Effect of Various Collagen Cross Linkers on the Bond Strength of Dentin Bonding Agents to the Dentin

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ABSTRACT

Introduction: Improvement of the mechanical properties of type 1 collagen may be advantageous during bonding procedures. So various collagen cross linkers are used in this review which are responsible for modification of dentinal substrates, thereby increasing the resin dentin bonds. The aim of the study was to systematically gather and evaluate effect of collagen cross linkers on the bond strength of dentin bonding agents to the dentin.

Material and methods: A systemetic search was conducted using pubmed, google, google scholar and manual search using DPU search library sources were searched from 2005- 31st December 2015. All cross reference lists of selected studies were also screened. Two reviewers assessed the eligibility of studies. All in vitro studies are considered. Review, case reports, abstracts, letters to editors, editorials and in vivo studies are excluded. All the extracted molars and incisors are taken in these studies.

Results: 60 articles from pubmed search was relevant according to the inclusion criteria. An addition of 7 others articles are included from other sources. A total of 23 records were screened according to the title and selected. A final of 8 articles were used for detailed evaluation in this systematic review after assessment of full text. All the collagen cross linkers showed statistically higher bond strengths values.

Conclusion: All collagen cross linkers increased the bond strength values to dentin substrates with different adhesive systems used.

Keywords: Dentin, Collagen Cross Linkers, Bond Strength, Dentin Bonding Agents

INTRODUCTION

Adhesive restorations are routinely used to replace carious dental tissue, broken or chipped tooth and replacement of defective resin restorations.[1] Dentin is composed of two phases: an inorganic, and an organic phase of predominantly Type 1 collagen.

Quality of the bond strength and its durability is greatly influenced by the structural integrity and mechanical properties of collagen fibrils. Adhesive resin monomers infiltrate and encapsulate the exposed collagen fibrils to form a hybrid layer.[4] Degradation of hybrid layer adversely affects the resin dentin bonds, which can eventually lead to the failure of adhesive restorations.[6]

Mechanical properties of collagen can be increased by forming intra and intermolecular and intermicrofibrillar cross links.

Proanthocynidins are naturally biocompatible collagen cross linker. Proanthocynidin has the ability to bind proline rich proteins such as collagen, and facilitate the enzyme proline hydroxylase activity, essential for collagen biosynthesis.[7]

Chlorhexidine, potent non specific matrix metalloproteinases inhibitor has been reported to arrest degradation of hybrid layer.[6]

Hesperidin has shown cross linking property, arrested collagen degradation and demineralization.[6]

Glutaraldehyde (GD) and Genipin (GE), cross-linking agents has been shown to improve the mechanical properties.[4]

Riboflavin has the ability to produce free radicals when photo activated with UV or visible light. When riboflavin is photo activated and light is absorbed forming covalent cross links between adjacent collagen molecules.[8]

Systematic reviews have gained an important position in the dental literature, aiding in clinical decision making. So far, no systematic review on the effectiveness of collagen cross linkers on the bond strength has been performed. The aim of this study was to gather and evaluate, in a systematic manner, available data on effect of various collagen cross linkers on the bond strength of dentin bonding agents to the dentin.

Focused Question

What is the effect of collagen cross linkers on the bond strength of dentin bonding agents to the dentin.

Objectives were to evaluate and compare the bond strength of dentin bonding agents to the dentin after pre treatment with collagen cross linkers.

MATERIAL AND METHODS

Eligibility Criteria

Inclusion criteria

1. Articles in English or those having detailed summary in English.
2. Studies published between 1st January 2005 and 31st December 2015.
3. In vitro studies.
4. Studies showing the effect of various collagen cross linkers on the bond strength of the dentin and Studies using the self etch as well as two step etch, rinse and bond adhesives.

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Exclusion criteria

1. Review, case reports, abstracts, letters to editors, and in vivo studies are excluded.
2. Studies assessing the bond strength without the use collagen cross linkers.
3. Studies that did not use any objective method to assess the bond strength.

PICOS

P - Participants: Extracted teeth
I - Intervention: collagen cross linkers
C - Comparison: between various collagen linkers and with where cross linker is not used.
O - Outcome: bond strength of composite to the dentin.
S - Study design: In vitro study.

INFORMATION SOURCES

Internet sources of evidence were used in the search of appropriate papers satisfying the study purpose: Google Scholar, Google, manual search using DPU college library resources. All cross reference lists of the selected studies were screened for additional papers that could meet the eligibility criteria of the study. The databases were searched from 1st January 2005 up to and including December 2015 using the search strategy.

STUDY SELECTION

Preliminary screening consisted total of 60 articles out of which 23 articles were selected. At first the papers were screened by title and abstract. As a second step, full text papers were obtained For full-text screening, the following criteria were taken into consideration: In vitro studies.Studies involving the collagen cross linkers which are calculating the bond strengths. Finally a total of 8 articles were included.

DATA COLLECTION PROCESS

A standard pilot form in excel sheet was initially used and then all those headings not applicable for review were removed. Data extraction was done for one article and this form was reviewed by an expert and finalized. This was followed by data extraction for all the articles.

Data items

The data items included were:

1. Author – The name of the author
2. Year of publication – The year in which the study was published.
3. Study design – In Vitro studies
4. Sample size – Number of extracted teeth used
5. Products – different collagen cross linkers
6. Technique – method used to evaluate the bond strength
7. Subgroups - subgroups based on different concentrations of collagen cross linkers and at various time intervals.
8. Confounders – affected dentin used in one study
9. Bonding agents – different generations of bonding agents used.
10. Bond strength – microshear and micro tensile bond strengths were evaluated.
11. Mean – mean of the bond strengths were recorded
12. Standard deviation – standard deviation of the bond strengths were recorded.
13. Conclusion – result of the study
14. Remark – comments of the author

DISCUSSION

SUMMARY OF EVIDENCE

G V Macedo et al (2009) hypothesized that crosslinking in dentin Collagen improves bond strength. This study investigated the effects of 5%glutaraldehyde and 6.5% grape seed extract treated for 1hour, induced crosslinking on the dentin bond strengths of sound and caries-affected dentin, and on the stability of dentin collagen. Their results demonstrated that the application of chemical crosslinking agents to etched dentin prior to bonding procedures significantly enhanced the dentin bond strengths of cariesaffected and sound dentin. All sound dentin groups showed significantly higher bond strengths when compared with their caries affected groups. Regardless of dentin substrate no statistically significant differences were observed between glutaraldehyde and grape seed extract.[2] There was no statistically significant difference between the TBS values of GE-treated samples and control groups (44.13 MPa and 43.70 MPa respectively, p =0.7178).[4]

Aiman Al Ammar (2009) et al[4] investigated the effect of three different crosslinking agents (Glutaraldehyde [GD], Grapeseed extract [GSE], and Genipin [GE]) on the tensile bond strength (TBS) of resin dentin bonds. Dentin surfaces were randomly divided according to the dentin treatment: Control group (no treatment), 5% GD, 6.5% GSE or 0.5% GE. Teeth were restored either with One Step Plus or Adper Single Bond Plus adhesive systems and resin composite.

The highest bond strength was observed for GSE treated groups (74.4 MPa, p <.0001), which was statistically higher than all the other experimental groups. GD treatment also resulted in a statistically increase in the TBS when compared to the control group (68.96 MPa, p <0.0001).

Carina Strano Castellan et al (2010) characterized the properties of dentin matrix treated with two Proanthocynidin rich crosslinking agents and their effect on dentin bonded interfaces.

Sound human molars were demineralized and either treated with one of two crosslinking agents (6.5%grape seed GSE and6.5% cocoa seed COE extractor left untreated. The effect of GSE or COE on the resin bond strength was evaluated after10 or 60 min of exposure time. Dentin resin bonds significantly increased following treatment with GSE regardless of the application time adhesive system used.[7]

A Cova et al (2011) have reported collagen cross-linking after exposure to riboflavin followed by ultraviolet-A (UVA) exposure. This is first to investigate the effect of a riboflavin-containing primer on adhesive interface stability and dentinal matrix metalloproteinase activity. Human dentin treated with 0.1% riboflavin, exposed to UVA for 2 min, and bonded with a two-step etch-and-rinse adhesive. Specimens were subjected to micro tensile bond strength tests and pulled to failure after storage for 24 hrs., 6 mos., or 1 yr. The use of the experimental primer containing UVA-activated riboflavin

Dentin	Dentin discs
Collagen cross linkers	Proanthocyanidin or sodium ascorbate or glutaraldehyde or genipin
Bond strength	Shear bond strength/ micro tensile bond strength
Composite resins	Adhesive resins or dental composite
Dentin bonding agents	Adhesives system or Self etch, or 2-step and 3-step adhesive
Riboflavin	Collagen cross linker
chlorhexidine	Collagen cross linker

Table-1: Dentin

Sr. No.	Search strategy	Number of articles	Number of selected articles	After Duplicate Removal
LD1	Dentin AND Collagen cross linkers AND Bond strength AND Composite resins AND Dentin bonding agents	4	4	4
LD2	Dentin AND collagen cross linkers AND bond strength AND composite resins.	3	3	0
LD3	Proanthocyanidin and dentin and composite resins.	4	4	1
LD4	Collagen cross linking agents and dentin and matrix metalloproteinases.	9	4	0
LD 5	Riboflavin, Proanthocynidin and collagen cross linkers.	8	1	1
LD6	Sodium ascorbate and collagen cross linkers	13	2	0
LD7	Collagen cross linkers and dentin	11	2	1
Other sources		7	7	1
Total		60	28	8

Table-2: Search strategy

before XP Bond application (Group 1) increased the immediate bond strength compared with control specimens. Over the next 6 mos., the riboflavin cross-linked specimens showed small but significant ($p < 0.05$) 19.8% reductions in bond strength, while the untreated control fell 41%. After storage for 1 yr., the riboflavin cross-linked specimens showed no further significant loss of bond strength (30.4%), while the control specimens fell to a cumulative loss of 52.5% of their original values. In conclusion, dentinal collagen cross-linking induced by riboflavin/UVA increased immediate bond strength.[8]

Amr S.Fawzy et al (2012) investigated the effect of photo-activation of riboflavin either by ultraviolet (UVA) or visible blue light (BL) on the bond strength to dentin and resin/dentin interface morphology. Dentin beams were demineralized, treated with 0.1% or 1% riboflavin solution for 5min and photo-activated with UVA or BL for 20s. The ultimate tensile strength (UTS was assessed Riboflavin was photo-activated separately with UVA or BL followed by photo-polymerization of the bonding resin with BL (two-step) or both riboflavin photo-activation and bonding resin photo-polymerization were done in one-step using BL. Photoactivation by blue light using one step adhesive systems did not show significant effect as that of two step photo activation.

Two step photo activation of riboflavin by UVA significantly enhanced the micro tensile bond strengths at 24 and 4 months compared to control group. Photo activation by blue light had no significant effect on enhancing the micro tensile bond strength of both 0.1 and 1% riboflavin cross-linked specimens at 24 hour compared to control group., however it led significantly higher value after 4 months storage. One step photo activation of riboflavin by blue light of 0.1% did not enhance the micro tensile bond strengths while 1% showed decreased bond strengths values.[5]

Sakhamuri Srinivasulu et al (2012)[3] evaluated the shear bond strength of composite resin to deep dentin, bonded using a self etch adhesive, after treatment with two collagen cross linkers at varying time intervals. The proximal deep dentin was exposed and the specimens were divided based on the surface treatment of dentin prior tobonding as follows: Group I (n = 12, control): Group II (n = 24): Dentin surface treated with 10% sodium ascorbate; and group III (n = 24): Dentin surface pretreated with 6.5%proanthocyanidin. Groups II and III were further divided into two subgroups based on the pre-treatment time of 5 and 10 min.

Higher shear bond strength to deep dentin was observed in teeth treated with 10% sodium ascorbate and 6.5% proanthocyanidin compared to control group.

Islam S et al (2012) aimed to investigate the effect of incorporation of natural cross-linkers into the primer of a self-etching adhesive on resin-dentine bond strength. Flat dentine surfaces were prepared from extracted human molar teeth and were applied with the following self-etching primers. The 0.5% hesperidin (HPN), 0.5% chlorhexidine (CHX) or 0.5% grape seed extract (GSE) was incorporated into Clearfil SE primer (Kuraray Medical, Inc.). The original SE primer served as control. Following primer application, the teeth were bonded with Clearfil SE bond, restored with resin composite and stored in water for 24 h at 37 °C. The bonded specimens were sectioned into beams and subjected to micro tensile bond testing. Tukey post hoc test revealed that incorporation of HPN significantly increased μTBS, The GSE-incorporated group significantly decreased μTBS, while CHX-incorporated group did not show any statistical significant difference when compared with the control

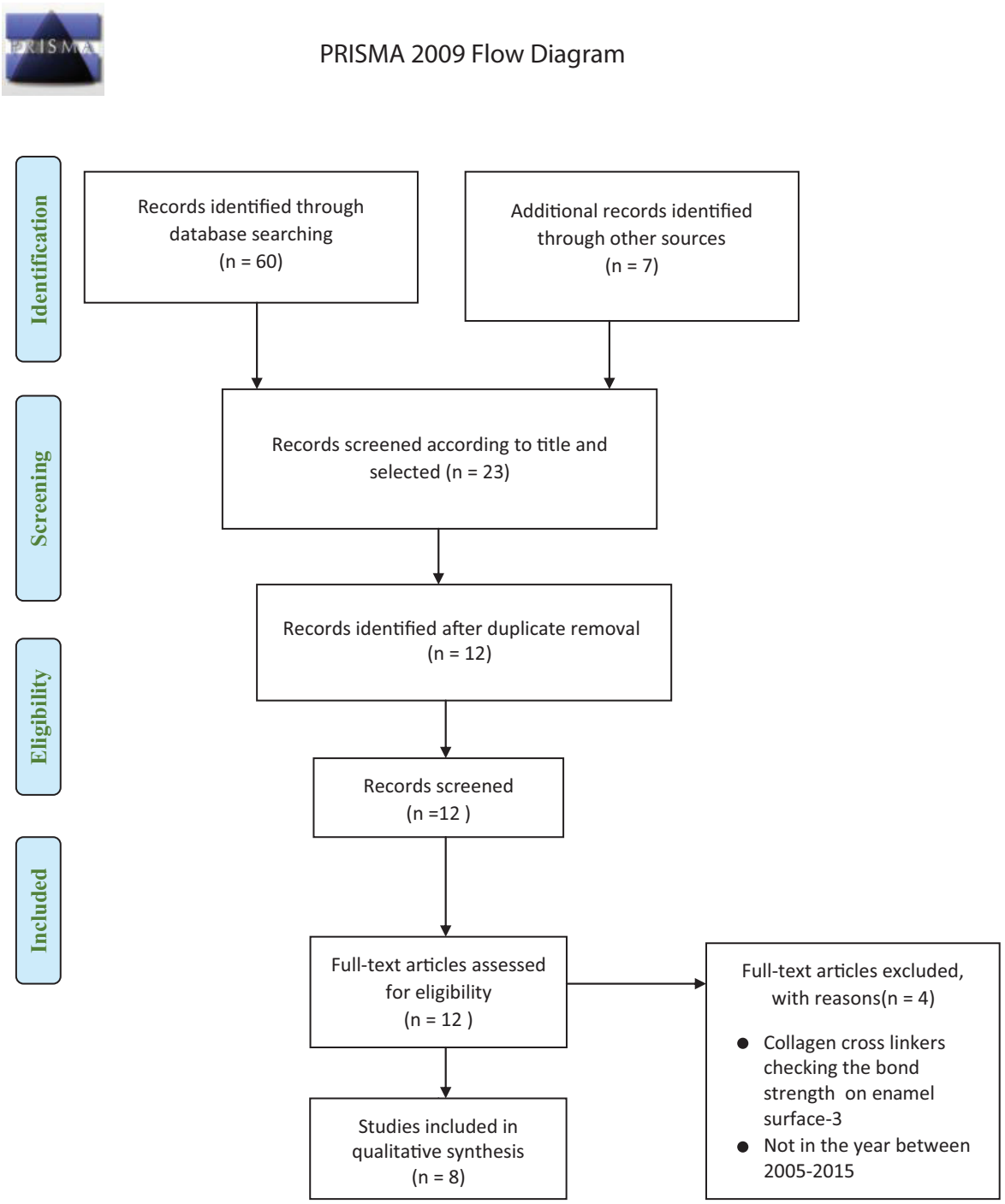

Figure-1: PRISMA 2009 Flow Diagram

group.[6]

Umer Daood (2015) modified two-step experimental etch-and rinse dentin adhesive with different Concentrations of riboflavin and studied its effect on the bond strength with different concentrations of riboflavin (m/m, 0, 1%, 3%, 5% and 10%). Micro-tensile bond testing was performed with scanning electron microscopy to analyse the failure of deboned beams. Modification with 1% and 3% riboflavin increased the micro-tensile bond strength compared to the control at 24 hour and 9-month storage. Raman analysis revealed that 1% and 3%riboflavin adhesives specimens showed relatively higher resin infiltration. The incorporation of riboflavin in the experimental two-step etch-and-rinse adhesive at 3% (m/m) improved the immediate bond strengths and bond durability after 9-month storage in artificial saliva without adversely affecting the degree of conversion of the adhesive monomers and resin infiltration. The 3% RF-modified group showed the highest micro TBS compared to the control and all other experimental groups after a 24-h storage in artificial saliva. In contrast, the 10% RF-modified specimens showed the lowest micro TBS compared to all other groups. Storing the resin-dentin beams for 9 months in artificial saliva significantly decreased the micro TBS within each of the control and the RF-modified groups. Only 1% and 3% RF-modified groups showed significantly higher μTBS after a 9-month storage compared to the control group.

As for the 24-h storage, the 10% RF-modified group showed the least μTBS after a 9-month storage subjected to micro tensile bond testing (μTBS). The GSE-incorporated group significantly decreased μTBS, H and EM, when compared with the other groups ($p < 0.006$); while CHX-incorporated group did not show any statistical significant difference when compared with the control group.[8]

All cross linked specimens with different concentrations of riboflavin photo activated either with ultraviolet or blue light showed statistically higher tensile strength values as compared to control groups irrespective of the concentrations used however photo activation by ultraviolet significantly increased the tensile strength compared to photo activation by blue light. With the limited scope of this study 1 to 5% riboflavin gave better bond strengths as compared to 10% irrespective of the time and the activation of one step bond is not as good as two step.[5]

Studies by Carina, S.srinivaslu and Aiman et al showed significantly higher tensile bond strengths of Proanthocynidin values as compared to their experimental and control groups irrespective of the pretreatment times and also on sound and demineralized dentin substrates.[4,7,3]

Glutaraldehyde has been investigated in various studies as a potential collagen cross-linking agent. Glutaraldehyde reacts primarily with ε-amino groups of lysyl (or hydrolysyl) residues by using its aldehyde functional groups. An experiment proposed by Ritter et al suggested that the presence of exogenous cross-links induced by Glutaraldehyde were sufficient to positively affect the mechanical properties of the exposed dentin matrix and consequently increase the TBS.

Studies of Aiman and G.V.macedo et al used 5% Glutaraldehyde for 1 hour and found significant effect on micro tensile bond strengths values[2,11]

Sodium ascorbate is an important component in synthesis of hydroxyproline and hydroxylysine in collagen. Hydroxyproline serves to stabilize collagen triple helix, and hydroxylysine is necessary for formation of intermolecular cross-links in collagen.

Dentin surface pretreated with 10% sodium ascorbate based on the pretreatment time of five minutes and 10 minutes showed significantly higher mean shear bond strength values in the control group. However no significant difference in shear bond strength values was found between the two pretreatment times However when it is compared with or grape seed extract, then grape seed extract has shown significantly higher bond strength values.[3]

CONCLUSION

Within the limitation of in vitro studies it can be concluded that all the collagen cross linkers increased the bond strength values to dentin substrates with different adhesive systems used. Further studies are required using similar parameters of concentration, time of application, and method of evaluation to reach to a definitive protocol for the application of collagen cross linkers.

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