2]. The dentin substrate presents unique challenges for bonding because of its heterogeneous composition, high organic content, tubular structure, and intrinsic moisture [3]. Following acid conditioning, the exposed collagen matrix serves as a scaffold for resin infiltration [4]. However, incomplete resin

penetration and subsequent degradation of collagen fibrils by endogenous enzymes such as matrix metalloproteinases (MMPs) and cysteine cathepsins can compromise bond durability over time [5]. Therefore, strategies aimed at stabilizing the dentin collagen matrix have become an area of considerable interest in adhesive dentistry [6].

Dentin collagen biomodification has emerged as a promising approach for enhancing the mechanical properties and degradation resistance of the hybrid layer [7]. Biomodification involves the application of collagen cross-linking agents that strengthen the collagen network, increase its resistance to enzymatic degradation, and improve the stability of resin–dentin bonds [8]. By inducing additional inter- and intramolecular cross-links within collagen fibrils, these agents enhance the mechanical properties of dentin and preserve the integrity of the adhesive interface under aging conditions [9].

Among the various collagen cross-linking agents investigated, proanthocyanidin has received considerable attention due to its natural origin and potent cross-linking ability [10]. Proanthocyanidins are polyphenolic compounds commonly extracted from grape seed and other plant sources [11]. These compounds interact with collagen through hydrogen bonding and hydrophobic interactions, resulting in increased collagen stiffness, enhanced tensile strength, and reduced susceptibility to enzymatic degradation. Several studies have demonstrated that proanthocyanidin treatment improves bond strength and significantly enhances the long-term stability of resin–dentin interfaces [12].

Riboflavin-mediated ultraviolet (UV) photocrosslinking represents another innovative approach for dentin biomodification [13]. Riboflavin, also known as vitamin B2, acts as a photosensitizer that generates reactive oxygen species upon exposure to ultraviolet light [14]. These reactive species induce covalent cross-linking within collagen fibrils, thereby strengthening the dentin matrix [15]. Riboflavin/UV photocrosslinking has been extensively utilized in ophthalmology for corneal stabilization and has recently gained attention in restorative dentistry because of its potential to improve collagen durability and adhesive performance [16].

Carbodiimide (1-ethyl-3-(3-dimethylaminopropyl) carbodiimide; EDC) is a synthetic cross-linking agent that promotes direct covalent bonding between collagen molecules without becoming incorporated into the collagen matrix [17]. In addition to its cross-linking activity, carbodiimide has been shown to inactivate endogenous matrix metalloproteinases and reduce collagen degradation [18]. Because of its low cytotoxicity and effective stabilization of dentin collagen, carbodiimide has emerged as a promising biomodification agent for improving the longevity of adhesive restorations.

Self-adhesive resin cements have become increasingly popular because they simplify clinical procedures by eliminating the need for separate etching and bonding steps [19]. These materials contain acidic functional monomers capable of simultaneously demineralizing and infiltrating dental hard tissues [20]. Self-adhesive resin cements reduce technique sensitivity and chairside time while providing acceptable mechanical and adhesive properties. However, their interaction with dentin remains less predictable than conventional adhesive systems, particularly over extended periods [21]. Therefore, enhancing dentin substrate stability before cementation may represent a viable strategy for improving the long-term performance of self-adhesive resin cements [22].

Several investigations have evaluated the effect of collagen cross-linkers on immediate bond strength; however, their influence on long-term bond durability remains a subject of ongoing research [23]. While some studies have reported significant improvements in bond stability following biomodification, others have found variable outcomes depending on the cross-linking agent, application protocol, adhesive system, and aging method employed [24]. Furthermore, direct comparisons among proanthocyanidin, riboflavin/UV photocrosslinking, and carbodiimide under standardized experimental conditions remain limited [25].

Artificial aging methods such as thermocycling and long-term water storage are commonly used to simulate the oral environment and assess the durability of adhesive interfaces [26]. Furthermore, direct comparisons among proanthocyanidin, riboflavin/UV photocrosslinking, and carbodiimide under standardized experimental conditions remain limited. [27]. Therefore, evaluating the aged microtensile bond strength of self-adhesive resin cements following dentin biomodification is essential for determining the clinical relevance of these interventions [28].

Given the growing interest in collagen biomodification and the limited comparative evidence available, further investigation is warranted [29]. Understanding the relative effectiveness of different cross-linking agents may assist clinicians in selecting appropriate pretreatment strategies to enhance restoration longevity and reduce adhesive failures [30].

Therefore, the present study was designed to evaluate the influence of dentin collagen biomodification using proanthocyanidin, riboflavin/UV photocrosslinking, and carbodiimide on the aged microtensile bond strength of self-adhesive resin cements. The null hypothesis tested was that no significant difference would exist among the various biomodification protocols with respect to long-term bond durability.

METHODOLOGY

Study Design

This in vitro experimental study was conducted to evaluate the influence of dentin collagen biomodification using proanthocyanidin, riboflavin/UV photocrosslinking, and carbodiimide on the aged microtensile bond strength of self-adhesive resin cements.

Study Setting

The study was carried out in the Department of Conservative Dentistry and Endodontics in collaboration with the Department of Dental Materials over a period of six months.

Sample Size

A total of **100 freshly extracted human permanent molars** were included in the study. The sample size was determined based on previous bond strength studies evaluating dentin collagen cross-linking agents and was considered adequate to detect significant differences among the study groups.

Inclusion Criteria

- Extracted human permanent molars with intact coronal dentin.
- Teeth free from caries, restorations, cracks, and developmental defects.
- Teeth extracted for periodontal or orthodontic reasons.

Exclusion Criteria

- Carious teeth.
- Restored or endodontically treated teeth.
- Teeth exhibiting enamel or dentin cracks.
- Teeth with developmental anomalies or structural defects.

Specimen Preparation

Following extraction, teeth were cleaned of soft tissue debris and stored in 0.1% thymol solution until use. The occlusal enamel was removed using a water-cooled diamond saw to expose flat mid-coronal dentin surfaces. The exposed dentin surfaces were polished with 600-grit silicon carbide paper under running water to create a standardized smear layer.

Group Allocation

The specimens were randomly divided into five groups (n = 20):

Group I (Control)

No dentin biomodification performed prior to cementation.

Group II (Proanthocyanidin Group)

Dentin treated with 6.5% proanthocyanidin solution for 60 seconds.

Group III (Riboflavin/UV Group)

Dentin treated with 0.1% riboflavin solution followed by ultraviolet irradiation for 120 seconds.

Group IV (Carbodiimide Group)

Dentin treated with 0.3 M carbodiimide solution for 60 seconds.

Group V (Combined Biomodification Group)

Dentin treated sequentially with proanthocyanidin and carbodiimide to evaluate synergistic effects.

Dentin Biomodification Procedures

Proanthocyanidin Application

A 6.5% proanthocyanidin solution was applied to the dentin surface using a microbrush for 60 seconds, followed by gentle air drying.

Riboflavin/UV Photocrosslinking

A 0.1% riboflavin solution was applied for 60 seconds. The surface was then irradiated using a UV light source (365 nm) for 120 seconds.

Carbodiimide Application

A 0.3 M carbodiimide solution was actively applied for 60 seconds and subsequently rinsed with distilled water.

Combined Treatment

Proanthocyanidin was applied for 60 seconds followed by carbodiimide application for an additional 60 seconds.

Cementation Procedure

A standardized composite resin block measuring 5 mm × 5 mm × 4 mm was fabricated for each specimen. Self-adhesive resin cement was mixed according to the manufacturer's instructions and applied between the dentin surface and composite block. A constant seating load of 1 kg was applied for 5 minutes to ensure uniform cement thickness. Excess cement was removed and light curing was performed for 40 seconds from each side.

Aging Protocol

Each group was further subdivided into:

Immediate Testing Subgroup (n = 10)

Specimens stored in distilled water at 37°C for 24 hours before testing.

Aged Testing Subgroup (n = 10)

Specimens subjected to 10,000 thermocycles between 5°C and 55°C with a dwell time of 30 seconds and subsequently stored in distilled water for six months.

Microtensile Bond Strength Testing

Following storage, specimens were sectioned longitudinally in both x and y directions using a precision diamond saw to obtain resin–dentin sticks with a cross-sectional area of approximately 1 mm².

Each stick was attached to a microtensile testing jig using cyanoacrylate adhesive and loaded to failure in a universal testing machine at a crosshead speed of 1 mm/min.

Microtensile bond strength (μTBS) was calculated using:

μTBS (MPa) = Failure Load (N) ÷ Cross-sectional Area (mm²)

Failure Mode Analysis

Fractured specimens were examined under a stereomicroscope at 40× magnification and classified as:

- Adhesive failure
- Cohesive failure in dentin
- Cohesive failure in resin cement
- Mixed failure

Outcome Measures

Primary Outcome

- Aged microtensile bond strength (MPa).

Secondary Outcomes

- Immediate bond strength.
- Percentage reduction following aging.
- Distribution of failure modes.

Statistical Analysis

Data were analyzed using SPSS version 25.0 (IBM Corp., USA). Results were expressed as mean ± standard deviation. One-way ANOVA followed by Tukey's post hoc test was used for intergroup comparisons. Independent Student's t-test was used to compare immediate and aged bond strengths within groups. A p-value < 0.05 was considered statistically significant.

RESULTS

Distribution of Specimens

A total of 100 dentin specimens were included in the study and equally distributed among five groups (n = 20). Each group was further subdivided into immediate and aged testing subgroups (n = 10 each). No specimen was lost during preparation, aging, or testing procedures.

Immediate Microtensile Bond Strength

The immediate microtensile bond strength values demonstrated significant differences among the study groups ($p < 0.001$). The Combined Biomodification Group showed the highest bond strength (33.14 ± 2.48 MPa), followed by the Proanthocyanidin Group (31.46 ± 2.72 MPa), Carbodiimide Group (30.28 ± 2.63 MPa), and Riboflavin/UV Group (29.82 ± 2.51 MPa). The Control Group exhibited the lowest immediate bond strength (26.18 ± 2.65 MPa).

Table 1. Immediate Microtensile Bond Strength

Group	n	Mean ± SD (MPa)
Control	10	26.18 ± 2.65
Proanthocyanidin	10	31.46 ± 2.72
Riboflavin/UV	10	29.82 ± 2.51
Carbodiimide	10	30.28 ± 2.63
Combined Treatment	10	33.14 ± 2.48

ANOVA: $F = 14.62$, $p < 0.001$

Aged Microtensile Bond Strength

Following thermocycling and six months of water storage, bond strength values decreased in all groups. However, biomodification groups demonstrated significantly higher aged bond strength than the control group. The Combined Treatment Group maintained the highest aged bond strength (30.52 ± 2.29 MPa), whereas the Control Group showed the lowest value (18.92 ± 2.44 MPa).

Table 2. Aged Microtensile Bond Strength

Group	n	Mean ± SD (MPa)
Control	10	18.92 ± 2.44
Proanthocyanidin	10	28.11 ± 2.35
Riboflavin/UV	10	25.67 ± 2.41

Carbodiimide	10	26.74 ± 2.52
Combined Treatment	10	30.52 ± 2.29

ANOVA: F = 29.84, p < 0.001

Comparison of Immediate and Aged Bond Strength

All groups exhibited a reduction in bond strength following aging. The Control Group demonstrated the greatest reduction (27.7%), whereas the Combined Treatment Group showed the least reduction (7.9%), indicating superior resistance to degradation.

Table 3. Comparison Between Immediate and Aged Bond Strength

Group	Immediate Mean ± SD (MPa)	Aged Mean ± SD (MPa)	Reduction (%)	p-value
Control	26.18 ± 2.65	18.92 ± 2.44	27.7	0.001*
Proanthocyanidin	31.46 ± 2.72	28.11 ± 2.35	10.6	0.018*
Riboflavin/UV	29.82 ± 2.51	25.67 ± 2.41	13.9	0.012*
Carbodiimide	30.28 ± 2.63	26.74 ± 2.52	11.7	0.015*
Combined Treatment	33.14 ± 2.48	30.52 ± 2.29	7.9	0.041*

*Statistically significant at $p < 0.05$.

Failure Mode Analysis

Failure mode analysis demonstrated that adhesive failures predominated in the Control Group, whereas mixed failures were more frequently observed in the biomodification groups. The Combined Treatment Group exhibited the highest proportion of mixed failures, suggesting a stronger and more stable resin–dentin interface.

Table 4. Distribution of Failure Modes After Aging

Group	Adhesive Failure n (%)	Mixed Failure n (%)	Cohesive Failure n (%)
Control	8 (80%)	2 (20%)	0 (0%)
Proanthocyanidin	4 (40%)	5 (50%)	1 (10%)
Riboflavin/UV	5 (50%)	4 (40%)	1 (10%)
Carbodiimide	4 (40%)	5 (50%)	1 (10%)
Combined Treatment	3 (30%)	6 (60%)	1 (10%)

Chi-square test: $\chi^2 = 10.72$, p = 0.031

Summary of Findings

Dentin collagen biomodification significantly enhanced the aged microtensile bond strength of self-adhesive resin cements. The Combined Treatment Group exhibited the highest immediate and aged bond strength values and the lowest reduction after aging. Among the individual biomodification protocols, proanthocyanidin demonstrated superior performance, followed by carbodiimide and riboflavin/UV photocrosslinking. The Control Group showed the greatest bond degradation and the highest frequency of adhesive failures. These findings indicate that collagen cross-linking strategies improve resin–dentin bond durability by stabilizing the collagen matrix and reducing aging-related degradation.

DISCUSSION

The present study evaluated the influence of dentin collagen biomodification using proanthocyanidin, riboflavin/UV photocrosslinking, and carbodiimide on the aged microtensile bond strength of self-adhesive resin cements. The results demonstrated that all biomodification protocols significantly improved bond durability compared with the untreated control group. The combined biomodification protocol exhibited the highest immediate and aged bond strength values, followed by proanthocyanidin, carbodiimide, and riboflavin/UV photocrosslinking. Furthermore, biomodified groups showed lower bond degradation after aging and a greater proportion of mixed failures, indicating enhanced stability of the resin–dentin interface.

The superior performance of the biomodification groups may be attributed to the stabilization of exposed dentin collagen fibrils through additional cross-link formation and inhibition of endogenous collagenolytic enzymes. Cross-linking agents strengthen the collagen matrix, improve its mechanical properties, and reduce susceptibility to hydrolytic and enzymatic degradation, thereby enhancing the longevity of adhesive bonds. These findings support the concept that collagen biomodification can serve as an effective strategy for preserving hybrid layer integrity and improving long-term clinical outcomes.

Castellan et al. (2010) [31] reported that proanthocyanidin significantly enhanced dentin collagen cross-linking and improved bond strength stability by increasing collagen stiffness and resistance to enzymatic degradation. The superior aged bond strength observed in the Proanthocyanidin Group in the present study corroborates their findings and suggests that natural collagen cross-linkers can effectively improve resin–dentin bond durability.

Liu et al. (2011) [32] demonstrated that carbodiimide treatment effectively inactivated matrix metalloproteinases and preserved the hybrid layer, resulting in improved long-term bond stability. Similar improvements were observed in the Carbodiimide Group of the present study, which maintained significantly higher aged bond strength values than the untreated control group.

Bedran-Russo et al. (2014) [33] investigated riboflavin/UV-induced collagen cross-linking and reported enhanced mechanical properties of dentin collagen along with improved resistance to degradation. Consistent with their observations, the Riboflavin/UV Group in the present study demonstrated significantly higher aged bond strength compared with untreated dentin, although its performance was slightly lower than that of proanthocyanidin and carbodiimide.

Mazzoni et al. (2017) [34] emphasized the importance of natural and synthetic collagen cross-linkers in improving dentin matrix stability and preserving the hybrid layer. Their findings support the overall results of the present study, where all biomodification protocols significantly enhanced bond durability and reduced aging-related degradation when compared with the control group.

Tezvergil-Mutluay et al. (2015) [35] reported that dentin biomodification strategies reduce collagen degradation and improve the longevity of adhesive interfaces by preserving collagen integrity and minimizing enzymatic breakdown. The superior performance of the Combined Treatment Group in the present investigation further supports the concept that multiple cross-linking mechanisms may provide synergistic benefits, resulting in greater stabilization of the dentin matrix and enhanced resistance to long-term degradation.

Failure mode analysis further supported the bond strength findings. The predominance of adhesive failures in the Control Group indicated a weaker resin–dentin interface, whereas the increased frequency of mixed failures in the biomodification groups reflected stronger and more durable bonding. The Combined Treatment Group exhibited the highest proportion of mixed failures, suggesting improved interfacial integrity and resistance to aging.

Overall, the findings of the present study demonstrate that dentin collagen biomodification significantly enhances the aged microtensile bond strength of self-adhesive resin cements. Among the evaluated protocols, the combined use of proanthocyanidin and carbodiimide produced the most favorable outcomes, indicating that synergistic collagen stabilization may offer greater protection against hybrid layer degradation. These findings support the incorporation of collagen cross-linking strategies into adhesive procedures to improve restoration longevity and clinical success.

Limitations

This study was conducted under in vitro conditions and may not completely replicate the biological and mechanical complexities of the oral environment. Only one self-adhesive resin cement and specific concentrations of biomodification agents were evaluated. Although thermocycling and water storage simulated aging, they cannot fully reproduce long-term clinical conditions. Furthermore, only sound dentin was investigated, limiting extrapolation to caries-affected or sclerotic dentin. Therefore, long-term clinical studies are required to validate the present findings.

CONCLUSION

Dentin collagen biomodification significantly improved the aged microtensile bond strength of self-adhesive resin cements. The combined proanthocyanidin and carbodiimide treatment demonstrated the highest bond durability and the least degradation after aging. Among the individual agents, proanthocyanidin exhibited the most favorable performance. Riboflavin/UV photocrosslinking and carbodiimide also enhanced bond stability compared with untreated dentin. Therefore, collagen biomodification may be considered an effective strategy for improving the longevity of resin–dentin bonds.

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