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LITERATURE REVIEW:

Does the Application of Anti-Erosive Substances on Eroded Dentin Affect Bond Strength? A Systematic Review

¿La aplicación de sustancias antierosivas en dentina erosionada afecta la resistencia adhesiva? Una revisión sistemática

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ABSTRACT: This systematic review evaluated whether using anti-erosive agents as a pretreatment of eroded dentin before bonding with resin composite affects the bond strength. A search was conducted by two reviewers in the PubMed, Embase, Scopus, Web of Science, and Science Direct databases in January 2023. Articles that employed artificially eroded human dentin and performed treatment prior to adhesion with anti-erosive substances were eligible. A validated tool with 12 items regarding *in vitro* studies was used to assess the risk of bias in the selected articles, obtaining a final score for each study. Four *in vitro* studies were included in this systematic review. Most studies used the microtensile bond strength test; most failures were adhesive or mixed. No tested substance negatively affected the bond strength to eroded dentin. Sodium fluoride (NaF), tin-containing fluoride (Sn/F) and silver diamine fluoride ($Ag(NH_3)_2F$) have been proven not to interfere with or improve bond strength to eroded dentin.

KEYWORDS: Dental erosion; Dentin; Tooth remineralization; Fluorides; Dental bonding; Operative dentistry; Systematic review.

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RESUMEN: Esta revisión sistemática evaluó si el uso de agentes antierosivos como tratamiento previo de la dentina erosionada antes de la adhesión de la resina compuesta afecta la resistencia adhesiva. Dos revisores realizaron una búsqueda en las bases de datos PubMed, Embase, Scopus, Web of Science y Science Direct en enero de 2023. Fueron seleccionados los artículos que empleaban dentina humana erosionada artificialmente y realizaban un tratamiento con sustancias antierosivas antes de la adhesión. Se utilizó una herramienta validada con 12 ítems referentes a estudios *in vitro* para evaluar el riesgo de sesgo en los artículos seleccionados, obteniendo una puntuación final para cada estudio. En esta revisión sistemática se incluyeron cuatro estudios *in vitro*. La mayoría de los estudios utilizaron la prueba de resistencia de unión por microtracción; la mayoría de las fallas fueron adhesivas o mixtas. Ninguna sustancia evaluada afectó negativamente la resistencia adhesiva a la dentina erosionada. El fluoruro de sodio (NaF), el fluoruro conteniendo estaño (Sn/F) y el fluoruro diamino de plata ($Ag(NH_3)_2F$) demostraron no interferir o mejorar la resistencia adhesiva a la dentina erosionada.

PALABRAS CLAVE: Erosión dental; Dentina; Remineralización dental; Fluoruros; Adhesión dental; Operatoria dental; Revisión sistemática.

INTRODUCTION

Dental erosion is the demineralization of teeth caused by acids from non-bacterial sources (1). Restoration using resin composites is effective in repairing lost tooth structure and is even recommended in cases of severe tooth wear (2). However, bonding these restorations can be challenging, as the adhesive system may have difficulty establishing bonds with the eroded dentin tissue (3). In vitro studies suggest that adhesion to eroded dentin requires additional interventions, such as the prior grinding of the dentin surface, to enhance long-term performance (4).

Furthermore, dentin bonding is critical due to the moist and organic nature of the substrate. Eroded dentin exhibits a region of deeper demineralization that exacerbates this challenge (5). Factors such as reduced availability of mineral bonding sites necessitate the preparation of this substrate to ensure the integrity of the bond when applying the adhesive system and the resin composite (6). Dentin erosion also increases nanoleakage due to greater water incorporation in the matrix, which undermines the structure of the hybrid layer. Consequently, anti-erosive compounds have been proposed to enhance bond strength on these substrates (7), once they may either replenish the lost mineral content or prevent the erosive process by forming a protective layer (8).

Anti-erosive substances investigated are typically used for conservative treatments to manage the erosive condition and prevent lesions. These agents act on the mineral content to restore the crystalline structure and facilitate additional chemical bonds (9,10). The literature categorizes these anti-erosive agents into four main groups: fluorides, organic compounds, calcium-based agents, and other anti-erosive substances (7). Fluoride compounds are the most prevalent but have limited effectiveness, requiring either higher concentrations or more frequent applications to significantly mitigate erosion (11).

Although many primary studies have examined the *in vitro* effects of these anti-erosive agents on mineral content, there remains a lack of synthesized results in the literature that could guide researchers in identifying the most effective approaches prior to resin composite bonding to eroded dentin (12). Therefore, this systematic review aimed to evaluate, through a synthesis of in vitro studies, whether the application of anti-erosive substances as a pretreatment affects bond strength on human permanent eroded dentin.

METHODS

This systematic review followed the Preferred Reporting Items for Systematic Reviews guidelines (the PRISMA 2020 statement) and was registered in the Open Science Framework (DOI number https://doi.org/10.17605/OSF.IO/XZY2F).

The PICOS (Population, Intervention, Comparison, Outcomes and Study) strategy used was: P - eroded dentin, I - application of anti-erosive agents, C - eroded dentin not submitted to anti-erosive treatment, O - bond strength, S - *in vitro*. The research question was according to the PICOS strategy: Does the application of anti-erosive substances on eroded dentin affect bond strength?

ELIGIBILITY CRITERIA

Original articles evaluating the adhesion on eroded human dentin previously treated with anti-erosive substances were eligible. Case reports, clinical trials, reviews, studies whose anti-erosive substance has empirical effect with no proven treatment protocol, studies with proteolytic inhibitors, and studies that evaluated cements were excluded. No language criteria were applied.

DATA SOURCES

The source databases were PubMed, Embase, Scopus, Web of Science, and Science Direct and database search was performed on January 17th, 2023. A manual search was also performed in Google Scholar with the search algorithm. In addition, the reference lists were reviewed for studies that were left out of the selection.

SEARCH STRATEGY

From the eligibility criteria, the search algorithm was developed: “eroded dentin” OR “eroded tooth” OR “tooth erosion” OR “tooth erosions” OR erosive OR erosively OR “dental erosion” OR “dental erosions” OR “dentin erosion” OR “dentine erosion” OR “erosive dental wear” OR “erosive tooth wear” OR “erosive challenge” OR “erosion challenge” OR “erosive challenges” OR “erosion challenges”.

And "antierosive" OR “anti-erosive” OR “anti-erosion” OR antiacid OR “anti-acid” OR "acid neutralization" OR fluorine OR fluoride OR fluorides OR “topical fluoride” OR “topical fluorides” OR “sodium fluoride” OR “sodium fluorides” OR “calcium fluoride” OR “tin fluoride” OR “tin fluorides” OR “stannous fluoride” OR “stannous fluorides” OR arginine OR phosphate OR phosphates OR “calcium phosphate” OR “calcium phosphates” OR “potassium compound” OR “potassium compounds” OR casein OR caseins OR chitosan OR “cariostatic agent” OR “cariostatic agents” OR toothpaste OR toothpastes OR dentifrice OR dentifrices OR mouthwash OR mouthwashes OR "salivary parameters".

And “bond strength” OR bond OR bonding OR adhesive OR adhesives OR adhesion OR “dentin adhesive” OR “dentin adhesives” OR “adhesive system” OR “adhesive systems” OR “hybrid layer” OR “adhesion stability” OR “adhesive stability” OR “bond stability” OR “bonding stability” OR "adhesion durability" OR “adhesive durability” OR "bond durability" OR "bonding durability".

SELECTION AND DATA COLLECTION PROCESS

Two independent reviewers (BBTLCS and RASJ) performed the selection through a prior screening by titles, abstracts, and a full reading of the texts according to the eligibility criteria. The results were imported into the Rayyan website (https://www.rayyan.ai) to remove duplicates and select articles. A third reviewer resolved selection disagreements (MJFC).

For data collection, two reviewers (BBTLCS and RASJ) independently extracted the data from the articles into a table in Microsoft Office Word 2019; a third reviewer was the intermediator of the process. The Kappa test was performed to confirm the agreement between reviewers from the selected articles. The data extracted were: author/year of publication/country, number of samples, sample size calculation and randomization, type of tooth storage, artificial erosion protocol, anti-erosion pre-treatment, adhesive system, mode of adhesive system application, restorative material, method of bond strength evaluation, aging, bond strength for each group, failure mode analysis, predominant failure mode, and main results. If some information was unavailable or unclear in the article, the authors were contacted via e-mail. If they did not respond within two weeks, the article was excluded for lack of information.

RISK OF BIAS ASESSMENT

The risk of bias assessment was based on a validated tool for *in vitro* studies by Sheth *et al*. (13). In it, 12 items are evaluated: 1) Clearly stated aims/objectives, 2) Detailed explanation of sample size calculation, 3) Detailed explanation of sampling technique, 4) Details of the comparison group, 5) Detailed explanation of methodology, 6) Operator details, 7) Randomization, 8) Method of measurement of outcome, 9) Outcome assessor details, 10) Blinding, 11) Statistical analysis, and 12) Presentation of results.

If the information was adequately specified, the reviewer scored "2", if it was inadequately specified, scored "1", if the information was not specified, scored "0" and if the information is not necessary for the article, scored as "not applicable". A total score was obtained for each study which is applied to the following formula to obtain the final score:

Final score = (Total score × 100) / (2 × number of applicable criteria)

Studies scoring >70% were classified as low risk of bias, those scoring 50% to 70% as medium risk of bias, and those scoring <50% as high risk of bias.

The two independent reviewers (BBTLCS and RASJ) obtained a Kappa value of 86%, with a confidence interval (CI) between 0.76-0.96. Two further calculations were performed with the third reviewer (MJFC), who did not initially participate in selecting the articles but resolved the inconsistencies. The Kappa value obtained between BBTLCS and MJFC was 90% (CI = 0.82-0.92). The Kappa value between RASJ and MJFC was 82% (CI = 0.72 - 0.92).

RESULTS

The main result evaluated was the mean bond strength between the adhesive and the eroded dentin previously treated with anti-erosive substances. Secondarily, the mean bond strength between the adhesive and the eroded control group. The type of anti-erosive substance used, the substance's application mode, the adhesive system/adhesive strategy and the predominant failure mode were also observed.

A total of 574 articles were initially exported to the Rayyan website. The tool allowed the removal of duplicates and the submission of titles and abstracts for reading by the two blinded reviewers. A total of 164 duplicates were removed. After the two reviewers' titles and abstract reading of the 422 articles, with the resolution of inconsistencies by the third reviewer, ten studies remained. Of these, 1 article was not found in its full version, and only nine could be read in full. After a full reading, five articles were removed according to the inclusion and exclusion criteria, remaining four studies (Figure 1).

The selection resulted in studies published between 2013 and 2021 by groups from different countries (14-17): Brazil [1], India [1] and Switzerland [2]. All studies used artificially eroded human dentin treated with anti-erosive substances that acted on the mineral content before the adhesion of restorations. Only one study adequately specified information about sample size calculation (17) and three studies adequately reported randomization (14,16,17). Artificial erosion was performed by cycling with a citric acid solution (14-16) or a soft drink (17). All the teeth were healthy before the experimental protocol, so they were primary dentin. Additionally, all the anti-erosion agents went through a washing process before the adhesive system was used.

The anti-erosive pretreatments were the application of fluoride solutions (14-17), tin chloride (14,15), casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) (16) or calcium sodium phosphosilicate (Novamin) (16).

Among the four articles, two showed that anti-erosive pretreatments increased the bond strength of adhesive systems on eroded dentin (14,17). The bond strength values were higher when using a NaF solution or SnF mouth rinse in demineralization process of eroded dentin (14), different from using a $SnCl_2$/AmF solution immediately before the application of adhesive system (15). When compared to eroded dentin previously treated with CPP-ACP (11.97 to 12.12 MPa), Novamin (11.66 to 11.97 MPa) or NaF (11.56 to 12.40 MPa), the untreated eroded dentin showed similar values (11.80 to 11.83 MPa) (16). The 38% silver diamine fluoride ($Ag(NH_3)_2F$) with or without iodide potassium (KI) showed bond strength of 39.38 to 41.57 MPa, different from the values of 33.74 to 36.56 MPa of untreated eroded dentin (17).

Most studies evaluated bonding by microtensile bond strength (14,15,17) and only one by microshear bond strength (16). One article evaluated long-term bond strength, showing that regardless of prior treatment with a $SnCl_2$/AmF solution, the average bond strength decreased within one year of storage at 37°C (15). The failure modes were evaluated by all articles with predominating adhesive and mixed failures. Two studies used adhesives in self-etch mode (14,15), and two compared etch-and-rinse and self-etch modes (16,17).

Other analyses applied to the treated eroded dentin were scanning electron microscopy (SEM) performed by all studies (14-17), energy dispersive X-ray spectroscopy (EDX) (14,15,17) and degree of conversion (17). The main results are shown in Table 1.

One study showed low risk of bias (17) and the other three showed medium risk of bias (14-16). The items "detailed explanation of sample size calculation", "operator details", "outcome assessor details," and "blinding" received the lowest scores (Figure 2).

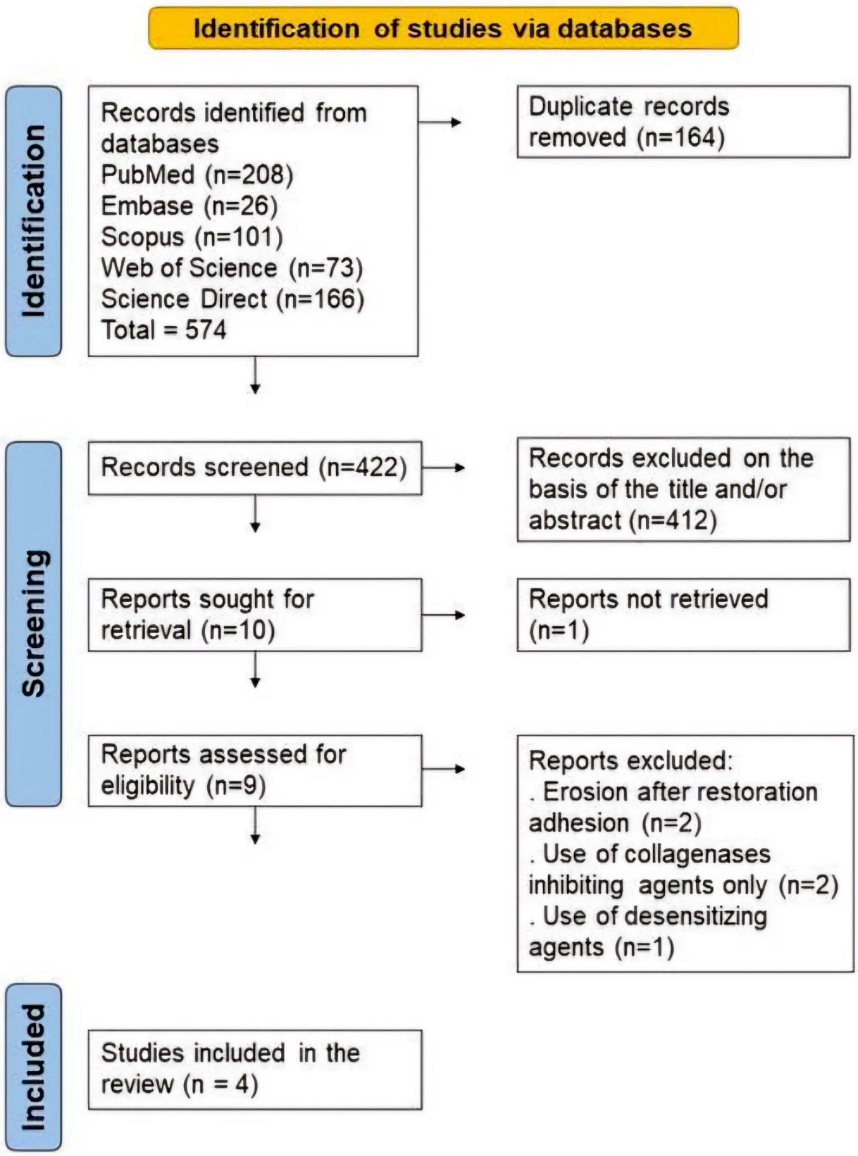

Figure 1. Search flowchart according to the PRISMA Statement.

Table 1. Main results of included studies.

Author Year Country	Anti-erosive pretreatments	Mode and time of application of the anti-erosive substance	Regions of tooth evaluated	Adhesive system (Adhesive strategy)	Bond stren-gth test (Storage time)	Statistical difference between untreated and treated eroded dentin groups	Predominant failure mode
Flury *et al*. (14) 2013 Switzerland	NaF solution (NaF 500 ppm, pH 4.5) Sn/F mouth rinse (Elmex® erosion protection, GABA International, Switzerland) (125 ppm F as amine fluoride [AmF], 375 ppm F as NaF, and 800 ppm Sn as $SnCl_2$, pH 4.5)	Anti-erosive solutions were applied after the first and the last demineralization period. (Cyclic de- and remineralization procedure was done 6 times per day for 10 days). Anti-erosive solutions were used for two minutes and then rinsed for 1 min with tap water.	Coronal surface	Clearfil SE Bond (SE)	Microtensile (24 h)	Sn/F-treated> NaF-treated > untreated eroded dentin	Untreated (Group 2a): Adhesive failures between adhesive system and dentin. NaF-treated (Group 3a): Adhesive failures between adhesive system and dentin. Sn/F-treated (Group 4a): Mixed adhesive failure.
Zumstein *et al*. (15) 2018 Switzerland	$SnCl_2$/AmF solution (800 ppm Sn^{2+}, 500 ppm F; pH 4.5)	Treatment was before application of the adhesive system. Solution was agitated 15 s, water rinse 15 s, and gently blow dry 5 s.	Coronal surface	Clearfil SE Bond (SE) Scotchbond Universal (SE)	Microtensile (24 h)	Clearfil SE Bond and Scotchbond Universal: $SnCl_2$/AmF-treated = untreated eroded dentin	Clearfil SE Bond and Scotchbond Universal: Untreated: Adhesive failure at dentin-adhesive interface. $SnCl_2$/AmF-treated: Adhesive failure at dentin-adhesive interface.
Krithi *et al*. (16) 2020 India	NaF-based paste (Glister, Amway enterprises, Hong Kong) CPP-ACP-based paste (GC Tooth Mousse, GC corporation, Japan) Novamin-based paste (Sensodyne, GSK Group of companies, India)	Paste was made into slurry by dissolving dentifrice (5 g) in water (10 ml) and then applied and brushed with the help of an electric toothbrush for 2 minutes. Paste was used after every acid challenge 3 times per day for 90 days.	Cervical surface	Adper Single Bond 2 (E&R) Clearfil SE Bond (SE)	Microshear (24 h)	Adper Single Bond 2 and Clearfil SE Bond: NaF-treated = CPP-ACP-treated = Novamin-treated = Untreated eroded dentin	Adper Single Bond 2 and Clearfil SE Bond: Fracture pattern was predominantly mixed in all groups.

Author Year Country	Anti-erosive pretreatments	Mode and time of application of the anti-erosive substance	Regions of tooth evaluated	Adhesive system (Adhesive strategy)	Bond stren-gth test (Storage time)	Statistical difference between untreated and treated eroded dentin groups	Predominant failure mode
Cardenas *et al.* (17) 2021 Brazil	12% silver diamine fluoride (SDF) solution (Cariestop Cariostatic, Biodinâmica LTDA, Brazil) 38% silver diamine fluoride (Riva Star, SDI Limited, Australia) with or without iodide potassium (KI) solution.	Solutions were applied after erosive demineralization and before application of the adhesive system. In E&R groups, solutions were applied after acid etching. 12% SDF: Application for 3 minutes, rinsing for 30 seconds and air drying for 5 seconds. 38% SDF with or without KI: Application of the silver capsule with a silver brush, application of solution from the green capsule (KI) until the creamy precipitate turns clear, and rinse for 30 s and air-dry for 5 seconds to keep the surface slightly moist.	Coronal surface	Clearfil Universal Bond Quick (E&R and SE) Scotchbond Universal (E&R and SE)	Microtensile (24 h)	Clearfil Universal Bond Quick (E&R and SE) and Scotchbond Universal (SE): 38% SDF with KI (A) = 38% SDF without KI (A) = 12% SDF (A,B) ≥ Untreated eroded dentin (B) Scotchbond Universal (E&R): 38% SDF with KI (A) = 38% SDF without KI (A) = 12% SDF (A) > Untreated eroded dentin (B)	Clearfil Universal Bond Quick (E&R and SE) and Scotchbond Universal (E&R and SE): Untreated eroded dentin: Adhesive and mixed failures. 12% SDF-treated: Adhesive and mixed failures. 38% SDF with KI-treated: Adhesive and mixed failures. 38% SDF without KI-treated: Adhesive and mixed failures.

E&R: Etch-and-rinse strategy; SE: Self-etch strategy; SDF: silver diamine fluoride; KI: iodide potassium.

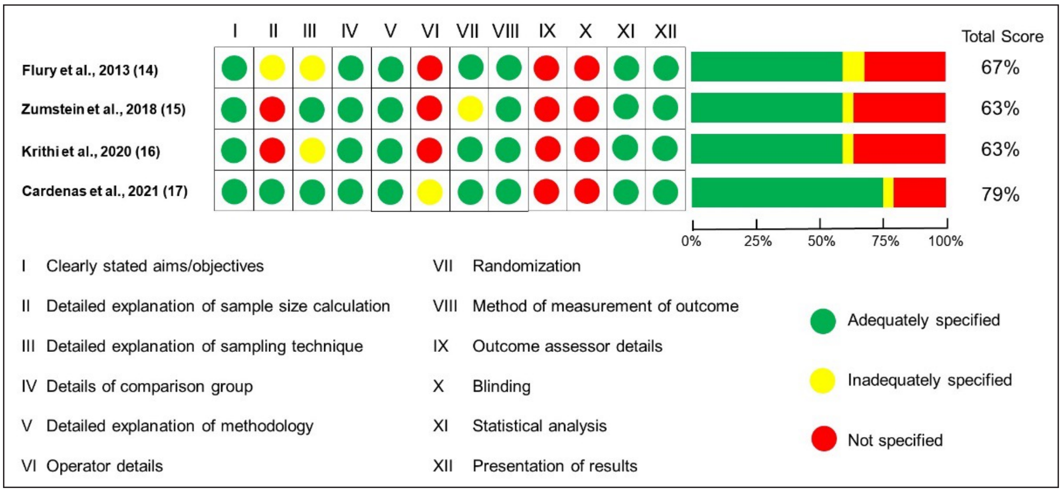

Figure 2. Risk of bias of included studies.

DISCUSSION

The results indicated that the effects of pretreatments on the bond strength of eroded dentin are inconsistent, with fluoride compounds such as sodium fluoride (NaF), tin-containing fluoride (Sn/F), and silver diamine fluoride ($Ag(NH_3)_2F$) showing improvements in adhesion. Conversely, CPP-ACP and Novamin demonstrated results comparable to untreated eroded dentin. Despite the promising findings, caution is warranted in interpreting these results due to the limited number of primary studies. Nevertheless, the synthesis presented in this systematic review is novel and original.

Fluoride compounds such as NaF, Sn/F, $Ag(NH_3)_2F$, and amine fluoride (AmF) address dentin hypersensitivity by forming a physical barrier through the precipitation of inorganic deposits on the dentin surface (18,19). Specifically, NaF showed promising bond strength results on eroded dentin when applied as a pure solution (14), in contrast to the water-diluted NaF-based dentifrice (16). These anti-erosive agents act on the dentin through several mechanisms. They generally form a protective layer on the tooth surface, modify the structure of hydroxyapatite crystals, alter the salivary pellicle, supply essential ions, neutralize acidity, and inhibit the activation of matrix metalloproteinases (MMPs). The actions above help protect the dentin from erosion and maintain its integrity (7,8).

When dentin undergoes erosion, minerals are depleted while the organic matrix remains intact. Thus, increased exposure of dentinal tubules and a fibrous intertubular structure occurs, creating a less adequate substrate for adhesion (5). Remineralization aims to restore the lost minerals and strengthen the dentin structure, recovering the mechanical properties and reducing the dentin permeability. Thus, the dentin becomes more suitable for adhesive procedures (20).

The efficacy of anti-erosive agents, such as fluoride and tin chloride, is significantly influenced by their concentrations. Variations in concentration across studies directly impact the bond strength to dentin, with higher concentrations potentially enhancing remineralization and increasing bond strength. Moreover, the method of application of these anti-erosive substances - whether through direct application, mouth rinse, or other methods

-plays a crucial role in determining the effectiveness of the treatment (14-17).

This variability may be attributed to the characteristics of the solutions used or to differences in the erosion challenge methodologies employed across the studies. However, other *in vitro* studies have reported a reduction in the progression of dentin erosion following the application of sodium fluoride (NaF) in various forms such as mouthwash, varnish, or dentifrice (21-23).

Mouthrinse applications can distribute anti-erosive agents more uniformly, resulting in more consistent outcomes on the treated surfaces. In contrast, direct applications may offer higher local concentrations but can lead to uneven distribution, affecting the uniformity of bond strength. Understanding the most effective application method is crucial in guiding clinical practices to optimize treatment outcomes (14-17).

A tin-containing fluoride (Sn/F) solution enhances bond strength values on eroded dentin by forming an amorphous acid-resistant layer (14). Moreover, Sn is retained on the negative charges of the demineralized organic matrix, making the collagen less polar and more accessible, which may contribute to these outcomes (22). However, the $SnCl_2$/AmF solution did not show improved bond strength, potentially due to differences in application methods. Flury *et al*. (14) applied the Sn/F solution for two minutes during the erosive challenge, whereas Zumstein *et al.* (15) applied the $SnCl_2$/AmF solution for only 15 seconds as an adhesive pretreatment.

Originally used to treat caries lesions, silver diamine fluoride has shown potential in remineralizing dentin and enhancing acid resistance. Bond strength studies on normal or carious dentin have shown no negative effects or improvement on adhesion (24-26), aligning with findings in this review (17). The mechanism by which silver diamine fluoride promotes the utilization of residual minerals as nucleation sites while inhibiting organic matrix metalloproteinases supports these positive results (27).

Krithi *et al*. (16), included in this synthesis, found that CPP-ACP-based and Novamin-based dentifrices did not improve bond strength compared to untreated eroded dentin. Casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) replaces Ca^{2+} and $[PO_4]^{-3}$ ions, forming a protective nanocoating layer against acids and its remineralizing effect is enhanced in the presence of fluoride (7,12). In erosive lesions, mineral deposition on the tooth surface results in higher microhardness values and reduced surface roughness (7). Calcium sodium phosphosilicate (NovaMin) is a bioactive glass capable of blocking dentinal tubules by forming apatite hydroxycarbonate, similar to hydroxyapatite (7,22). Some studies suggest that this compound and CPP-ACP increase acid resistance after tubular occlusion, potentially impeding adhesive infiltration (28).

Micro-tensile bond strength testing provides detailed insights into small, specific regions of a material and is less influenced by defects, although it is more technically challenging and time-consuming than traditional tensile strength testing. Conversely, traditional tensile bond strength testing is easier and faster, offering a general overview of bond strength in larger specimens. However, the macro test is more affected by defects, which can lead to decreased tensile strength and potentially less accurate results for uniform material evaluation (29).

The study by Zumstein *et al*. (15) was the only one that analyzed long-term bond strength, indicating a limitation in this synthesis, as long-term evaluations are crucial in assessing the degradation of the adhesive interface over time. However, the studies included in this review varied the substances used and adhesive strategies, with the strategy not shown to affect the performance of the adhesives, which were primarily universal and self-etch adhesive systems (14-17). This review allowed for a consideration that did not interfere with the comparative analysis between anti-erosive substances. Regarding these adhesive systems, the presence of the functional monomer 10-MDP, which can form stable calcium and phosphate complexes on hydroxyapatite, may also be favored by the greater presence of mineral sites in the treated substrate (30).

Future perspectives include the *in vitro* evaluation of additional anti-erosion substances as adhesive pretreatment on eroded dentin, particularly those with enhanced dentinal tubule penetration properties, such as nanoparticulate compounds. Additionally, innovative options for inducing regeneration of damaged dental tissues, such as silica particles and regenerative therapy with biomaterials and growth factors, are under consideration. Further inclusion of long-term analyses would be valuable to understand how non-invasive treatments of non-carious lesions may affect the durability of restorations on this substrate.

CONCLUSION

This systematic review showed that CPP-ACP and Novamin applied as a pretreatment of eroded dentin did not alter bond strength, while fluoride substances such as NaF, Sn/F and ($Ag(NH_3)_2F$) improved bond strength. However, further primary studies evaluating the same substances could be conducted to enhance the reliability of the results found in this synthesis study.

AUTHOR CONTRIBUTION STATEMENT

Conceptualization, design and writing-original draft: B.B.T.L.C.S and B.C.D.B
Literature review, methodology, data curation, Writing-proofreading and editing: B.B.T.L.C.S. and R.A.S.J.
Supervision and critical review: M.J.F.C., C.P.H. and B.C.D.B.

CONFLICT OF INTEREST

The authors of the manuscript "Does the application of anti-erosive substances on eroded dentin affect bond strength? A systematic review" declare no conflict of interest.

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