International Journal of
Molecular Sciences

MDPI

Review

Biomimetic Remineralization Strategies for Dentin Bond Stability—Systematic Review and Network Meta-Analysis

Rosário Costa [1,*], Joana Reis-Pardal [2,3], Sofia Arantes-Oliveira [4], João Cardoso Ferreira [1], Luis Filipe Azevedo [2,3] and Paulo Melo [1,5]

[1] Faculty of Dental Medicine, Department of Operative Dentistry, University of Porto, Rua Dr. Manuel Pereira da Silva, 4200-393 Porto, Portugal; jcferreira@fmd.up.pt (J.C.F.); pmelo@fmd.up.pt (P.M.)
[2] CINTESIS@RISE—Center for Health Technology and Services Research (CINTESIS), Health Research Network Associated Laboratory (RISE), University of Porto, 4200-450 Porto, Portugal; jrpardal@med.up.pt (J.R.-P.); lazevedo@med.up.pt (L.F.A.)
[3] Department of Community Medicine, Information and Health Decision Sciences (MEDCIS), Faculty of Medicine, University of Porto, Alameda Prof. Hernâni Monteiro, 4200-319 Porto, Portugal
[4] Department of Dental Biomaterials, Faculty of Dental Medicine, University of Lisbon, Cidade Universitária, Rua Prof.ª Teresa Ambrósio, 1600-277 Lisbon, Portugal; sofiaaol@campus.ul.pt
[5] EpiUnit, ITR, Institute of Public Health, University of Porto, Rua das Taipas, n° 135, 4050-600 Porto, Portugal
* Correspondence: mrcosta@fmd.up.pt; Tel.: +351-220-901-100

Abstract: This systematic review and network meta-analysis aimed to evaluate the bond strength of artificial caries-affected dentin (ACAD) of permanent human teeth with and without biomimetic remineralization (BR), assessed based on in vitro studies. Following PRISMA guidelines, we conducted a systematic search until June 2023, identifying 82 eligible articles for full-text analysis. We assessed the study characteristics, methodological quality, and summary results. Bond strength was examined immediately and after artificial aging using three bond strength tests. We performed meta-regressions (using OpenBUGS software) to explore the relationship between the independent variable's adhesive application technique (Etch-and-Rinse or Self-Etch) and ACAD protocol (chemical or biological) and the dependent variable of bond strength. Additionally, we conducted random-effect NMAs (using CINEMA software) to compare the effect of multiple interventions per application technique and ACAD protocol simultaneously. Among the included studies that compared various BR strategies, most studies (19 out of 22) presented a medium risk of bias. In some comparisons, the meta-regression results revealed a significant association between bond strength at 24 h and both the adhesive application technique and the ACAD protocol. Our findings indicate the potential of BR to enhance bond strength in human ACAD in in vitro settings.

Keywords: adhesives; biomimetic material; dentin-bonding agents; tooth demineralization; tooth remineralization

Academic Editors: Iacob Bogdan-Cezar and Ede Bodoki

Received: 1 March 2025
Revised: 5 April 2025
Accepted: 6 April 2025
Published: 8 April 2025

Citation: Costa, R.; Reis-Pardal, J.; Arantes-Oliveira, S.; Ferreira, J.C.; Azevedo, L.F.; Melo, P. Biomimetic Remineralization Strategies for Dentin Bond Stability—Systematic Review and Network Meta-Analysis. *Int. J. Mol. Sci.* **2025**, *26*, 3488. https://doi.org/10.3390/ijms26083488

1. Introduction

Dentin-bonding procedures pose persistent challenges in Operative Dentistry despite the currently significant successes achieved in enamel bonding [1]. A well-documented issue in the literature is the gradual deterioration of the adhesive systems' bond strength to dentin over time, primarily due to hybrid layer degradation [2]. This compromise in dentin bonding significantly limits the lifespan of adhesive restorations [3].

The ideal dentin-bonding process involves exposing the collagen network and facilitating the penetration of chelating agents or acidic functional monomers to form the

crucial hybrid layer [4]. However, a portion of the exposed collagen matrix remains unfilled with resin monomers, rendering it susceptible to hydrolytic degradation over time, thus jeopardizing the longevity of dentin bonding due to nanoleakage. The incomplete water removal within hydrophilic resin monomers also creates a weak point in resin-dentin bonds [5,6]. These phenomena have led to the exploration of an innovative approach to improve dentin adhesion: the biomimetic remineralization (BR) of collagen fibrils exposed during biomineralization [7,8].

There are two primary BR strategies: incorporating mineral-promoting agents into adhesives or restorative materials and applying pre-treating solutions before adhesive systems [9,10]. For the first strategy, researchers have developed experimental adhesive systems or restorative materials containing bioactive components like calcium phosphate or other inorganic materials that supply mineral ions to remineralize the resin–dentin interface [11,12]. The second strategy involves solutions containing non-collagenous proteins or template analogs to stimulate intra/extra-fibrillar mineralization [13,14]. These remineralizing agents facilitate the formation of nanometric apatite crystals, which replace excess water, mimicking physiological remineralization [14], thus enhancing the structural integrity of dentin and extending the longevity of the dentin–composite resin bonding interface [7,15,16]. Some studies have also suggested that these agents can inhibit the degradation of exposed collagen by attracting calcium to it [17].

Therefore, it is essential to analyze the challenges posed by dentin-bonding procedures and the potential advantages of BR procedures. This systematic review uses a comprehensive network meta-analysis (NMA) to assess and compare the bond strength of human artificial caries-affected dentin (ACAD) with and without BR evaluated in in vitro studies.

2. Materials and Methods

2.1. Search Strategy

This systematic review was registered in PROSPERO and performed according to the PRISMA statement [18]. On June 2023, PubMed, ISI Web of Science, and SCOPUS were searched to identify potentially relevant studies. In addition to electronic databases, reference lists of included studies and relevant systematic reviews were also searched. The complete search strategies are available in Appendix A.

2.2. Outcomes

The primary outcome of this systematic review was determining the mean difference between the bond strength of ACAD with and without BR using different adhesive application techniques, including Etch-and-Rinse (ER) or Self-Etch (SE), and ACAD protocols, including chemical or biological.

2.3. Eligibility Criteria

The following inclusion criteria were established: experimental or quasi-experimental in vitro studies investigating the influence of any BR procedure on the ACAD–adhesive interface's bond strength; having a control group (dentin without BR) for comparison; ACAD protocols in which agents were applied immediately prior to bonding; outcomes measured based on shear, micro-shear, or micro-tensile bond strength (SBS, μSBS, μTBS) tests. The exclusion criteria included studies with doped materials or modified adhesive systems.

The terms "caries-affected dentin", "demineralized dentin", and "artificial eroded dentin" were considered as references to ACAD. ACAD consists of human dentin tissue artificially demineralized to mimic the characteristics of dentin affected by carious changes. It is created by exposing dentin tissue to acidic or demineralizing solutions to remove mineral content, leading to softening and structural alterations like those observed in

natural caries-affected dentin [19–21]. This demineralization process is performed in a laboratory setting to replicate the conditions and properties of carious dentin.

The BR procedures considered included any technique aimed at restoring and strengthening damaged or demineralized dentin in a way that mimicked the tooth's natural remineralization process [3,22].

2.4. Data Extraction and Collection

Firstly, two authors (RC and JP) independently reviewed titles and abstracts to select articles for further assessment per their consensus. Disagreements were resolved by discussion until a consensus was reached. Full texts of the selected articles were retrieved, and the same two authors further evaluated and independently extracted data from them. The reference lists of the included full texts were also screened and cross-referred.

In the case of missing/unclear items (e.g., missing bond strength measurements, missing standard deviation values, uncertain number of samples used) or inconsistent data within or between sources (e.g., differences in data between text and figures, bond strength measurements only in figures), the authors of the respective studies were contacted via e-mail. Two follow-up e-mails were sent with a one-week interval.

The search results from the online databases were imported to Endnote20 (Clarivate, Philadelphia, USA), where duplicates were removed. The Rayyan app [23] was used to keep records and assist in abstract screening, full-text review, and data extraction. Data for the systematic review and NMA were extracted using a custom-made Excel worksheet.

The following items were extracted from each source: authors; year of publication; study randomization; risk of bias; means and standard deviations; number of samples; ACAD protocol (chemical or biological); BR procedure; adhesive type used (ER, SE, or universal) and adhesive application technique; method of bond strength assessment; outcome measurement time point (24 h or after artificial aging method).

The authors classified and grouped the treatments by active substance into nine groups: fluorine, calcium phosphate, peptide, silica, hydroxyapatite, flavonoids, calcium, and 2-hydroxyethyl methacrylate/ethylene glycol dimethacrylate (HEMA/EDGMA).

2.5. Risk of Bias Assessment

Two authors (RC and JP) independently assessed the risk of bias in the included in vitro studies according to the QUIN tool [24]. Disagreements were resolved by discussion until a consensus was reached. Each study was graded accordingly as having high, medium, or low risk based on the final score of the tool: low risk of bias if >70%, medium risk of bias if 50–70%, and high risk of bias if <50%.

2.6. Data Synthesis and Statistical Analysis

2.6.1. Qualitative Synthesis

Qualitative evidence synthesis was performed via descriptive analysis of the studies' characteristics, methodologic quality, and summary results using a narrative description and summary tables, providing a clear overview of the individual study characteristics, main findings, and methodological assessments.

2.6.2. Quantitative Synthesis

Quantitative syntheses were performed via random-effects NMA of the mean difference between the intervention and control groups. NMAs were conducted using the CINEMA software (https://cinema.ispm.unibe.ch/), based on the R software (https://www.r-project.org/) packages meta an netmeta [25,26], using the adhesive application technique and ACAD protocol and including all possible pair-wise comparisons based on direct and indirect evidence. In accordance with the Cochrane guidelines [27], when trials had more than two arms, we

combined interventions into a single group if they belonged to the same intervention category. When more than one independent treatment–comparator pair existed in each study, we treated them as if they pertained to independent studies. Following the Cochrane guidelines [27], standard deviations were imputed from other included studies in cases where they were not available in the manuscript and could not be obtained upon contact with the authors.

The rating of confidence in the results was assessed following the CINEMA approach by evaluating the following domains: within-study bias, reporting bias, indirectness, imprecision, heterogeneity, and incoherence. The minimal clinically important difference was established by consensus of the authors as 7 megapascals (MPa).

In addition, since it has been reported that the adhesive application technique (ER vs. SE) [8,25–27] and the ACAD protocol (chemical vs. biological) [7,28] might influence the BR treatment's effect, we explored the effects of these two covariates in NMA effects estimates based on random-effects Bayesian meta-regressions using the OpenBUGS software version 3.2.3 (Code in Appendix A). Within a random-effects Bayesian framework, the OpenBUGS software [28] was also used to estimate each intervention's posterior median ranks and probability to be the best.

Finally, to assess the robustness of the results obtained from NMAs, as assumptions change, we conducted the following two sensitivity analyses:

1. Random selection of one treatment intervention: Instead of combining interventions belonging to the same intervention category, as in the main analysis, we randomly selected only one.
2. Removal of SBS test results: Instead of including all bond strength tests, as in the main analysis, we included only results from μSBS and μTBS tests.

3. Results and Discussion

3.1. Search Results

In the electronic search, 1874 records were identified after eliminating duplicates. Only 82 were selected for full-text screening. The reasons for the exclusion of screened full texts are shown in Appendix A Table A1. After critical appraisal, 23 remaining articles were included in our systematic review and 22 in the NMA. A PRISMA flow diagram of the complete process is illustrated in Figure 1.

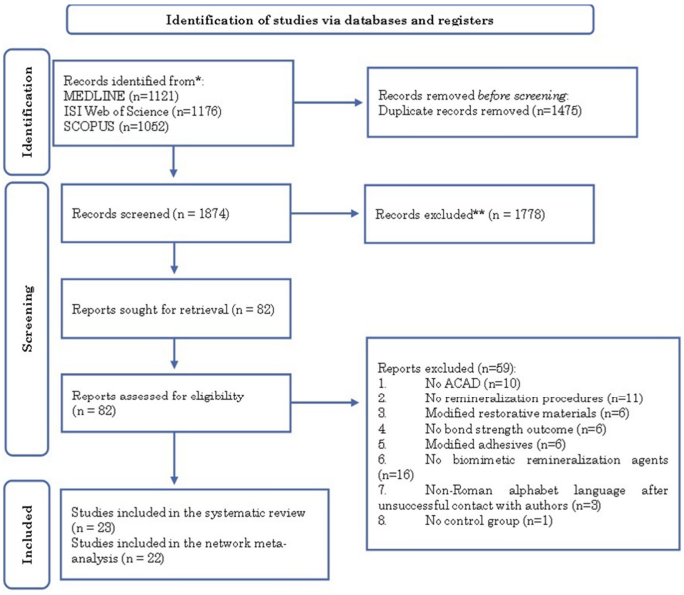


Figure 1. PRISMA 2020 flow diagram of literature search for new systematic reviews [18]. Identification *; screening **.

3.2. Characteristics of Included Studies

Table 1 displays the characteristics of the included studies, interventions, and outcomes. Of the 23 studies in the systematic review, 16 were experimental [8,15,29–42] and 7 were quasi-experimental [7,14,43–47]. One study was excluded from the NMA because it lacked reporting data, which could not be obtained upon direct contact with the authors (Appendix A Tables A2–A4).

All 22 studies in the NMA performed immediate (24 h) bond strength measurements. Of these studies, 13 investigated the ER technique associated with the chemical ACAD protocol [7,8,29–31,33–35,38–40,46], 5 investigated the ER with the biological ACAD [7,15,32,37,44], 13 investigated the SE with the chemical ACAD [8,14,31,33–36,41,43,45,47–49], and only 1 investigated the SE with the biological ACAD [37]; the latter was insufficient to perform an NMA. In turn, 11 studies measured bond strength after artificial aging of the specimens: 4 used thermocycling [14,32,38,50], and 7 stored them in a fluid solution for months [15,29,39,40,43,44,47].

Overall, both immediate and aged bond strength in the ACAD benefited from BR. The artificial aging method globally diminished bond strength values, and thermocycling caused the lowest bond strength.

Table 1. Characteristics of the included studies, interventions, and outcomes.

	Study/Year	RoB (Score)	Study Type	ACAD	BRP	Groups	N (Teeth)	Mean (SD)	AT	OM Test
24 h measurement										
ER + C	Altinci et al., 2018 [40]	M (50)	Exp.	32% phosphoric acid	Control	Control	9	35.27 (4.63) [a]	ER	µTBS
					F	NaF + 6 mM F		34.7 (4.63) [a]		
						NaF + 24 mM F		54.66 (4.63) [a]		
						NaF + 179 mM F		47.11 (4.63) [a]		
						KF + 6 mM F		51.8 (4.63) [a]		
						KF + 24 mM F		48.56 (4.63) [a]		
						KF + 179 mM F		47.58 (4.63) [a]		
						CaF2 + 6 mM F		36.34 (4.63) [a]		
						CaF2 + 24 mM F		39.49 (4.63) [a]		
						CaF2 + 179 mM F		48.47 (4.63) [a]		
						Excite F		48.84 (4.63) [a]		
	Barbosa-Martins et al. (A) 2018 [8]	M (54)	Exp.	6% CMC	Control	Control	6	26.38 (8.64)	ER	µTBS
					F	NaF		33.43 (10.41)		
					CaP	CPP-ACP		45.25 (8.82)		
					Pept.	P11-4		46.42 (12.03)		
	Barbosa-Martins et al. (B) 2018 [7]	M (54)	Quasi-Exp.	6% CMC	Control	Control	6	21.96 (5.92)	ER	µTBS
					F	NaF		33.43 (10.42)		
					CaP	CPP-ACP		45.25 (8.83)		
					Pept.	P11-4		46.42 (12.03)		
	Bauer et al., 2018 [29]	M (50)	Exp.	35% phosphoric acid	Control	Control	13	17 (4.1)	ER	SBS
					CaP	5% NbG		17.9 (5)		
						10%NbG		15.8 (6.4)		
						20%NbG		16.6 (4.4)		
						40%NbG		15.8 (4.1)		

Table 1. *Cont.*

	Study/Year	RoB (Score)	Study Type	ACAD	BRP	Groups	N (Teeth)	Mean (SD)	AT	OM Test
ER + C	Cardenas et al., 2021 [30]	M (63)	Exp.	pH cycling	Control	Control	5	33.74 (3.6)	Univ.	µTBS
					F	SDF 12%		38.03 (3.5)		
						SDF 38%		39.68 (2.7)		
						SDF 38% without KI		39.38 (2.5)		
					Control	Control		34.9 (3.3)		
					F	SDF 12%		42.45 (2.9)		
						SDF 38%		40.47 (4.2)		
						SDF 38% without KI		41.3 (2.5)		
	Chen et al., 2020 [c]	M (54)	Quasi-Exp.	pH cycling	Control	Control	4	13.8 (3.35) [a]	Univ.	µTBS
					CaP	Ca/P-PILP		23.8 (3.35) [a]		
					Pept.	PAA-PASP		14 (3.35) [a]		
					CaP	Ca/P		11.9 (3.35) [a]		
	Cifuentes-Jimenez et al., 2021 [31]	M (50)	Exp.	pH cycling	Control	Control	5	31.4 (4.63) [a]	ER	µTBS
					F	Cariestop		15.1 (4.63) [a]		
						RivaStar1		10.1 (4.63) [a]		
						RivaStar2		7.5 (4.63) [a]		
						Saforide		23.2 (4.63) [a]		
	Gungormus et al., 2021 [33]	M (50)	Exp.	37% phosphoric acid	Control	Control	10	15.38 (1.3)	ER	SBS
					CaP	NPR 60 min		15.85 (1.44)		
					Pept.	PR 10 min		20.81 (1.74)		
						PR 30 min		20 (1.68)		
						PR 60 min		16.21 (1.1)		
	Krithi et al., 2020 [34]	M (54)	Exp.	0.5% citric acid	Control	Control	15	11.83 (0.43)	ER	µSBS
					F	NaF		11.56 (0.15)		
					CaP	CPP-ACP		12.12 (0.57)		
						Novamin		11.66 (0.28)		
					Ca	Non-Fidated		11.94 (0.27)		
	Meng et al., 2021 [35]	M (50)	Exp.	1% citric acid	Control	Control	8	46.8 [b] (4.63) [a]	Univ.	µTBS
					Hap	Biorepair		50.72 [b] (4.63) [a]		
						Dontodent Sensitive		50.71 [b] (4.63) [a]		
						nHAp		51.24 [b] (4.63) [a]		
					Control	Control		50.41 [b] (4.63) [a]		
					Hap	Biorepair		53.38 [b] (4.63) [a]		
						Dontodent Sensitive		54.5 [b] (4.63) [a]		
						nHAp		55.63 [b] (4.63) [a]		
					Control	Control		46.85 [b] (4.63) [a]		
					Hap	Biorepair		50.77 [b] (4.63) [a]		
						Dontodent Sensitive		53.82 [b] (4.63) [a]		
						nHAp		55 [b] (4.63) [a]		
	Pulidindi et al., 2021 [38]	M (63)	Exp.	37% phosphoric acid	Control	Control	15	48.84 (4.63) [a]	ER	µTBS
					Pept.	P11-4		38.66 (4.63) [a]		
					CaP	CPP-ACP		34.07 (4.63) [a]		
					Control	Control		22.63 (4.63) [a]		
					Pept.	P11-4		25.37 (4.63) [a]		
					CaP	CPP-ACP		23.62 (4.63) [a]		

Table 1. *Cont.*

	Study/Year	RoB (Score)	Study Type	ACAD	BRP	Groups	N (Teeth)	Mean (SD)	AT	OM Test
ER + C	Van Duker et al., 2019 [46]	H (46)	Quasi-Exp.	7 days in ADS	Control	Control	10	23.5 (10.7)	Univ.	µTBS
					F	SDF 38%		19.8 (8.4)		
						SDF 38% without KI		7.9 (6.6)		
	Yang et al., 2018 [39]	M (50)	Exp.	1% citric acid	Control	Control	10	46.5 [b] (4.63) [a]	ER	µTBS
					CaP	CPP-ACP		42.6 [b] (4.63) [a]		
						Novamin		43.3 [b] (4.63) [a]		
					Control	Control		22.3 [b] (4.63) [a]		
					CaP	CPP-ACP		41.2 [b] (4.63) [a]		
						Novamin		31.4 [b] (4.63) [a]		
ER + B	Barbosa-Martins et al. (B) 2018	M (54)	Quasi-Exp.	BHI+ S.Mutans	Control	Control	6	22.89 (2.68)	ER	µTBS
					F	NaF		26.94 (6.7)		
					CaP	CPP-ACP		47.95 (6.69)		
					Pept.	P11-4		42.07 (7.83)		
	Dávila-Sánchez et al., 2020 [32]	M (54)	Exp.	Cariogenic + S. Mutans	Control	Control	7	14.42 (4.43)	Univ.	µTBS
					Fls.	QUE		24.58 (4.9)		
						HES		18.41 (5.3)		
						RUT		26 (5.51)		
						NAR		24.64 (3.7)		
						PRO		20.66 (3.92)		
	de Sousa et al., 2019 [44]	M (50)	Quasi-Exp.	Cariogenic + S. Mutans	Control	Control	8	21.07 (3.24)	ER	µTBS
					Pept.	P11-4		42.07 (7.83)		
	Moreira et al., 2021 [15]	M (54)	Exp.	Cariogenic + S. Mutans	Control	Control	8	25.4 (2.45)	ER	µTBS
					F	NaF		25.47 (4.8)		
					CaP	CPP-ACP		41.79 (5.85)		
					Pept.	P11-4		40.12 (3.62)		
	Siqueira et al., 2020 [37]	M (63)	Exp.	Cariogenic + S. Mutans	Control	Control	5	16.81 (3.5)	Univ.	µTBS
					F	SDF 12%		21.11 (4.1)		
						SDF 38%		24.36 (3.4)		
					Control	Control		19.89 (2.4)		
					F	SDF 12%		24.47 (3.4)		
						SDF 38%		26.32 (2)		
SE + C	Atomura et al., 2018 [43]	H (46)	Quasi-Exp.	7 days in ADS	Control	Control	unknown	48.3 (13)	SE	µTBS
					F	NaF		47.7 (8.6)		
						FCP complex		43.9 (14.3)		
	Barbosa-Martins et al. (A) 2018 [8]	M (54)	Exp.	48 h 6% CMC	Control	Control	6	25.38 (8.58)	SE	µTBS
					F	NaF		35.59 (9.18)		
					CaP	CPP-ACP		48.11 (11.71)		
					Pept.	P11-4		25.7 (8.95)		
	Cardenas et al., 2021 [30]	M (63)	Exp.	pH cycling	Control	Control	5	33.74 (3.6)	Univ.	µTBS
					F	SDF 12%		39.53 (4.2)		
						SDF 38%		41.31 (2)		
						SDF 38% without KI		40.55 (2.9)		
					Control	Control		36.56 (4.1)		
					F	SDF 12%		39.98 (1.7)		
						SDF 38%		41.08 (3)		
						SDF 38% without KI		41.57 (2.4)		

Table 1. *Cont.*

	Study/Year	RoB (Score)	Study Type	ACAD	BRP	Groups	N (Teeth)	Mean (SD)	AT	OM Test
SE + C	Chen et al., 2020 [14]	M (54)	Quasi-Exp.	pH cycling	Control	Control	4	13.8 (3.35) [a]	Univ.	μTBS
					CaP	Ca/P-PILP		23.8 (3.35) [a]		
					Pept.	PAA-PASP		14 (3.35) [a]		
					CaP	Ca/P		11.9 (3.35) [a]		
					Control	Control		9.2 (3.35) [a]		
					CaP	Ca/P-PILP		15.1 (3.35) [a]		
					Pept.	PAA-PASP		9.3 (3.35) [a]		
					CaP	Ca/P		9.8 (3.35) [a]		
	Cifuentes-Jimenez et al., 2021 [31]	M (50)	Exp.	pH cycling	Control	Control	5	31.4 (3.35) [a]	SE	μTBS
					F	Cariestop		9.6 (3.35) [a]		
						Saforide		8.03 (3.35) [a]		
	Gungormus et al., 2021 [33]	M (50)	Exp.	37% phosphoric acid	Control	Control	10	15.38 (1.3)	SE	SBS
					CaP	NPR 60 min		15.49 (1.17)		
					Pept.	PR 10 min		18.93 (0.99)		
						PR 30 min		19.62 (0.9)		
						PR 60 min		21.73 (1.57)		
	Krithi et al., 2020 [34]	M (54)	Exp.	0.5% citric acid	Control	Control	15	11.83 (0.43)	SE	μSBS
					F	NaF		12.4 (0.18)		
					CaP	CPP-ACP		11.97 (0.39)		
						Novamin		11.97 (0.17)		
					Ca	Non-Fidated		10.62 (0.11)		
	Meng et al., 2021 [35]	M (50)	Exp.	1% citric acid	Control	Control	8	46.8 [b] (3.35) [a]	Univ.	μTBS
					Hap	Biorepair		47.62 [b] (3.35) [a]		
						Dontodent Sensitive		51.89 [b] (3.35) [a]		
						nHAp		51.89 [b] (3.35) [a]		
					Control	Control		56.3 [b] (3.35) [a]		
					Hap	Biorepair		51.62 [b] (3.35) [a]		
						Dontodent Sensitive		57.47 [b] (3.35) [a]		
						nHAp		58.39 [b] (3.35) [a]		
					Control	Control		56.8 [b] (3.35) [a]		
					Hap	Biorepair		52.25 [b] (3.35) [a]		
						Dontodent Sensitive		50.8 [b] (3.35) [a]		
						nHAp		56.1 [b] (3.35) [a]		
	Paik et al., 2022 [42]	M (50)	Exp.	35% phosphoric acid	Control	Control	4	21.66 (3.35) [a]	Univ.	μTBS
					Fls.	ICT		24.4 (3.35) [a]		
						FIS		26.81 (3.35) [a]		
						SIB		25.65 (3.35) [a]		
						CPIC		25.97 (3.35) [a]		
						ICT + C		30.63 (3.35) [a]		
						FIS + C		25.63 (3.35) [a]		
						SIB + C		24.76 (3.35) [a]		

Table 1. *Cont.*

	Study/Year	RoB (Score)	Study Type	ACAD	BRP	Groups	N (Teeth)	Mean (SD)	AT	OM Test
SE + C	Pei et al., 2019 [36]	M (50)	Exp.	1% citric acid	Control	Control	4	43.61 (3.35) [a]	SE	µTBS
					Hap	Biorepair		33.16 (3.35) [a]		
						Dontodent Sensit.		35.41 (3.35) [a]		
						nHAp		46.92 (3.35) [a]		
					Control	Control		47.47 (3.35) [a]		
					Hap	Biorepair		43.47 (3.35) [a]		
						Dontodent Sensit.		42.3 (3.35) [a]		
						nHAp		41.24 (3.35) [a]		
	Priya et al., 2020 [45]	H (46)	Quasi-Exp.	37% phosphoric acid	Control	Control	13	6.677 (1.254)	Univ.	SBS
					F	VivaSens		3.332 (0.78)		
						MS Coat F		3.127 (0.478)		
					HEMA	GLUMA Desensit.		4.572 (0.718)		
						Systemp		9.697 (1.127)		
	Zang et al., 2018 [41]	M (50)	Exp.	37% phosphoric acid	Control	Control	6	19.73 [b] (2.108)	Univ.	SBS
					SiO_2	Charged meso-porous		20.57 [b] (2.244)		
	Zumstein et al., 2018 [47]	M (50)	Quasi-Exp.	pH cycling	Control	Control	20	24.7 (8.1) [c]	SE	µTBS
					F	$SnCl_2$/AmF4		23.3 (8.2) [c]		
					Control	Control		23.73 (8) [c]	Univ.	
					F	$SnCl_2$/AmF4		21.39 (6.8) [c]		
SE + B	Siqueira et al., 2020 [37]	M (63)	Exp.	Cariogenic + S. Mutans	Control	Control	5	16.81 (3.5)	Univ.	µTBS
					F	SDF 12%		20.02 (4.6)		
						SDF 38%		25.21 (3)		
					Control	Control		19.61 (3.3)		
					F	SDF 12%		23.82 (4.4)		
						SDF 38%		27.16 (3.6)		
TMC measurement										
ER + C	Pulidindi et al., 2021 [38]	M (63)	Exp.	37% phosphoric acid	Control	Control	15	48.84 (4.63) [a]	ER	µTBS
					Pept.	P11-4		25.37 (4.63) [a]		
					CaP	CPP-ACP		23.62 (4.63) [a]		
ER + B	Dávila-Sánchez et al., 2020 [32]	M (54)	Exp.	Cariogenic + S. Mutans	Control	Control	7	14.42 (4.43)	Univ.	µTBS
					Fls.	QUE		12.02 (5.21)		
						HES		15.73 (6.07)		
						RUT		21.08 (4.75)		
						NAR		22.12 (2.92)		
						PRO		17.2 (2.72)		
SE + C	Chen et al., 2020 [14]	M (54)	Quasi-Exp.	pH cycling	Control	Control	4	13.8 (3.35) [a]	Univ.	µTBS
					CaP	Ca/P-PILP		15.1 (3.35) [a]		
					Pept.	PAA-PASP		9.3 (3.35) [a]		
					CaP	Ca/P		9.8 (3.35) [a]		
	Paik et al., 2022 [42]	M (50)	Exp.	35% phosphoric acid	Control	Control	4	21.66 (3.35) [a]	Univ.	µTBS
					Fls.	ICT		20.53 (3.35) [a]		
						FIS		19.4 (3.35) [a]		
						SIB		22.04 (3.35) [a]		
						CPIC		23.43 (3.35) [a]		
						ICT + C		26.74 (3.35) [a]		
						FIS + C		23.42 (3.35) [a]		
						SIB + C		25.17 (3.35) [a]		

Table 1. *Cont.*

	Study/Year	RoB (Score)	Study Type	ACAD	BRP	Groups	N (Teeth)	Mean (SD)	AT	OM Test
Storage in a fluid solution for 3-month measurement										
ER + C	Bauer et al., 2018 [29]	M (50)	Exp.	35% phosphoric acid	Control	Control	13	17 (4.1)	ER	SBS
					CaP	5% NbG		11.8 (3.7)		
						10%NbG		13.9 (3.2)		
						20%NbG		13.2 (2.7)		
						40%NbG		14.7 (2.9)		
SE + C	Atomura et al., 2018 [43]	H (46)	Quasi-Exp.	7 days in ADS	Control	Control	unknown	48.3 (13)	SE	µTBS
					F	NaF		42.6 (12.1)		
						FCP complex		47.4 (9.2)		
Storage in a fluid solution for 6-month measurement										
ER + C	Altinci et al., 2018 [40]	M (50)	Exp.	32% phosphoric acid	Control	Control	9	35.27 (4.63) [a]	ER	µTBS
					F	NaF + 6 mM F		50.31 (4.63) [a]		
						NaF + 24 mM F		49.28 (4.63) [a]		
						NaF+179 mM F		47.73 (4.63) [a]		
						KF + 6 mM F		41.95 (4.63) [a]		
						KF + 24 mM F		51.53 (4.63) [a]		
						KF + 179 mM F		54.29 (4.63) [a]		
						CaF2 + 6 mM F		52.25 (4.63) [a]		
						CaF2+24 mM F		41.1 (4.63) [a]		
						CaF2+179 mM F		40.85 (4.63) [a]		
						Excite F		46.22 (4.63) [a]		
	de Sousa et al., 2019 [44]	M (50)	Quasi-Exp.	Cariogenic + S. Mutans	Control	Control	8	21.07 (3.24)	ER	µTBS
					Pept.	P11-4		31.98 (3.44)		
	Moreira et al., 2021 [15]	M (54)	Exp.	Cariogenic + S. Mutans	Control	Control	8	25.4 (2.45)	ER	µTBS
					F	NaF		18.36 (5.5)		
					CaP	CPP-ACP		36.55 (4.27)		
Storage in a fluid solution for 12-month measurement										
ER + C	Altinci et al., 2018 [40]	M (50)	Exp.	32% phosphoric acid	Control	Control	9	35.27 (4.63) [a]	ER	µTBS
					F	NaF + 6 mM F		51.63 (4.63) [a]		
						NaF + 24 mM F		45.56 (4.63) [a]		
						NaF + 179 mM F		39.31 (4.63) [a]		
						KF + 6 mM F		40.01 (4.63) [a]		
						KF + 24 mM F		51.85 (4.63) [a]		
						KF + 179 mM F		36.48 (4.63) [a]		
						CaF2 + 6 mM F		33.06 (4.63) [a]		
						CaF2 + 24 mM F		38.24 (4.63) [a]		
						CaF2 + 179 mM F		0.88 (4.63) [a]		
						Excite F		42.4 (4.63) [a]		

Table 1. *Cont.*

	Study/Year	RoB (Score)	Study Type	ACAD	BRP	Groups	N (Teeth)	Mean (SD)	AT	OM Test
ER + C	Yang et al., 2018 [39]	M (50)	Exp.	1% citric acid	Control	Control	10	46.5 [b] (4.63) [a]	ER	µTBS
					CaP	CPP-ACP		41.2 [b] (4.63) [a]		
						Novamin		31.4 [b] (4.63) [a]		
SE + C	Zumstein et al., 2018 [51]	M (50)	Quasi-Exp.	pH cycling	Control	Control	20	24.7 (8.1) [c]	SE	µTBS
					F	SnCl2/AmF4		16.3 (6.36) [c]		
					Control	Control		15.43 (6.53) [c]	Univ.	
					F	SnCl2/AmF4		14.12 (7.12) [c]		
Storage in a fluid solution for 18-month measurement										
ER + B	Moreira et al., 2021 [15]	M (54)	Exp.	Cariogenic + S. Mutans	Control	Control	8	25.4 (2.45)	ER	µTBS
					F	NaF		7.81 (4.48)		
					CaP	CPP-ACP		26.01 (3.28)		
					Pept.	P11-4		25.24 (3.98)		

[a]—Input SD Values; [b]—Information given by authors; [c]—Information from another meta-analysis. Legend: B—Biological; C—Chemical; RoB—Risk of bias; ACAD—Artificial caries-affected dentin; BRP—Biomimetic remineralization procedure; SD—Standard deviation; AT—Adhesive technique; OM—Outcome measurement; ADS—Artificial demineralization solution; M—Medium; H—High; Exp.—Experimental; ER—Etch-and-Rinse; SE—Self-Etch; Univ.—Universal; F—Fluorine; Ca—Calcium; CaP—Calcium phosphate; Pept.—Peptide; FLs—Flavonoids; SiO_2—Silica; Hap—Hidroxiapatite; HEMA—2-hydroxyethyl methacrylate; TMC—Thermocycling; µTBS—microtensile bond strength; SBS—shear bond strength; µSBS—microshear bond strength.

3.3. Meta-Regressions

3.3.1. Influence of the Adhesive Technique on NMA Effect Estimates

The meta-regression results showed that the ER technique performed better than the SE in four NMA comparisons: control vs. calcium phosphate, control vs. peptide, fluorine vs. calcium phosphate, and fluorine vs. peptide. On the contrary, the SE technique performed better in the NMA comparison of peptide vs. hydroxyapatite. In all other comparisons, both techniques demonstrated similar performance (Appendix A Table A5).

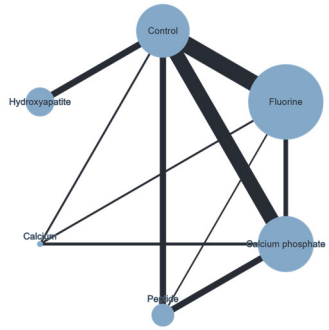
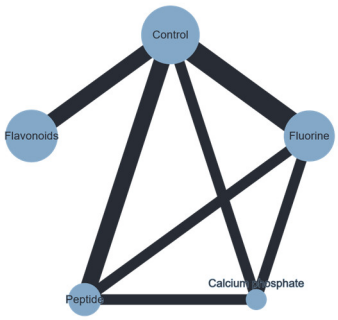
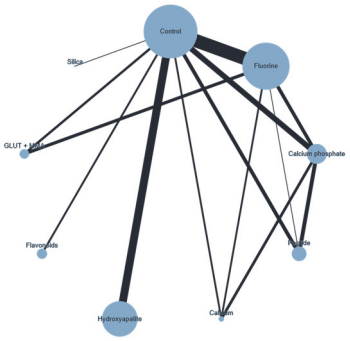
3.3.2. Influence of the ACAD Protocol on NMA Effect Estimates

Regarding the influence of different ACAD protocols on NMA effect estimates, the chemical ACAD protocol resulted in higher bond strength values than the biological ACAD protocol in nine NMA comparisons: control vs. fluorine, control vs. calcium phosphate, control vs. peptide, control vs. HEMA, control vs. flavonoids, control vs. calcium, control vs. hydroxyapatite, fluorine vs. calcium phosphate, and fluorine vs. peptide. In all other comparisons, both protocols performed similarly (Appendix A Table A6).

3.4. Network Meta-Analysis

Plots for the three performed NMAs are shown in Table 2.

Table 2. Network meta-analysis plots.

Plot of the NMA ER + Chemical ACAD	Plot of the NMA ER + Biological ACAD	Plot of the NMA SE + Chemical ACAD
		

Note: Black lines connect biomimetic remineralization interventions that were compared head-to-head. The size of each node (circle) provides a measure of the sample size. The thickness of the line provides a measure of the number of direct comparisons between two interventions. Legend: ACAD—Artificial caries-affected dentin; ER—Etch-and-Rinse; NMA—Network meta-analysis; SE- Self-Etch.

Table 3 shows the NMA results from the BR intervention network.

Table 3. Network meta-analysis results from the network of biomimetic remineralization interventions.

NMA	NMA Results							
ER + chemical	Calcium							
	0.596 (−7.289, 8.482)	Calcium Phosphate						
	−0.508 (−8.207, 7.191)	−1.105 (−4.828, 2.619)	Control					
	−0.628 (−8.504, 7.248)	−1.224 (−5.931, 3.482)	−0.120 (−3.783, 3.544)	Fluorine				
	4.333 (−5.240,13.906)	3.736 (−3.063, 0.536)	4.841 (−0.848,10.530)	4.960 (−1.806,11.727)	HAp			
	4.044 (−4.923, 3.011)	3.448 (−1.833, 8.729)	4.553 (−0.635, 9.740)	4.672 (−1.320,10.665)	−0.288 (−7.988, 7.411)	Peptide		
ER + biological	Calcium Phosphate							
	−21.209 (−25.954, −16.463)	Control						
	−12.771 (−20.538, −5.003)	8.438 (2.289, 14.587)	Flavonoids					
	−17.012 (−22.103, −11.920)	4.197 (1.080, 7.314)	−4.241 (−11.135, 2.652)	Fluorine				
	−2.914 (−8.210, 2.382)	18.295 (14.418, 22.172)	9.857 (2.588, 17.126)	14.098 (9.684, 18.512)	Peptide			
SE + chemical	Calcium							
	2.663 (−2.395, 7.722)	Calcium Phosphate						
	1.124 (−3.670, 5.917)	−1.539 (−4.817, 1.738)	Control					
	5.728 (−2.442,13.897)	3.065 (−4.318, 10.447)	4.604 (−2.011, 11.219)	Flavonoids				
	0.523 (−4.358, 5.404)	−2.140 (−5.787, 1.506)	−0.601 (−2.932, 1.730)	−5.205 (−12.219, 1.809)	Fluorine			
	3.023 (−3.815, 9.861)	0.360 (−5.589, 6.309)	1.899 (−3.210, 7.009)	−2.705 (−11.063, 5.654)	2.500 (−2.603, 7.603)	HEMA		
	−1.792 (−7.415, 3.831)	−4.455 (−8.857, −0.053)	−2.916 (−5.854, 0.023)	−7.520 (−14.758, −0.281)	−2.315 (−6.066, 1.436)	−4.815 (−10.709, 1.079)	HAp	
	2.654 (−3.216, 8.524)	−0.009 (−4.076, 4.058)	1.530 (−2.373, 5.434)	−3.074 (−10.755, 4.607)	2.131 (−2.213, 6.475)	−0.369 (−6.728, 5.990)	4.446 (−0.440, 9.332)	Peptide
	1.964 (−5.802, 9.730)	−0.699 (−7.633, 6.234)	0.840 (−5.270, 6.950)	−3.764 (−12.769, 5.241)	1.441 (−5.099, 7.980)	−1.059 (−9.024, 6.906)	3.756 (−3.024, 10.536)	−0.690 (−7.941, 6.560)	Silica

Note: The data in each cell are the mean difference with 95% confidence intervals for the network comparison of row-defining treatment versus column-defining treatment. Negative values favor the intervention in the column. Statistically significant results are in bold and gray. Legend: ER—Etch-and-Rinse; SE—Self-Etch; HAp—Hydroxyapatite; HEMA—2-hydroxyethyl methacrylate.

The contribution tables are displayed in Appendix A, Tables A7–A9.

3.4.1. ER Technique with Chemical ACAD Protocol

The results of this NMA suggested that no statistically significant differences existed between any BR interventions in any of the network comparisons.

3.4.2. ER Technique with Biological ACAD Protocol

When the ER technique and the biological ACAD protocol were used together, 8 of the 10 BR intervention network comparisons achieved statistically significant results: the calcium phosphate intervention compared to control (MD: −21.209, 95% CI: −25.954, −16.463), flavonoids (MD: −12.771, 95% CI: −20.538, −5.003), and fluorine (MD: −17.012, 95% CI: −22.103, −11.920); the flavonoids intervention compared to control (MD: 8.438, 95% CI: 2.289, 14.587); the peptide intervention compared to control (MD: 18.295, 95% CI: 14.418, 22.172), flavonoids (MD: 9.857, 95% CI: 2.588, 17.126), and fluorine (MD: 14.098, 95% CI: 9.684, 18.512); and the fluorine intervention compared to control (MD:4.197, 95% CI: 1.080, 7.314).

3.4.3. SE Technique with Chemical ACAD Protocol

When the SE technique and the chemical ACAD protocol were used together, only 2 of the 36 BR intervention network's comparisons achieved statistically significant results: the calcium phosphate (MD: −4.455, 95% CI: −8.857, −0.053) and the flavonoids (MD: −7.520, 95% CI: −14.758, −0.281) interventions compared to hydroxyapatite.

3.5. NMA Confidence Ratings

The confidence ratings for each NMA can be found in Appendix A, Tables A10–A12.

3.5.1. ER Technique with Chemical ACAD Protocol

In this NMA, two direct comparisons (calcium vs. control and control vs. fluorine) and one indirect comparison (hydroxyapatite vs. peptide) presented very low confidence, mainly due to major imprecision, heterogeneity, or incoherence concerns. The remaining indirect and direct comparisons presented a low or moderate confidence rating.

3.5.2. ER Technique with Biological ACAD Protocol

In this NMA, all the direct and indirect comparisons presented a moderate confidence rating.

3.5.3. SE Technique with Chemical ACAD Protocol

A low confidence rating was observed for six direct comparisons (calcium phosphate vs. peptide, calcium vs. fluorine, control vs. HEMA, control vs. SiO_2, fluorine vs. HEMA, and fluorine vs. peptide) and two indirect ones (calcium vs. hydroxyapatite and HEMA vs. peptide), mostly due to major concerns in heterogeneity, incoherence, and within-study bias. The remaining comparisons presented a moderate confidence rating.

3.6. Rankings

The treatment rankings and probability of ranking best are displayed in Table 4.

Table 4. Treatment rankings and probability of ranking best.

NMA	Ranks and Probability of Ranking Best				
		Rank			
		Mean	Median	CrI95%	Probability of ranking best (%)
ER + chemical	Control	4.66	5	(3.6)	0.05^{-4}
	Fluorine	4.66	5	(2.6)	0.64
	CaP	3.75	4	(2.6)	1.75
	Peptide	1.92	2	(1.5)	41.55
	Calcium	4.06	4	(1.6)	9.91
	HAp	1.97	2	(1.5)	**46.10**

Table 4. *Cont.*

NMA	Ranks and Probability of Ranking Best				
		Rank			
		Mean	Median	CrI95%	Probability of ranking best (%)
ER + biological	Control	4.98	5	(5.5)	0.00
	Fluorine	3.89	4	(4.5)	0.00
	CaP	1.15	1	(1.2)	**85.24**
	Peptide	1.86	2	(1.2)	14.56
	FLs	3.12	3	(3.4)	0.20
		Rank			
		Mean	Median	CrI95%	Probability of ranking best (%)
SE + chemical	Control	5.49	6	(3.6)	0.11
	Fluorine	5.96	6	(3.9)	0.32
	CaP	3.28	3	(1.7)	12.41
	Peptide	4.77	4	(1.9)	5.01
	Calcium	6.00	7	(1.9)	4.15
	HAp	7.89	8	(4.9)	0.09
	FLs	2.75	2	(1.9)	**46.36**
	HEMA	4.03	3	(1.9)	17.49
	Silica	4.85	5	(1.9)	14.05

Note: Interventions ranked best are highlighted in bold. Legend: ER—Etch-and-Rinse; SE—Self-Etch; CrI—Credible interval; CaP—Calcium phosphate; FLs—Flavonoids, HAp—Hydroxyapatite; HEMA—2-hydroxyethyl methacrylate.

3.6.1. ER Technique with Chemical ACAD Protocol

Among all the treatments in the NMA, hydroxyapatite achieved the highest probability of being the best treatment (46.10%), closely followed by peptide (41.55%).

3.6.2. ER Technique with Biological ACAD Protocol

In this NMA, calcium phosphate ranked first, with an 85.24% probability of being the best BR treatment.

3.6.3. SE Technique with Chemical ACAD Protocol

Compared to the other treatments in the NMA, flavonoids achieved the highest probability of being best (46.36%), followed by HEMA (17.49%).

3.7. Sensitivity Analyses

The sensitivity analyses for each NMA can be found in Appendix A, Tables A13–A15.

3.7.1. ER Technique with Chemical ACAD Protocol

Both sensitivity analyses showed results like those of the main analysis.

3.7.2. ER Technique with Biological ACAD Protocol

In this NMA, a sensitivity analysis where studies measuring the outcome with SBS tests were excluded was impossible because none used this test to assess the outcome. In the sensitivity analysis where we randomly selected one treatment intervention instead of combining interventions from the same category, the flavonoids vs. peptide comparison result lost statistical significance due to the loss of precision.

3.7.3. SE Technique with Chemical ACAD Protocol

When we excluded studies using SBS tests from the NMA, the flavonoids vs. hydroxyapatite comparison ceased to show differences between the two interventions due to a loss of precision. When we randomly selected 1 treatment intervention instead of combining interventions from the same category, 8 of the 36 NMA comparison conclusions changed from not showing differences between the interventions to favoring one of them.

3.8. Discussion

This systematic review aimed to unravel the intricate interactions among different BR procedures and their influence on bond strength in human ACAD by analyzing and comparing bond strength from various in vitro studies through NMA. NMA allows for the integration of data from direct and indirect comparisons, enabling a more precise estimation of treatment effects and a deeper understanding of optimal treatment options. Ultimately, this systematic review and NMA aspires to contribute to the existing knowledge on dentin-bonding procedures and offer valuable insights into the effectiveness of BR. The findings may help clinicians make informed decisions regarding dentin-bonding strategies for improved treatment outcomes [51].

This study's systematic review and NMA have shed light on the potential benefits of BR for bond strength in human ACAD, measured both immediately and after artificial aging. Its findings indicate that BR protocols are promising in enhancing restorative materials' bonding performance on demineralized dentin surfaces. [52]

ACAD's compromised nature negatively affects bond strength, and its surface is more challenging for bonding due to the incomplete infiltration of adhesives into the exposed collagen matrix [53]. Furthermore, the low pH associated with ACAD promotes the activation and activity of proteolytic enzymes, accelerating the breakdown of non-infiltrated collagen and the hybrid layer [37,48].

Our NMA findings highlighted differences between chemical and biological ACAD protocols. Chemical protocols consistently yielded higher bond strength results than biological, agreeing with previous research [54]. This difference may derive from the thicker demineralization layer associated with chemical protocols and the excessive softness of the primary dentine resulting from microbiological approaches [54].

The NMA also revealed variations in bond strength depending on the adhesive application technique. With their additional acid-etching stage, ER techniques proved more efficient in dissolving the smear layer than SE methods, which have a less acidic composition and are more sensitive [20]. Additionally, SE relies on chemical interactions with calcium ions, often found in lower concentrations in ACAD. Consequently, ER techniques yielded significantly higher bond strength values than SE, in line with the existing literature [31,33,53,55]. Moreover, when considering the ACAD surface, ER consistently demonstrated higher bond strength than SE materials [53].

This systematic review's 23 in vitro studies showed medium heterogeneity, reflecting variations in ACAD protocols, aging methods, and bond strength tests. Thus, random-effects models were employed throughout the NMA investigation. Artificial aging methods, such as thermocycling and months of storage, generally reduce bond strength. Thermocycling promoted the most extreme breakdown of the bond interface and caused the lowest bond strength, even with associated BR, which is consistent with other studies [56]. However, different bond strength tests were used in the included investigations, which could affect the measurement results, and aspects such as specimen preparation and geometry, loading configuration, and material characteristics were not considered [3,57,58].

BR overall increased the bond strength values, even after artificial aging methods [10,58]. Nonetheless, the limited availability of studies reporting BR associated with bond strength restricts the exploration of these relationships [22]. Incorporating these BR methods into dental treatments can potentially enhance the durability and quality of the resin–dentin interface, offering promising avenues for improving clinical outcomes in restorative dentistry. In the NMA on ER with chemical ACAD, hydroxyapatite was the most effective treatment (46.10%), closely followed by peptide (41.55%), despite the low confidence in some comparisons. In the NMA on ER with biological ACAD, calcium phosphate emerged as the top-ranking BR (85.24%), significantly surpassing the control, flavonoids, and fluo-

ride treatments. However, the NMA on SE with chemical ACAD showed low confidence in various comparisons, with flavonoids having the highest probability (46.36%) of being more effective, followed by HEMA (17.49%). These findings highlight the nuanced effectiveness of BR, influenced by different protocols and compositions. Most investigations on BR have shown its ability to remineralize ACAD in a basic manner. However, because they were carried out in vitro, their application in clinical contexts remains unexplored [22].

This study has some limitations. Most notably, in vitro studies lack the complexity of the oral environment, including oral biofluids and microbial interactions [3,22,52,56,57]. The absence of real dental caries development processes in the ACAD models is also a limitation. Future studies should address these shortcomings for a more comprehensive understanding of the clinical applicability of BR.

Another limitation is related to the sensitivity analysis for the NMA on SE with chemical ACAD. In this network, when we randomly selected one treatment intervention instead of combining interventions from the same category, 8 out of the 36 NMA comparisons changed their conclusions from not showing differences between the interventions to favoring one of them. Despite this, we are confident that combining multiple arms related to the same intervention yields more reliable estimates because it does not waste useful data and evidence, as outlined and in accordance with the Cochrane recommendations. Moreover, regardless of the strategy used to cope with multiple-arm trials, six of the eight comparisons that had their conclusions changed in the sensitivity analysis were based solely on indirect evidence, which inherently carries less confidence than scenarios where direct evidence is also available.

Despite these limitations, our findings suggest that BR can enhance bond strength in ACAD, offering potential benefits for clinical practice. Dental professionals can use this knowledge to optimize treatment approaches, improve patient outcomes, and extend the longevity of adhesive bonding materials [3,22,52,57,58]. Future research should include randomized clinical trials to confirm the findings.

4. Conclusions

In conclusion, through a systematic review and NMAs, we showed that bond strength degraded after biological or chemical ACAD protocols. As a result, surface preparation with BR procedures prior to bonding is advised to increase the bonding of ER and SE adhesives.

Author Contributions: R.C. contributed to concepts, design, the definition of intellectual content, literature search, data acquisition, and article preparation. J.R.-P. contributed to concepts, design, the definition of intellectual content, literature search, data acquisition, statistical analysis, and article preparation. J.C.F. contributed to the definition of intellectual content and article preparation. S.A.-O. contributed to the definition of intellectual content and article preparation. L.F.A. contributed to concepts, design, the definition of intellectual content, statistical analysis, and critically revised the manuscript. P.M. contributed to concepts, design, the definition of intellectual content, and critically revised the manuscript. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: The study was approved by the local "Comissão de Ética para a Saúde da Faculdade de Medicina Dentária da Universidade do Porto"-"Projeto no 22/2021".

Data Availability Statement: The data that support the findings of this study are available from the corresponding author, Rosário Costa, upon reasonable request.

Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

NMA	Network meta-analysis
ACAD	Artificial caries-affected dentin
BR	Biomimetic remineralization

Appendix A

Appendix A.1. Search Strategies

PubMed: 1121 retrieved records

#1 Light-Curing of Dental Adhesives [MeSH] OR Self-Curing of Dental Resins [MeSH] OR adhesi*[tw] OR (bond*[tw] AND strength[tw])

#2 biomimetic*[tw] OR Biomimetics [MeSH] OR mineraliz*[tw] OR biomineraliz*[tw] OR Biomineralization [MeSH] OR remineraliz*[tw] OR Tooth Remineralization [MeSH] OR ((Dental Caries [MeSH] OR cari*[tw] OR eroded[tw] OR desensitized[tw]) AND (pre-treat*[tw] OR pretreat*[tw] OR treat*[tw] OR therap*[tw]))

#3 Dentin-Bonding Agents [MeSH] OR (dentin[tw] AND bond*[tw])

#1 AND #2 AND #3

ISI Web of Science: 1176 retrieved records

#1 adhesi* OR (bond* AND strength) (All Fields)

#2 biomimetic* OR mineraliz* OR biomineraliz* OR remineraliz* OR ((cari* OR eroded OR desensitized) AND (pre-treat* OR pretreat* OR treat* OR therap*)) (All Fields)

#3 dentin AND bond* (All Fields)

#1 AND #2 AND #3

SCOPUS: 1052 retrieved records

#1 TITLE-ABS-KEY (adhesi* OR (bond* AND strength))

#2 TITLE-ABS-KEY (biomimetic* OR mineraliz* OR biomineraliz* OR remineraliz* OR ((cari* OR eroded OR desensitized) AND (pre-treat* OR pretreat* OR treat* OR therap*)))

#3 TITLE-ABS-KEY (dentin AND bond*)

#1 AND #2 AND #3

Table A1. Reasons for excluding studies after accessing full texts.

Studies	Reason for Exclusion
Doozandeh et al. (2015) [57]	1—Without ACAD
Bergamin et al. (2016)[58]	1—Without ACAD
Ghani et al. (2017) [59]	1—Without ACAD
Komori et al. (2009) [60]	1—Without ACAD
Leal et al. (2017) [61]	1—Without ACAD
Luong et al. (2020) [62]	1—Without ACAD
Meraji et al. (2018) [63]	1—Without ACAD
Prasansuttiporn et al. (2020) [64]	1—Without ACAD
Sajjad et al. (2022) [65]	1—Without ACAD
Yilmaz et al. (2017) [66]	1—Without ACAD
Castellan et al. (2010) [67]	2—Without remineralization procedures
Okuyama et al. (2011) [68]	2—Without remineralization procedures
Wang et al. (2012) [69]	2—Without remineralization procedures
de-Melo et al. (2013) [70]	2—Without remineralization procedures
Carvalho et al. (2016) [71]	2—Without remineralization procedures
Deari et al. (2017) [72]	2—Without remineralization procedures
Giacomini et al. (2017) [73]	2—Without remineralization procedures
Rodrigues et al. (2017) [74]	2—Without remineralization procedures

Table A1. *Cont.*

Studies	Reason for Exclusion
Imiolczyk et al. (2017) [75]	2—Without remineralization procedures
Stape et al. (2021) [76]	2—Without remineralization procedures
Hartz et al. (2022) [77]	2—Without remineralization procedures
Wang et al. (2016) [78]	3—Modified Materials
Moda et al. (2018) [79]	3—Modified Materials
Choi et al. (2020) [80]	3—Modified Materials
Abdelshafi et al. (2021) [81]	3—Modified Materials
Al-Qahtani et al. (2021) [82]	3—Modified Materials
Khor et al. (2022) [83]	3—Modified Materials
Adebayo et al. (2010) [84]	4—Without bond strength measurement
Liu et al. (2011) [85]	4—Without bond strength measurement
Chen et al. (2016) [86]	4—Without bond strength measurement
Bortolotto et al. (2017) [87]	4—Without bond strength measurement
Liang et al. (2017) [88]	4—Without bond strength measurement
Wang et al. (2021) [89]	4—Without bond strength measurement
Zhou et al. (2016) [90]	5—Modified adhesive
Flury et al. (2017) [91]	5—Modified adhesive
Ye et al. (2017) [92]	5—Modified adhesive
Liang et al. (2018) [93]	5—Modified adhesive
Cardenas et al. (2021) [48]	5—Modified adhesive
Hasegawa et al. (2021) [94]	5—Modified adhesive
Bridi et al. (2012) [95]	6—Not biomimetic remineralization agents
Castellan et al. (2013) [96]	6—Not biomimetic remineralization agents
Monteiro et al. (2013) [97]	6—Not biomimetic remineralization agents
Abu Nawareg et al. (2016) [98]	6—Not biomimetic remineralization agents
Lee et al. (2017) [99]	6—Not biomimetic remineralization agents
Prasansuttiporn et al. (2017) [100]	6—Not biomimetic remineralization agents
Ramezanian Nik et al. (2017) [101]	6—Not biomimetic remineralization agents
Costa et al. (2019) [102]	6—Not biomimetic remineralization agents
Fialho et al. (2019) [103]	6—Not biomimetic remineralization agents
Landmayer et al. (2020) [104]	6—Not biomimetic remineralization agents
Costa et al. (2021) [105]	6—Not biomimetic remineralization agents
Giacomini et al. (2021) [106]	6—Not biomimetic remineralization agents
Shioya et al. (2021) [107]	6—Not biomimetic remineralization agents
Xu et al. (2021) [108]	6—Not biomimetic remineralization agents
Atay et al. (2022) [109]	6—Not biomimetic remineralization agents
Lemos et al. (2022) [110]	6—Not biomimetic remineralization agents
Zhang et al. (2015) [111]	7—Non-Roman Alphabet language after unsuccessful contact with authors
Wang et al. (2017) [112]	7—Non-Roman Alphabet language after unsuccessful contact with authors
Meng et al. (2022) [113]	7—Non-Roman Alphabet language after unsuccessful contact with authors
Kim et al. (2020) [13]	8—Missing control group

Table A2. Reasons for excluding studies from network meta-analyses.

Study	Reason for Exclusion
Atomura et al. (2018) [43]	Standard deviation and sample size (N) missing and authors did not respond to emails.

Table A3. Data information.

Study	Data Information
Zumstein et al. (2018) [50]	Missing data obtained from another meta-analysis by Wiegand et al., 2021 [57]. Authors did not respond to emails.

Table A4. Authors providing data via email, upon request.

Study	Data Information
Barbosa-Martins et al. (A) (2018) [8]	Unit of statistical analysis
Barbosa-Martins et al. (B) (2018) [7]	Unit of statistical analysis
de Sousa et al. (2019) [44]	Unit of statistical analysis
Moreira et al. (2021) [15]	Unit of statistical analysis
Meng et al. (2021) [35]	Mean and SD values
Pei et al. (2019) [36]	Unit of statistical analysis
Pulidindi et al. (2021) [38]	Unit of statistical analysis
Yang et al. (2018) [39]	Mean and SD values and unit of statistical analysis
Zang et al. (2018) [41]	Mean and SD values and unit of statistical analysis

Appendix A.2. OpenBUGS Code for Random Effects Meta-Regression Model with a Subgroup Indicator Covariate

```
# Normal likelihood, identity link, subgroup
# Random effects model for multi-arm trials

model{ # *** PROGRAM STARTS

for(i in 1:ns){ # LOOP THROUGH STUDIES
w[i,1] <- 0 # adjustment for multi-arm trials is zero for control arm
delta[i,1] <- 0 # treatment effect is zero for control arm
mu[i] ~ dnorm(0,.0001) # vague priors for all trial baselines
for (k in 1:na[i]) { # LOOP THROUGH ARMS
var[i,k] <- pow(se[i,k],2) # calculate variances
se[i,k] ~ dunif(0,10) # vague prior for SE
prec[i,k] <- 1/var[i,k] # set precisions
y[i,k] ~ dnorm(theta[i,k],prec[i,k]) # binomial likelihood

theta[i,k] <- mu[i] + delta[i,k] + (beta[t[i,k]]-beta[t[i,1]]) * x[i]# model for linear predictor, covariate effect relative to treat in arm 1

#Deviance contribution
dev[i,k] <- (y[i,k]-theta[i,k])*(y[i,k]-theta[i,k])*prec[i,k]
}
# summed residual deviance contribution for this trial
resdev[i] <- sum(dev[i,1:na[i]])
for (k in 2:na[i]) { # LOOP THROUGH ARMS
# trial-specific LOR distributions
delta[i,k] ~ dnorm(md[i,k],taud[i,k])
# mean of LOR distributions, with multi-arm trial correction
md[i,k] <- d[t[i,k]] - d[t[i,1]] + sw[i,k]
# precision of LOR distributions (with multi-arm trial correction)
taud[i,k] <- tau *2*(k-1)/k
# adjustment, multi-arm RCTs
w[i,k] <- (delta[i,k] - d[t[i,k]] + d[t[i,1]])
# cumulative adjustment for multi-arm trials
sw[i,k] <- sum(w[i,1:k-1])/(k-1)
}
```

```
}
totresdev <- sum(resdev[]) #Total Residual Deviance
d[1]<-0 # treatment effect is zero for control arm

beta[1] <- 0 # covariate effect is zero for reference treatment

# vague priors for treatment effects
for (k in 2:nt){ # LOOP THROUGH TREATMENTS
d[k] ~ dnorm(0,.0001) # vague priors for treatment effects
beta[k] <- B # common covariate effect
}

B ~ dnorm(0,.0001) # vague prior for covariate effect

sd ~ dunif(0,5) # vague prior for between-trial SD
tau <- pow(sd,-2) # between-trial precision = (1/between-trial variance)

# treatment effect when covariate = z[j]
for (k in 1:nt){ # LOOP THROUGH TREATMENTS
for (j in 1:nz) { dz[j,k] <- d[k] + (beta[k]-beta[1])*z[j] }
}

# All pairwise comparisons, if nt>2
for (c in 1:(nt-1)) {
for (k in (c+1):nt) {
# when covariate is zero
diff[c,k] <- (d[c] - d[k])
#at covariate=z[j]


for (j in 1:nz) {
diff.j[c,k] <- (dz[j,c] - dz[j,k])
}}}

} # *** PROGRAM ENDS
```

Appendix A.3. Meta-Regression

Table A5. Meta-regression results evaluating the influence of adhesive application type (er vs. se) on treatment effects at 24 h.

NMA Comparison	Mean	95% CrI
CTRL:F	0.8846	(−1.72; 3.52)
CTRL:CaP	**−3.351**	**(−6.664; −0.03009)**
CTRL:Pept.	**−5.384**	**(−9.103; −1.65)**
CTRL:SiO_2	−0.8296	(−10.72; 9.049)
CTRL:HEMA	−1.728	(−10.22; 6.768)
CTRL:FLs	−4.982	(−12.35; 2.382)
CTRL:Ca	0.3152	(−5.575; 6.211)
CTRL:HAp	1.223	(−2.536; 4.98)
F:CaP	**−4.236**	**(−7.499; −0.9842)**

Table A5. *Cont.*

NMA Comparison	Mean	95% CrI
F:Pept.	**−6.268**	**(−9.996; −2.552)**
F:SiO_2	−1.714	(−11.95; 8.521)
F:HEMA	−2.613	(−11.1; 5.868)
F:FLs	−5.867	(−13.45; 1.726)
F:Ca	−0.5694	(−6.352; 5.196)
F:HAp	0.3381	(−3.942; 4.631)
CaP:Pept.	−2.032	(−5.601; 1.525)
CaP:SiO_2	2.522	(−7.906; 12.94)
CaP:HEMA	1.623	(−7.297; 10.54)
CaP:FLs	−1.631	(−9.428; 6.172)
CaP:Ca	3.666	(−2.196; 9.529)
CaP:HAp	4.574	(−0.07638; 9.248)
Pept.:SiO_2	4.554	(−6.013; 15.1)
Pept.:HEMA	3.656	(−5.425; 12.76)
Pept.:FLs	0.4015	(−7.578; 8.394)
Pept.:Ca	5.699	(−0.6984; 12.08)
Pept.:HAp	**6.606**	**(1.658; 11.56)**
SiO_2:HEMA	−0.8984	(−13.94; 12.13)
SiO_2:FLs	−4.153	(−16.46; 8.18)
SiO_2:Ca	1.145	(−10.37; 12.64)
SiO_2:HAp	2.052	(−8.496; 12.66)
HEMA:FLs	−3.254	(−14.41; 7.904)
HEMA:Ca	2.043	(−8.051; 12.17)
HEMA:HAp	2.951	(−6.264; 12.18)
FLs:Ca	5.297	(−3.932; 14.52)
FLs:HAp	6.205	(−1.944; 14.31)
Ca:HAp	0.9075	(−5.872; 7.675)

Note: Negative mean values favor ER application type. Statistically significant results are highlighted in bold. Legend: Control (CTRL), Fluorine (F), Calcium Phosphate (CaP), Peptide (Pept.), Silica (SiO_2), Flavonoids (FLs), Calcium (Ca), Hydroxyapatite (HAp), Credible Interval (Crl).

Table A6. Meta-regression results evaluating the influence of acad protocol type (chemical vs. biological) on treatment effects at 24 h.

NMA Comparison	Mean	95% CrI
CTRL:F	**−7.588**	**(−11.3; −3.877)**
CTRL:CaP	**−12.97**	**(−17.32; −8.628)**
CTRL:Pept.	**−14.2**	**(−18.64; −9.77)**
CTRL:SiO_2	−10.15	(−20.78; 0.5214)
CTRL:HEMA	**−10.62**	**(−19.71; −1.499)**
CTRL:FLs	**−11.2**	**(−18.69; −3.706)**
CTRL:Ca	**−9.321**	**(−15.94; −2.717)**
CTRL:HAp	**−9.208**	**(−14.65; −3.78)**
F:CaP	**−5.381**	**(−8.621; −2.139)**
F:Pept.	**−6.617**	**(−10.3; −2.935)**
F:SiO_2	−2.563	(−12.68; 7.6)
F:HEMA	−3.031	(−11.43; 5.39)
F:FLs	−3.61	(−11.2; 3.981)
F:Ca	−1.734	(−7.48; 3.999)
F:HAp	−1.62	(−5.972; 2.749)
CaP:Pept.	−1.236	(−4.793; 2.332)
CaP:SiO_2	2.818	(−7.433; 13.12)
CaP:HEMA	2.35	(−6.401; 11.14)
CaP:FLs	1.77	(−6.08; 9.585)
CaP:Ca	3.647	(−2.149; 9.428)
CaP:HAp	3.761	(−0.8584; 8.391)
Pept.:SiO_2	4.055	(−6.382; 14.52)
Pept.:HEMA	3.586	(−5.386; 12.55)
Pept.:FLs	3.007	(−4.964; 10.97)

Table A6. *Cont.*

NMA Comparison	Mean	95% CrI
Pept.:Ca	4.884	(−1.454; 11.21)
Pept.:HAp	4.997	(−0.001725; 10.01)
SiO_2:HEMA	−0.4682	(−13.38; 12.48)
SiO_2:FLs	−1.048	(−13.4; 11.32)
SiO_2:Ca	0.829	(−10.56; 12.18)
SiO_2:HAp	0.9427	(−9.562; 11.42)
HEMA:FLs	−0.5796	(−11.75; 10.58)
HEMA:Ca	1.297	(−8.708; 11.3)
HEMA:HAp	1.411	(−7.759; 10.56)
FLs:Ca	1.877	(−7.369; 11.12)
FLs:HAp	1.991	(−6.31; 10.31)
Ca:HAp	0.1137	(−6.606; 6.846)

Note: Negative mean values favor Chem ACAD protocol type. Statistically significant results are highlighted in bold. Legend: Control (CTRL), Fluorine (F), Calcium Phosphate (CaP), Peptide (Pept.), Silica (SiO_2), Flavonoids (FLs), Calcium (Ca), Hydroxyapatite (HAp), Credible Interval (Crl).

Appendix A.4. Contribution Tables

Table A7. Per-comparison contribution matrix for the ER with chemical network.

NMA Treatment Effect/Comparisons	Ca:CaP	Ca:CTRL	Ca:F	CaP:CTRL	CaP:F	CaP:Pept.	CTRL:F	CTRL:HAp	CTRL:Pept.	F:Pept.
Mixed estimates										
CaP:CTRL	2.935	2.375	0.56	**63.32**	7.4	7.4783	8.4533	0	6.985	0.4933
CaP:F	4.195	0.0675	4.2625	22.975	**31.11**	6.1242	25.1317	0	2.2242	3.9
CaP:Pept.	1.1317	0.6967	0.435	16.795	5.04	**52.39**	0.535	0	18.0267	4.94
Ca:CaP	**38.27**	15.92	11.94	17.4467	7.655	2.7583	3.2517	0	1.725	1.0333
Ca:CTRL	15.095	**36.58**	15.3917	13.445	0.125	1.775	14.73	0	2.3117	0.5367
Ca:F	12.5817	15.78	**38.56**	3.1633	7.905	1.5133	18.9033	0	0.04	1.5533
CTRL:F	0.5775	2.515	3.0925	8.505	8.155	0.2275	**70.38**	0	3.3875	3.16
CTRL:HAp	0	0	0	0	0	0	0	**100**	0	0
CTRL:Pept.	0.8633	0.8783	0.015	14.86	1.5317	17.255	7.2017	0	**51.7**	5.685
F:Pept.	1.5167	0.5925	2.1092	3.9225	10.465	15.9042	25.565	0	22.235	**17.69**
Indirect estimates										
CaP:HAp	2.0033	1.5833	0.42	31.66	4.9333	5.0267	5.7233	43.6233	4.6567	0.37
Ca:HAp	10.2008	18.29	10.3225	8.9633	0.1	1.3375	9.82	38.8133	1.74	0.4025
Ca:Pept.	17.22	16.965	12.4708	0.7075	1.7067	19.6342	4.2742	0	20.5317	6.49
F:HAp	0.4445	1.6767	2.1212	5.6992	5.4367	0.182	35.19	44.8545	2.2887	2.1067
HAp:Pept.	0.6475	0.6595	0.012	9.9067	1.1495	11.7037	4.9275	41.3437	25.85	3.79

Note: Columns refer to comparisons with direct data and rows to NMA treatment effects. The data in each cell show how much (in %) each direct comparison contributes to the NMA treatment effects. The values in bold and grey identify the percentage each direct comparison contributes to the corresponding NMA comparison treatment effect. Legend: Control (CTRL), Fluorine (F), Calcium Phosphate (CaP), Peptide (Pept.), Calcium (Ca), Hidroxiapatite (HAp).

Table A8. Per-comparison contribution matrix for the ER with biological network.

NMA Treatment Effect/Comparisons	CaP:CTRL	CaP:F	CaP:Pept.	CTRL:FLs	CTRL:F	CTRL:Pept.	F:Pept.
Mixed estimates							
CaP:CTRL	**47.08**	13.7	12.3317	0	14.5567	11.475	0.8567
CaP:F	17.525	**40.42**	11.1833	0	19.6783	2.1533	9.03
CaP:Pept.	16.035	11.5217	**43.84**	0	1.0367	17.0717	10.485
CTRL:FLs	0	0	0	**100**	0	0	0
CTRL:F	6.015	6.345	0.33	0	**71.49**	8.075	7.745
CTRL:Pept.	7.505	1.1033	8.6083	0	12.8783	**58.13**	11.775
F:Pept.	0.9933	8.17	9.1633	0	21.8183	20.825	**39.04**
Indirect estimates							
CaP:FLs	23.54	9.1333	8.2925	40.9658	9.7758	7.65	0.6425
FLs:F	4.01	4.2575	0.2475	45.1658	35.745	5.4108	5.1633
FLs:Pept.	5.0033	0.8275	5.8308	42.7458	8.6775	29.065	7.85

Note: Columns refer to comparisons with direct data and rows to NMA treatment effects. The data in each cell show how much (in %) each direct comparison contributes to the NMA treatment effects. The values in bold and grey identify the percentage each direct comparison contributes to the corresponding NMA comparison treatment effect. Legend: Control (CTRL), Fluorine (F), Calcium Phosphate (CaP), Peptide (Pept.), Calcium (Ca), Flavonoids (FLs).

Table A9. Per-comparison contribution matrix for the SE with chemical network.

NMA Treatment Effect/Comparisons	Ca:CaP	Ca:CTRL	Ca:F	CaP:CTRL	CaP:F	CaP:Pept.	CTRL: FLS	CTRL:F	CTRL: HEMA	CTRL:HAp	CTRL:Pept.	CTRL:SiO_2	F:HEMA	F:Pept.
Mixed estimates														
CaP:CTRL	5.215	3.955	1.26	**51.94**	9.345	8.4575	0	10.425	0.4725	0	8.165	0	0.4725	0.2925
CaP:F	6.4433	0.7333	5.71	20.78	**29.56**	5.3175	0	23.9333	1.1025	0	3.5225	0	1.1025	1.795
CaP:Pept.	1.9783	1.3433	0.635	14.09	4.5933	**54.07**	0	2.3683	0.13	0	17.932	0	0.13	2.73
Ca:CaP	**41.85**	14.96	11.2705	15.37	8.04	2.8205	0	2.5325	0.168	0	2.2905	0	0.168	0.53
Ca:CTRL	13.2408	**37.83**	16.005	10.395	0.6525	2.1933	0	15.825	0.6925	0	2.3333	0	0.6925	0.14
Ca:F	11.2397	16.065	**39.64**	3.365	6.74	1.1347	0	19.125	0.773	0	0.468	0	0.773	0.6667
CTRL:FLs	0	0	0	0	0	0	**100**	0	0	0	0	0	0	0
CTRL:F	0.4375	2.85	3.2875	5.19	5.3533	0.6008	0	**72.96**	3.15	0	1.8108	0	3.15	1.21
CTRL:HEMA	0.174	0.9567	1.1307	1.74	1.8025	0.2365	0	18.35	**52.86**	0	0.6432	0	21.6898	0.4067
CTRL:HAp	0	0	0	0	0	0	0	0	0	**100**	0	0	0	0
CTRL:Pept.	1.553	1.29	0.263	11.88	2.5467	15.9797	0	5.8717	0.248	0	**56.8**	0	0.248	3.31
CTRL:SiO_2	0	0	0	0	0	0	0	0	0	0	0	**100**	0	0
F:HEMA	0.174	0.9433	1.1173	1.72	1.78	0.234	0	18.125	21.4223	0	0.634	0	**53.44**	0.4
F:Pept.	2.31	0.455	2.765	3.8833	9.255	15.4483	0	28.2333	1.265	0	26.07	0	1.265	**9.05**
Indirect estimates														
CaP:FLs	3.5907	2.6367	0.954	25.97	6.23	5.6773	41.468	7.04	0.378	0	5.4433	0	0.378	0.234
CaP:HEMA	4.1842	1.6142	2.57	23.36	12.08	4.2917	0	3.6925	24.7767	0	3.495	0	19.1392	0.7967
CaP:HAp	3.5907	2.6367	0.954	25.97	6.23	5.6773	0	7.04	0.378	41.468	5.4433	0	0.378	0.234
CaP:SiO_2	3.5907	2.6367	0.954	25.97	6.23	5.6773	0	7.04	0.378	0	5.4433	41.468	0.378	0.234
Ca:FLs	9.097	18.915	10.685	6.93	0.522	1.645	38.697	10.55	0.552	0	1.75	0	0.552	0.105
Ca:HEMA	8.9795	17.48	17.97	5.1542	2.6933	1.132	0	1.0295	22.5367	0	0.932	0	21.8928	0.2
Ca:HAp	9.097	18.915	10.685	6.93	0.522	1.645	0	10.55	0.552	38.697	1.75	0	0.552	0.105
Ca:Pept.	17.575	16.975	11.148	0.668	1.6767	19.9197	0	5.6533	0.298	0	22.258	0	0.298	3.52
Ca:SiO_2	9.097	18.915	10.685	6.93	0.522	1.645	0	10.55	0.552	0	1.75	38.697	0.552	0.105
FLs:F	0.35	1.9	2.25	3.46	3.5825	0.4725	45.2192	36.48	2.1	0	1.2792	0	2.1	0.8067
FLs:HEMA	0.145	0.7175	0.8625	1.305	1.355	0.195	41.1858	12.2333	26.43	0	0.5	0	14.7558	0.305
FLs:HAp	0	0	0	0	0	0	50	0	0	50	0	0	0	0
FLs:Pept.	1.1862	0.9675	0.2187	7.92	1.91	11.0162	41.6228	4.1287	0.2067	0	28.4	0	0.2067	2.2067
FLs:SiO_2	0	0	0	0	0	0	50	0	0	0	0	50	0	0
F:HAp	0.35	1.9	2.25	3.46	3.5825	0.4725	0	36.48	2.1	45.2192	1.2792	0	2.1	0.8067
F:SiO_2	0.35	1.9	2.25	3.46	3.5825	0.4725	0	36.48	2.1	0	1.2792	45.2192	2.1	0.8067
HEMA:HAp	0.145	0.7175	0.8625	1.305	1.355	0.195	0	12.2333	26.43	41.1858	0.5	0	14.7558	0.305
HEMA:Pept.	1.4625	0.2	1.2625	4.635	4.37	10.4675	0	5.7817	25.81	0	26.757	0	15.3342	3.92
HEMA:SiO_2	0.145	0.7175	0.8625	1.305	1.355	0.195	0	12.2333	26.43	0	0.5	41.1858	14.7558	0.305
HAp:Pept.	1.1862	0.9675	0.2187	7.92	1.91	11.0162	0	4.1287	0.2067	41.623	28.4	0	0.2067	2.2067
HAp:SiO_2	0	0	0	0	0	0	0	0	0	50	0	50	0	0
Pept.:SiO_2	1.1862	0.9675	0.2187	7.92	1.91	11.0162	0	4.1287	0.2067	0	28.4	41.6228	0.2067	2.2067

Note: Columns refer to comparisons with direct data and rows to NMA treatment effects. The data in each cell show how much (in %) each direct comparison contributes to the NMA treatment effects. The values in bold and grey identify the percentage each direct comparison contributes to the corresponding NMA comparison treatment effect. Legend: Control (CTRL), Fluorine (F), Calcium Phosphate (CaP), Peptide (Pept.), Calcium (Ca), Flavonoids (FLs), Hidroxiapatite (HAp), Silica (SiO_2).

Appendix A.5. Confidence Rating Output of CINeMA Software

Table A10. Confidence rating table for the ER with chem network meta-analysis.

Comparison	Number of Studies	Within-Study Bias	Reporting Bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence Rating
Mixed estimates								
CaP:CTRL	1	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
CaP:F	1	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
CaP:Pept.	1	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Low
Ca:CaP	7	Some concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Ca:CTRL	3	Some concerns	Low risk	No concerns	No concerns	Major concerns	Major concerns	Very low
Ca:F	4	Some concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Moderate
CTRL:F	8	Some concerns	Low risk	No concerns	No concerns	Major concerns	Major concerns	Very low
CTRL:HAp	3	Some concerns	Low risk	No concerns	Some concerns	No concerns	Major concerns	Low
CTRL:Pept.	4	Some concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Moderate
F:Pept.	2	Some concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Moderate
Indirect estimates								
CaP:HAp	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	Low
Ca:HAp	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	Low
Ca:Pept.	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	Low
F:HAp	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Major concerns	Low
HAp:Pept.	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	Major concerns	Very low

Legend: Control (CTRL), Fluorine (F), Calcium Phosphate (CaP), Peptide (Pept.), Calcium (Ca), Hidroxiapatite (HAp). Different colors correspond to the Confidence Rating: orange for low, blue for moderate, pink for very low, yellow for some concern, green for no concern, and red for major concern.

Table A11. Confidence rating table for the ER with biol network meta-analysis.

ER with Biological								
Comparison	Number of Studies	Within-Study Bias	Reporting Bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence Rating
Mixed estimates								
CaP:CTRL	2	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
CaP:F	2	Some concerns	Some concerns	No concerns	No concerns	No concerns	No concerns	Moderate
CaP:Pept.	2	Some concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Moderate
CTRL:FLs	1	Some concerns	Some concerns	No concerns	No concerns	Some concerns	No concerns	Moderate
CTRL:F	4	Some concerns	Low risk	No concerns	No concerns	Some concerns	No concerns	Moderate
CTRL:Pept.	3	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
F:Pept.	2	Some concerns	Some concerns	No concerns	No concerns	No concerns	No concerns	Moderate
Indirect estimates								
CaP:FLs	0	Some concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Moderate
FLs:F	0	Some concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Moderate
FLs:Pept.	0	Some concerns	Low risk	No concerns	No concerns	Some concerns	No concerns	Moderate

Legend: Control (CTRL), Fluorine (F), Calcium Phosphate (CaP), Peptide (Pept.), Flavonoids (FLs). Different colors correspond to the Confidence Rating: blue for moderate, yellow for some concern and green for no concern.

Table A12. Confidence rating table for the SE with chem network meta-analysis.

SE with Chemical								
Comparison	Number of Studies	Within-Study Bias	Reporting Bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
Mixed estimates								
CaP:CTRL	1	Some concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Moderate
CaP:F	1	Some concerns	Low risk	No concerns	No concerns	Some concerns	No concerns	Moderate
CaP:Pept.	1	Some concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
Ca:CaP	4	Some concerns	Low risk	No concerns	No concerns	Some concerns	Some concerns	Moderate
Ca:CTRL	2	Some concerns	Low risk	No concerns	No concerns	Some concerns	No concerns	Moderate
Ca:F	3	Some concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Low
CTRL:FLs	1	Some concerns	Low risk	No concerns	Some concerns	No concerns	Some concerns	Moderate
CTRL:F	8	Some concerns	Low risk	No concerns	No concerns	Some concerns	No concerns	Moderate
CTRL:HEMA	1	Major concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Low
CTRL:HAp	5	Some concerns	Low risk	No concerns	No concerns	Some concerns	Some concerns	Moderate
CTRL:Pept.	3	Some concerns	Low risk	No concerns	No concerns	Some concerns	Some concerns	Moderate
CTRL:SiO_2	1	Some concerns	Low risk	No concerns	No concerns	Major concerns	Some concerns	Low
F:HEMA	1	Major concerns	Low risk	No concerns	Some concerns	No concerns	No concerns	Low
F:Pept.	1	Some concerns	Low risk	No concerns	No concerns	Some concerns	Major concerns	Low
Indirect estimates								
CaP:FLs	0	Some concerns	Low risk	No concerns	Some concerns	No concerns	Some concerns	Moderate
CaP:HEMA	0	Some concerns	Low risk	No concerns	Some concerns	No concerns	Some concerns	Moderate
CaP:HAp	0	Some concerns	Low risk	No concerns	Some concerns	No concerns	Some concerns	Moderate
CaP:SiO_2	0	Some concerns	Low risk	No concerns	Some concerns	No concerns	Some concerns	Moderate
Ca:FLs	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Some concerns	Moderate
Ca:HEMA	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Some concerns	Moderate
Ca:HAp	0	Some concerns	Low risk	No concerns	No concerns	Major concerns	Some concerns	Low
Ca:Pept.	0	Some concerns	Low risk	No concerns	No concerns	Some concerns	Some concerns	Moderate
Ca:SiO_2	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Some concerns	Moderate
FLs:F	0	Some concerns	Low risk	No concerns	Some concerns	No concerns	Some concerns	Moderate
FLs:HEMA	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Some concerns	Moderate
FLs:HAp	0	Some concerns	Low risk	No concerns	No concerns	Some concerns	Some concerns	Moderate
FLs:Pept.	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Some concerns	Moderate

Table A12. *Cont.*

Comparison	Number of Studies	SE with Chemical						
		Within-Study Bias	Reporting Bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
FLs:SiO_2	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Some concerns	Moderate
F:HAp	0	Some concerns	Low risk	No concerns	No concerns	Some concerns	Some concerns	Moderate
F:SiO_2	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Some concerns	Moderate
HEMA:HAp	0	Some concerns	Low risk	No concerns	Some concerns	No concerns	Some concerns	Moderate
HEMA:Pept.	0	Some concerns	Low risk	No concerns	No concerns	Major concerns	Some concerns	Low
HEMA:SiO_2	0	Some concerns	Low risk	No concerns	Some concerns	Some concerns	Some concerns	Moderate
HAp:Pept.	0	Some concerns	Low risk	No concerns	Some concerns	No concerns	Some concerns	Moderate
HAp:SiO_2	0	Some concerns	Low risk	No concerns	Some concerns	No concerns	Some concerns	Moderate

Legend: Control (CTRL), Fluorine (F), Calcium Phosphate (CaP), Peptide (Pept.), Silica (SiO_2), Flavonoids (FLs), Calcium (Ca), Hidroxiapatite (HAp). Different colors correspond to the Confidence Rating: orange for low, blue for moderate, yellow for some concern, green for no concern, and red for major concern.

Appendix A.6. Sensitivity Analyses

Table A13. Results of sensitivity analysis for ER with chemical network meta-analysis.

Random	Calcium					
	1.106 (−7.711, 9.922)	CaP				
	−0.123 (−8.738, 8.491)	−1.229 (−5.371, 2.913)	Control			
	−1.291 (−10.094, 7.512)	−2.397 (−7.595, 2.802)	−1.168 (−5.227, 2.892)	Fluorine		
	5.813 (−4.953, 16.580)	4.707 (−2.965, 12.380)	5.937 (−0.522, 12.395)	7.104 (−0.524, 14.733)	HAp	
	5.028 (−4.929, 14.984)	3.922 (−1.860, 9.704)	5.151 (−0.520, 10.822)	6.319 (−0.223, 12.860)	−0.786 (−9.381, 7.809)	Peptide
Without SB	Calcium					
	1.849 (−10.377, 14.074)	CaP				
	−1.065 (−12.941, 10.810)	−2.914 (−9.377, 3.549)	Control			
	−1.323 (−13.357, 10.710)	−3.172 (−10.460, 4.116)	−0.258 (−5.532, 5.016)	Fluorine		
	3.777 (−10.759, 18.313)	1.928 (−8.656, 12.513)	4.842 (−3.540, 13.225)	5.100 (−4.804, 15.004)	HAp	
	5.947 (−8.203, 20.096)	4.098 (−4.949, 13.145)	7.012 (−1.747, 15.771)	7.270 (−2.143, 16.683)	2.170 (−9.954, 14.293)	Peptide

Note: Data in each cell are mean difference (MD) with 95% confidence intervals (CI) for the network comparison of row-defining treatment versus column-defining treatment. Negative values favor the intervention in the column. Legend: Calcium Phosphate (CaP), Hydroxyapatite (HAp).

Table A14. Results of sensitivity analysis for ER with biological network meta-analysis.

Random	Calcium phosphate				
	−21.320 (−26.341, −16.299)	Control			
	−11.160 (−20.061, −2.258)	10.160 (2.810, 17.510)	Flavonoids		
	−17.063 (−22.451, −11.675)	4.257 (0.806, 7.708)	−5.903 (−14.023, 2.217)	Fluorine	
	−2.924 (−8.500, 2.652)	18.396 (14.256, 22.535)	**8.236 (−0.200, 16.672)**	14.139 (9.408, 18.870)	Peptide

Note: Data in each cell are mean difference (MD) with 95% confidence intervals (CI) for the network comparison of row-defining treatment versus column-defining treatment. Negative values favor the intervention in the column. In blue: results reaching a different conclusion from the main analysis.

Table A15. Results of sensitivity analysis for SE with chemical network meta-analysis.

Random	Calcium							
	1.938 (−2.927, 6.803)	CaP						
	1.437 (−3.182, 6.057)	−0.500 (−3.617, 2.616)	Control					
	10.407 (1.928, 18.887)	**8.470 (0.706, 16.233)**	**8.970 (1.859, 16.081)**	FLs				
	0.937 (−3.774, 5.649)	−1.000 (−4.507, 2.507)	−0.500 (−2.804, 1.804)	**−9.470 (−16.945, −1.995)**	Fluorine			
	0.768 (−5.753, 7.290)	−1.169 (−6.806, 4.467)	−0.669 (−5.510, 4.172)	**−9.639 (−18.241, −1.036)**	−0.169 (−5.004, 4.667)	HEMA		
	−3.124 (−8.605, 2.357)	−5.061 (−9.352, −0.771)	**−4.561 (−7.511, −1.611)**	−13.531 (−21.230, −5.832)	**−4.061 (−7.804, −0.318)**	−3.892 (−9.561, 1.776)	HAp	
	4.256 (−1.421, 9.932)	2.318 (−1.565, 6.201)	2.818 (−0.994, 6.632)	−6.152 (−14.220, 1.917)	**3.318 (−0.931, 7.568)**	3.487 (−2.601, 9.576)	**7.380 (2.559, 12.200)**	Peptide
	2.277 (−5.235, 9.789)	0.340 (−6.354, 7.033)	0.840 (−5.084, 6.764)	−8.130 (−17.385, 1.125)	**1.340 (−5.016, 7.696)**	**0.509** (−6.141, 9.159)	5.401 (−1.217, 12.019)	−1.978 (−9.024, 5.066)
Without SB	Calcium							
	3.937 (−3.398, 11.273)	CaP						
	0.117 (−6.760, 6.994)	−3.820 (−9.111, 1.471)	Control					
	4.721 (−6.357, 15.800)	0.784 (−9.386, 10.954)	4.604 (−4.082, 13.290)	FLs				
	0.254 (−6.695, 7.203)	−3.684 (−9.251, 1.884)	0.137 (−3.243, 3.516)	−4.467 (−13.787, 4.853)	Fluorine			
	−2.875 (−10.771, 5.021)	−6.812 (−13.373, −0.252)	−2.992 (−6.871, 0.887)	**−7.596 (−17.108, 1.916)**	−3.129 (−8.273, 2.016)	HAp		
	−2.811 (−11.987, 6.365)	−6.748 (−13.994, 0.498)	−2.928 (−9.722, 3.866)	−7.532 (−18.559, 3.495)	−3.065 (−10.240, 4.111)	0.064 (−7.759, 7.888)	Peptide	

Note: Data in each cell are mean difference (MD) with 95% confidence intervals (CI) for the network comparison of row-defining treatment versus column-defining treatment. Negative values favor the intervention in the column. In blue: results reaching a different conclusion from the main analysis. Legend: Calcium Phosphate (CaP), Hydroxyapatite (HAp), Flavonoids (FLs).

References

1. Swift, E.J., Jr. Dentin/enamel adhesives: Review of the literature. *Pediatr. Dent.* **2002**, *24*, 456–461. [PubMed]
2. Tjaderhane, L.; Nascimento, F.D.; Breschi, L.; Mazzoni, A.; Tersariol, I.L.; Geraldeli, S.; Tezvergil-Mutluay, A.; Carrilho, M.R.; Carvalho, R.M.; Tay, F.R.; et al. Optimizing dentin bond durability: Control of collagen degradation by matrix metalloproteinases and cysteine cathepsins. *Dent. Mater.* **2013**, *29*, 116–135. [CrossRef] [PubMed]
3. Yang, Y.; Xu, A.; Zhou, Z.; Shen, D.; Wu, Z.; Shi, Y. Mineralization strategy on dentin bond stability: A systematic review of in vitro studies and meta-analysis. *J. Adhes. Sci. Technol.* **2021**, *36*, 1666–1680. [CrossRef]
4. Pashley, D.H.; Tay, F.R.; Yiu, C.; Hashimoto, M.; Breschi, L.; Carvalho, R.M.D.; Ito, S. Collagen degradation by host-derived enzymes during aging. *J. Dent. Res.* **2004**, *83*, 216–221. [CrossRef]
5. Pashley, D.H.; Tay, F.R.; Breschi, L.; Tjaderhane, L.; Carvalho, R.M.; Carrilho, M.; Tezvergil-Mutluay, A. State of the art etch-and-rinse adhesives. *Dent. Mater.* **2011**, *27*, 1–16. [CrossRef]
6. Carrilho, M.R.O.; Geraldeli, S.; Tay, F.; De Goes, M.F.; Carvalho, R.M.; Tjäderhane, L.; Reis, A.F.; Hebling, J.; Mazzoni, A.; Breschi, L.; et al. In vivo preservation of the hybrid layer by chlorhexidine. *J. Dent. Res.* **2007**, *86*, 529–533. [CrossRef]
7. Barbosa-Martins, L.F.; Sousa, J.P.; Alves, L.A.; Davies, R.P.W.; Puppin-Rontanti, R.M. Biomimetic Mineralizing Agents Recover the Micro Tensile Bond Strength of Demineralized Dentin. *Materials* **2018**, *11*, 1733. [CrossRef]
8. Barbosa-Martins, L.F.; de Sousa, J.P.; de Castilho, A.R.F.; Puppin-Rontani, J.; Davies, R.P.W.; Puppin-Rontani, R.M. Enhancing bond strength on demineralized dentin by pre-treatment with selective remineralising agents. *J. Mech. Behav. Biomed. Mater.* **2018**, *81*, 214–221. [CrossRef]
9. Xu, A.-W.; Ma, Y.; Cölfen, H. Biomimetic mineralization. *J. Mater. Chem.* **2007**, *17*, 415–449. [CrossRef]
10. Cao, C.Y.; Mei, M.L.; Li, Q.L.; Lo, E.C.; Chu, C.H. Methods for biomimetic remineralization of human dentine: A systematic review. *Int. J. Mol. Sci.* **2015**, *16*, 4615–4627. [CrossRef]
11. Osorio, R.; Cabello, I.; Medina-Castillo, A.L.; Osorio, E.; Toledano, M. Zinc-modified nanopolymers improve the quality of resin-dentin bonded interfaces. *Clin. Oral Investig.* **2016**, *20*, 2411–2420. [PubMed]
12. Abuna, G.; Feitosa, V.P.; Correr, A.B.; Cama, G.; Giannini, M.; Sinhoreti, M.A.; Pashley, D.H.; Sauro, S. Bonding performance of experimental bioactive/biomimetic self-etch adhesives doped with calcium-phosphate fillers and biomimetic analogs of phosphoproteins. *J. Dent.* **2016**, *52*, 79–86. [CrossRef] [PubMed]
13. Kim, H.; Choi, A.; Gong, M.K.; Park, H.R.; Kim, Y.I. Effect of Remineralized Collagen on Dentin Bond Strength through Calcium Phosphate Ion Clusters or Metastable Calcium Phosphate Solution. *Nanomaterials* **2020**, *10*, 2203. [CrossRef] [PubMed]

14. Chen, R.; Jin, R.; Li, X.; Fang, X.; Yuan, D.; Chen, Z.; Yao, S.; Tang, R.; Chen, Z. Biomimetic remineralization of artificial caries dentin lesion using Ca/P-PILP. *Dent. Mater.* **2020**, *36*, 1397–1406. [CrossRef]
15. Moreira, K.M.; Bertassoni, L.E.; Davies, R.P.; Joia, F.; Hofling, J.F.; Nascimento, F.D.; Puppin-Rontani, R.M. Impact of biomineralization on resin/biomineralized dentin bond longevity in a minimally invasive approach: An "in vitro" 18-month follow-up. *Dent. Mater.* **2021**, *37*, e276–e289. [CrossRef]
16. Poggio, C.; Lombardini, M.; Vigorelli, P.; Ceci, M. Analysis of dentin/enamel remineralization by a CPP-ACP paste: AFM and SEM study. *Scanning* **2013**, *35*, 366–374.
17. Padovano, J.D.; Ravindran, S.; Snee, P.T.; Ramachandran, A.; Bedran-Russo, A.K.; George, A. DMP1-derived peptides promote remineralization of human dentin. *J. Dent. Res.* **2015**, *94*, 608–614.
18. Page, M.J.; McKenzie, J.E.; Bossuyt, P.M.; Boutron, I.; Hoffmann, T.C.; Mulrow, C.D.; Shamseer, L.; Tetzlaff, J.M.; Akl, E.A.; Brennan, S.E.; et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *BMJ* **2021**, *371*, n71.
19. Haj-Ali, R.; Walker, M.; Williams, K.; Wang, Y.; Spencer, P. Histomorphologic characterization of noncarious and caries-affected dentin/adhesive interfaces. *J. Prosthodont.* **2006**, *15*, 82–88.
20. Erhardt, M.C.; Toledano, M.; Osorio, R.; Pimenta, L.A. Histomorphologic characterization and bond strength evaluation of caries-affected dentin/resin interfaces: Effects of long-term water exposure. *Dent. Mater.* **2008**, *24*, 786–798.
21. Joves, G.J.; Inoue, G.; Nakashima, S.; Sadr, A.; Nikaido, T.; Tagami, J. Mineral density, morphology and bond strength of natural versus artificial caries-affected dentin. *Dent. Mater. J.* **2013**, *32*, 138–143. [CrossRef] [PubMed]
22. Dawasaz, A.A.; Togoo, R.A.; Mahmood, Z.; Ahmad, A.; Thirumulu Ponnuraj, K. Remineralization of Dentinal Lesions Using Biomimetic Agents: A Systematic Review and Meta-Analysis. *Biomimetics* **2023**, *8*, 159. [CrossRef] [PubMed]
23. Mourad Ouzzani, H.H. Zbys Fedorowicz, and Ahmed Elmagarmid. Rayyan—A web and mobile app for systematic reviews. *Syst. Rev.* **2016**, *5*, 210.
24. Sheth, V.H.; Shah, N.P.; Jain, R.; Bhanushali, N.; Bhatnagar, V. Development and validation of a risk-of-bias tool for assessing in vitro studies conducted in dentistry: The QUIN. *J. Prosthet. Dent.* **2022**, *131*, 1038–1042.
25. Nikolakopoulou, A.; Higgins, J.P.; Papakonstantinou, T.; Chaimani, A.; Del Giovane, C.; Egger, M.; Salanti, G. CINeMA: An approach for assessing confidence in the results of a network meta-analysis. *PLoS Med.* **2020**, *17*, e1003082. [CrossRef]
26. Papakonstantinou, T.; Nikolakopoulou, A.; Higgins, J.P.; Egger, M.; Salanti, G. CINeMA: Software for semiautomated assessment of the confidence in the results of network meta-analysis. *Campbell Syst. Rev.* **2020**, *16*, e1080.
27. Higgins, J.P.T.; Thomas, J.; Chandler, J.; Cumpston, M.; Li, T.; Page, M.J.; Welch, V.A. Chapter 6: Choosing Effect Measures and Computing Estimates of Effect. In *Cochrane Handbook for Systematic Reviews of Interventions*, version 6.3; Higgins, J.P.T., Li, T., Deeks, J.J., Eds.; Wiley: Hoboken, NJ, USA, 2022.
28. Jonas, D.E.; Wilkins, T.M.; Bangdiwala, S.; Bann, C.M.; Morgan, L.C.; Thaler, K.J.; Amick, H.R.; Gartlehner, G. Appendix A, WinBUGS Code Used in Bayesian Mixed Treatment Comparisons Meta-Analysis. In *Findings of Bayesian Mixed Treatment Comparison Meta-Analyses: Comparison and Exploration Using Real-World Trial Data and Simulation*; Agency for Healthcare Research and Quality: Rockville, MD, USA, 2013.
29. Bauer, J.; e Silva, A.S.; Carvalho, E.M.; Carvalho, C.N.; Carvalho, R.M.; Manso, A.P. A niobophosphate bioactive glass suspension for rewetting dentin: Effect on antibacterial activity, pH and resin-dentin bonding durability. *J. Int. J. Adhes. Adhes.* **2018**, *84*, 178–183.
30. Cardenas, A.F.M.; Siqueira, F.S.F.; Morales, L.A.R.; Araujo, L.C.R.; Campos, V.S.; Bauer, J.R.; Reis, A.; Loguercio, A.D. Influence of silver diamine fluoride on the adhesive properties of interface resin-eroded dentin. *Int. J. Adhes. Adhes.* **2021**, *106*, 102813.
31. Cifuentes-Jimenez, C.; Alvarez-Lloret, P.; Benavides-Reyes, C.; Gonzalez-Lopez, S.; Rodriguez-Navarro, A.B.; Bolaños-Carmona, M.V. Physicochemical and Mechanical Effects of Commercial Silver Diamine Fluoride (SDF) Agents on Demineralized Dentin. *J. Adhes. Dent.* **2021**, *23*, 557–567.
32. Dávila-Sánchez, A.; Gutierrez, M.F.; Bermudez, J.P.; Méndez-Bauer, M.L.; Hilgemberg, B.; Sauro, S.; Loguercio, A.D.; Arrais, C.A.G. Influence of flavonoids on long-term bonding stability on caries-affected dentin. *Dent. Mater.* **2020**, *36*, 1151–1160.
33. Gungormus, M.; Tulumbaci, F. Peptide-assisted pre-bonding remineralization of dentin to improve bonding. *J. Mech. Behav. Biomed. Mater.* **2021**, *113*, 104119. [CrossRef] [PubMed]
34. Krithi, B.; Vidhya, S.; Mahalaxmi, S. Microshear bond strength of composite resin to demineralized dentin after remineralization with sodium fluoride, CPP-ACP and NovaMin containing dentifrices. *J. Oral Biol. Craniofacial Res.* **2020**, *10*, 122–127. [CrossRef] [PubMed]
35. Meng, Y.; Huang, F.; Wang, S.; Li, M.; Lu, Y.; Pei, D.; Li, A. Bonding Performance of Universal Adhesives Applied to Nano-Hydroxyapatite Desensitized Dentin Using Etch-and-Rinse or Self-Etch Mode. *Materials* **2021**, *14*, 4746. [CrossRef] [PubMed]
36. Pei, D.; Meng, Y.; Li, Y.; Liu, J.; Lu, Y. Influence of nano-hydroxyapatite containing desensitizing toothpastes on the sealing ability of dentinal tubules and bonding performance of self-etch adhesive. *J. Mech. Behav. Biomed. Mater.* **2019**, *91*, 38–44. [CrossRef]
37. de Siqueira, F.S.F.; Morales, L.A.R.; Granja, M.C.P.; Melo, B.d.O.d.; Monteiro-Neto, V.; Reis, A.; Cardenas, A.F.M.; Loguercio, A.D. Effect of Silver Diamine Fluoride on the Bonding Properties to Caries-affected Dentin. *J. Adhes. Dent.* **2020**, *22*, 161–172.

38. Pulidindi, H.; Mandava, J.; Borugadda, R.; Ravi, R.; Angadala, P.; Penmatsa, P. Effect of remineralizing agents on resin-dentin bond durability of adhesive restorations: An in vitro. *J. Int. Oral Health* **2021**, *13*, 470–477.
39. Yang, H.; Chen, Z.; Yan, H.; Huang, C. Effects of calcium-containing desensitizers on the bonding stability of an etch-and-rinse adhesive against long-term water storage and pH cycling. *Dent. Mater. J.* **2018**, *37*, 122–129. [CrossRef]
40. Altinci, P.; Mutluay, M.; Tjäderhane, L.; Tezvergil-Mutluay, A. Microtensile bond strength to phosphoric acid-etched dentin treated with NaF, KF and CaF_2. *Int. J. Adhes. Adhes.* **2018**, *85*, 337–343. [CrossRef]
41. Zhang, L.; Sun, H.; Yu, J.; Yang, H.; Song, F.; Huang, C. Application of electrophoretic deposition to occlude dentinal tubules in vitro. *J. Dent.* **2018**, *71*, 43–48. [CrossRef]
42. Paik, Y.; Kim, J.H.; Yoo, K.H.; Yoon, S.Y.; Kim, Y.I. Dentin Biomodification with Flavonoids and Calcium Phosphate Ion Clusters to Improve Dentin Bonding Stability. *Materials* **2022**, *15*, 1494. [CrossRef]
43. Atomura, J.; Inoue, G.; Nikaido, T.; Yamanaka, K.; Uo, M.; Tagami, J. Influence of FCP-COMPLEX on bond strength and the adhesive artificial caries-affected dentin interface. *Dent. Mater. J.* **2018**, *37*, 775–782. [CrossRef] [PubMed]
44. de Sousa, J.P.; Carvalho, R.G.; Barbosa-Martins, L.F.; Torquato, R.J.S.; Mugnol, K.C.U.; Nascimento, F.D.; Tersariol, I.L.S.; Puppin-Rontani, R.M. The Self-Assembling Peptide P11-4 Prevents Collagen Proteolysis in Dentin. *J. Dent. Res.* **2019**, *98*, 347–354. [CrossRef] [PubMed]
45. Priya, C.L.; Naik, S.B.; Kumar, N.K.; Merwade, S.; Brigit, B.; Prabakaran, P. Evaluation of the bond strength of posterior composites to the dentin, treated with four different desensitizing agents—An In vitro study. *J. Int. Clin. Dent. Res. Organ.* **2020**, *12*, 38–41. [CrossRef]
46. Van Duker, M.; Hayashi, J.; Chan, D.C.; Tagami, J.; Sadr, A. Effect of silver diamine fluoride and potassium iodide on bonding to demineralized dentin. *Am. J. Dent.* **2019**, *32*, 143–146.
47. Zumstein, K.; Peutzfeldt, A.; Lussi, A.; Flury, S. The Effect of $SnCl_2$/AmF Pretreatment on Short- and Long-Term Bond Strength to Eroded Dentin. *Biomed. Res. Int.* **2018**, *2018*, 3895356. [CrossRef]
48. Cardenas, A.F.M.; Araujo, L.C.R.; Szesz, A.L.; Tavarez, R.R.d.J.; de Siqueira, F.S.F.; Reis, A.; Loguercio, A.D. Influence of Application of Dimethyl Sulfoxide on the Bonding Properties to Eroded Dentin. *J. Adhes. Dent.* **2021**, *23*, 589–598.
49. Cipriani, A.; Higgins, J.P.; Geddes, J.R.; Salanti, G. Conceptual and technical challenges in network meta-analysis. *Ann. Intern. Med.* **2013**, *159*, 130–137. [CrossRef]
50. Isolan, C.P.; Sarkis-Onofre, R.; Lima, G.S.; Moraes, R.R. Bonding to Sound and Caries-Affected Dentin: A Systematic Review and Meta-Analysis. *J. Adhes. Dent.* **2018**, *20*, 7–18. [CrossRef]
51. Marquezan, M.; Correa, F.N.; Sanabe, M.E.; Rodrigues Filho, L.E.; Hebling, J.; Guedes-Pinto, A.C.; Mendes, F.M. Artificial methods of dentine caries induction: A hardness and morphological comparative study. *Arch. Oral. Biol.* **2009**, *54*, 1111–1117. [CrossRef]
52. Ceballos, L.; Camejo, D.G.; Victoria Fuentes, M.; Osorio, R.; Toledano, M.; Carvalho, R.M.; Pashley, D.H. Microtensile bond strength of total-etch and self-etching adhesives to caries-affected dentine. *J. Dent.* **2003**, *31*, 469–477. [CrossRef]
53. Teixeira, G.S.; Pereira, G.K.R.; Susin, A.H. Aging Methods—An Evaluation of Their Influence on Bond Strength. *Eur. J. Dent.* **2021**, *15*, 448–453.
54. Hardan, L.; Bourgi, R.; Kharouf, N.; Mancino, D.; Zarow, M.; Jakubowicz, N.; Haikel, Y.; Cuevas-Suarez, C.E. Bond Strength of Universal Adhesives to Dentin: A Systematic Review and Meta-Analysis. *Polymers* **2021**, *13*, 814. [CrossRef] [PubMed]
55. Wiegand, A.; Lechte, C.; Kanzow, P. Adhesion to eroded enamel and dentin: Systematic review and meta-analysis. *Dent. Mater.* **2021**, *37*, 1845–1853. [CrossRef]
56. Niu, L.N.; Zhang, W.; Pashley, D.H.; Breschi, L.; Mao, J.; Chen, J.H.; Tay, F.R. Biomimetic remineralization of dentin. *Dent. Mater.* **2014**, *30*, 77–96. [CrossRef]
57. Doozandeh, M.; Firouzmandi, M.; Mirmohammadi, M. The Simultaneous Effect of Extended Etching Time and Casein Phosphopeptide-Amorphous Calcium Phosphate containing Paste Application on Shear Bond Strength of Etch-and-rinse Adhesive to Caries-affected Dentin. *J. Contemp. Dent. Pract.* **2015**, *16*, 794–799. [CrossRef]
58. Bergamin, A.C.P.; Bridi, E.C.; Amaral, F.L.B.; Turssi, C.P.; Basting, R.T.; Aguiar, F.H.B.; França, F.M.G. Influence of an arginine-containing toothpaste on bond strength of different adhesive systems to eroded dentin. *Gen. Dent.* **2016**, *64*, 67–73.
59. Ghani, S.; Khan, M.H.; Jindal, M.K.; Chaudhary, S.; Manuja, N. Comparative Evaluation of The Influence of Pre-Treatment With Cpp-Acp and Novamin On Dentinal Shear Bond Strength With Composite-An In Vitro Study. *Ann. Dent. Spec.* **2017**, *5*, 140–145.
60. Komori, P.C.P.; Pashley, D.H.; Tjäderhane, L.; Breschi, L.; Mazzoni, A.; de Goes, M.F.; Wang, L.; Carrilho, M.R. Effect of 2% chlorhexidine digluconate on the bond strength to normal versus caries-affected dentin. *Oper. Dent.* **2009**, *34*, 157–165. [CrossRef]
61. Leal, A.; Carvalho, C.; Maia-Filho, E.; Monteiro-Neto, V.; Carmo, M.; Maciel, A.; Bauer, J. Airborne-particle abrasion with niobium phosphate bioactive glass on caries-affected dentin-effect on the microtensile bond strength. *J. Adhes. Sci. Technol.* **2017**, *31*, 2410–2423. [CrossRef]
62. Luong, M.N.; Huang, L.; Chan, D.C.N.; Sadr, A. In Vitro Study on the Effect of a New Bioactive Desensitizer on Dentin Tubule Sealing and Bonding. *J. Funct. Biomater.* **2020**, *11*, 38. [CrossRef]

63. Meraji, N.; Nekoofar, M.H.; Yazdi, K.A.; Sharifian, M.R.; Fakhari, N.; Camilleri, J. Bonding to caries affected dentine. *Dent. Mater.* **2018**, *34*, e236–e245. [CrossRef] [PubMed]
64. Prasansuttiporn, T.; Thanatvarakorn, O.; Mamanee, T.; Hosaka, K.; Tagami, J.; Foxton, R.M.; Nakajima, M. Effect of antioxidant/reducing agents on the initial and long-term bonding performance of a self-etch adhesive to caries-affected dentin with and without smear layer-deproteinizing. *Int. J. Adhes. Adhes.* **2020**, *102*, 102648.
65. Sajjad, M.; Munir, N.; Inayat, N.; Qaiser, A.; Wajahat, M.; Khan, M.W. Shear Bond Strength Of Etch And Rinse Adhesives To Dentin- Comparison Of Bond Strength After Acid and Papacarie Pre-Treatment. *J. Ayub Med. Coll. Abbottabad* **2022**, *34*, 45–48.
66. Yilmaz, N.A.; Ertas, E.; Orucoglu, H. Evaluation of Five Different Desensitizers: A Comparative Dentin Permeability and SEM Investigation In Vitro. *Open Dent. J.* **2017**, *11*, 15–33.
67. Castellan, C.S.; Pereira, P.N.; Grande, R.H.; Bedran-Russo, A.K. Mechanical characterization of proanthocyanidin-dentin matrix interaction. *Dent. Mater.* **2010**, *26*, 968–973.
68. Okuyama, K.; Komatsu, H.; Yamamoto, H.; Pereira, P.N.R.; Bedran-Russo, A.K.; Nomachi, M.; Sato, T.; Sano, H. Fluorine analysis of human dentin surrounding resin composite after fluoride application by μ-PIGE/PIXE analysis. *Nucl. Instrum. Methods Phys. Res. Sect. B Beam Interact. Mater. At.* **2011**, *269*, 2269–2273. [CrossRef]
69. Wang, Y.; Liu, S.; Pei, D.; Du, X.; Ouyang, X.; Huang, C. Effect of an 8.0 arginine and calcium carbonate in-office desensitizing paste on the microtensile bond strength of self-etching dental adhesives to human dentin. *Am. J. Dent.* **2012**, *25*, 281–286.
70. de-Melo, M.A.S.; Goes, D.D.C.; de-Moraes, M.D.R.; Santiago, S.L.; Rodrigues, L.K.A. Effect of chlorhexidine on the bond strength of a self-etch adhesive system to sound and demineralized dentin. *Braz. Oral. Res.* **2013**, *27*, 218–224.
71. Carvalho, C.; Fernandes, F.P.; Freitas Vda, P.; Franca, F.M.; Basting, R.T.; Turssi, C.P.; Amaral, F.L. Effect of green tea extract on bonding durability of an etch-and-rinse adhesive system to caries-affected dentin. *J. Appl. Oral. Sci.* **2016**, *24*, 211–217. [CrossRef]
72. Deari, S.; Wegehaupt, F.J.; Taubock, T.T.; Attin, T. Influence of Different Pretreatments on the Microtensile Bond Strength to Eroded Dentin. *J. Adhes. Dent.* **2017**, *19*, 147–155.
73. Giacomini, M.C.; Scaffa, P.; Chaves, L.P.; Vidal, C.; Machado, T.N.; Honorio, H.M.; Tjaderhane, L.; Wang, L. Role of Proteolytic Enzyme Inhibitors on Carious and Eroded Dentin Associated With a Universal Bonding System. *Oper. Dent.* **2017**, *42*, E188–E196. [PubMed]
74. Rodrigues, R.V.; Giannini, M.; Pascon, F.M.; Panwar, P.; Bromme, D.; Manso, A.P.; Carvalho, R.M. Effect of conditioning solutions containing ferric chloride on dentin bond strength and collagen degradation. *Dent. Mater.* **2017**, *33*, 1093–1102. [CrossRef] [PubMed]
75. Imiolczyk, S.M.; Hertel, M.; Hase, I.; Paris, S.; Blunck, U.; Hartwig, S.; Preissner, S. The Influence of Cold Atmospheric Plasma Irradiation on the Adhesive Bond Strength in Non-Demineralized and Demineralized Human Dentin: An In Vitro Study. *Open Dent. J.* **2018**, *12*, 960–968.
76. Stape, T.H.S.; Mutluay, M.M.; Tjaderhane, L.; Uurasjarvi, E.; Koistinen, A.; Tezvergil-Mutluay, A. The pursuit of resin-dentin bond durability: Simultaneous enhancement of collagen structure and polymer network formation in hybrid layers. *Dent. Mater.* **2021**, *37*, 1083–1095.
77. Hartz, J.J.; Keller, S.P.; Tauböck, T.T.; Attin, T.; Wegehaupt, F.J. Influence of pretreatments on microtensile bond strength to eroded dentin using a universal adhesive in self-etch mode. *Int. J. Adhes. Adhes.* **2022**, *114*, 103108.
78. Wang, A.S.; Botelho, M.G.; Tsoi, J.K.H.; Matinlinna, J.P. Effects of silver diammine fluoride on microtensile bond strength of GIC to dentine. *Int. J. Adhes. Adhes.* **2016**, *70*, 196–203.
79. Moda, M.D.; Fagundes, T.C.; Briso, A.L.F.; Dos Santos, P.H. Analysis of the bond interface between self-adhesive resin cement to eroded dentin in vitro. *PLoS ONE* **2018**, *13*, e0208024.
80. Choi, Y.J.; Bae, M.K.; Kim, Y.I.; Park, J.K.; Son, S.A. Effects of microsurface structure of bioactive nanoparticles on dentinal tubules as a dentin desensitizer. *PLoS ONE* **2020**, *15*, e0237726.
81. Abdelshafi, M.A.; Fathy, S.M.; Elkhooly, T.A.; Reicha, F.M.; Osman, M.F. Bond strength of demineralized dentin after synthesized collagen/hydroxyapatite nanocomposite application. *J. Mech. Behav. Biomed. Mater.* **2021**, *121*, 104590.
82. Al-Qahtani, Y.M. Impact of graphene oxide and silver diamine fluoride in comparison to photodynamic therapy on bond integrity and microleakage scores of resin modified glass ionomer cement to demineralized dentin. *Photodiagnosis Photodyn. Ther.* **2021**, *33*, 102163.
83. Khor, M.M.; Rosa, V.; Sim, C.J.; Hong, C.H.L.; Hu, S. SMART: Silver diamine fluoride reduces microtensile bond strength of glass ionomer cement to sound and artificial caries-affected dentin. *Dent. Mater. J.* **2022**, *41*, 698–704. [CrossRef] [PubMed]
84. Adebayo, O.A.; Burrow, M.F.; Tyas, M.J. Resin-dentine interfacial morphology following CPP-ACP treatment. *J. Dent.* **2010**, *38*, 96–105. [CrossRef]
85. Liu, Y.; Mai, S.; Li, N.; Yiu, C.K.; Mao, J.; Pashley, D.H.; Tay, F.R. Differences between top-down and bottom-up approaches in mineralizing thick, partially demineralized collagen scaffolds. *Acta Biomater.* **2011**, *7*, 1742–1751. [CrossRef]
86. Chen, C.; Mao, C.; Sun, J.; Chen, Y.; Wang, W.; Pan, H.; Tang, R.; Gu, X. Glutaraldehyde-induced remineralization improves the mechanical properties and biostability of dentin collagen. *Mater. Sci. Eng. C Mater. Biol. Appl.* **2016**, *67*, 657–665. [CrossRef]

87. Bortolotto, T.; Ryabova, A.; Nerushay, I.; Kling, S.; Hafezi, F.; Garcia-Godoy, F.; Krejci, I. Effects of riboflavin, calcium-phosphate layer and adhesive system on stress-strain behavior of demineralized dentin. *Am. J. Dent.* **2017**, *30*, 179–184.
88. Liang, K.; Weir, M.D.; Reynolds, M.A.; Zhou, X.; Li, J.; Xu, H.H.K. Poly (amido amine) and nano-calcium phosphate bonding agent to remineralize tooth dentin in cyclic artificial saliva/lactic acid. *Mater. Sci. Eng. C Mater. Biol. Appl.* **2017**, *72*, 7–17. [CrossRef]
89. Wang, Y.; Green, A.; Yao, X.; Liu, H.; Nisar, S.; Gorski, J.P.; Hass, V. Cranberry Juice Extract Rapidly Protects Demineralized Dentin against Digestion and Inhibits Its Gelatinolytic Activity. *Materials* **2021**, *14*, 3637. [CrossRef]
90. Zhou, J.; Chiba, A.; Scheffel, D.L.; Hebling, J.; Agee, K.; Tagami, J.; Tan, J.; Abuelenain, D.; Nawareg, M.A.; Hassan, A.H.; et al. Cross-linked dry bonding: A new etch-and-rinse technique. *Dent. Mater.* **2016**, *32*, 1124–1132. [CrossRef]
91. Flury, S.; Lussi, A.; Peutzfeldt, A. Long-Term Bond Strength of Two Benzalkonium Chloride-Modified Adhesive Systems to Eroded Dentin. *Biomed. Res. Int.* **2017**, *2017*, 1207208. [CrossRef]
92. Ye, Q.; Spencer, P.; Yuca, E.; Tamerler, C. Engineered Peptide Repairs Defective Adhesive-Dentin Interface. *Macromol. Mater. Eng.* **2017**, *302*, 1600487. [CrossRef]
93. Liang, K.; Xiao, S.; Weir, M.D.; Bao, C.; Liu, H.; Cheng, L.; Zhou, X.; Li, J.; Xu, H.H.K. Poly (amido amine) dendrimer and dental adhesive with calcium phosphate nanoparticles remineralized dentin in lactic acid. *J. Biomed. Mater. Res. B Appl. Biomater.* **2018**, *106*, 2414–2424. [CrossRef] [PubMed]
94. Hasegawa, M.; Tichy, A.; Hosaka, K.; Kuno, Y.; Ikeda, M.; Nozaki, K.; Chiba, A.; Nakajima, M.; Tagami, J. Degree of conversion and dentin bond strength of light-cured multi-mode adhesives pretreated or mixed with sulfinate agents. *Dent. Mater. J.* **2021**, *40*, 877–884. [CrossRef] [PubMed]
95. Bridi, E.C.; Botelho Amaral, F.L.; Gomes França, F.M.; Martão Flório, F.; Basting, R.T. Influence of storage time on bond strength of self-etching adhesive systems to artificially demineralized dentin after a papain gel chemical–mechanical agent application. *Int. J. Adhes. Adhes.* **2012**, *38*, 31–37. [CrossRef]
96. Castellan, C.S.; Bedran-Russo, A.K.; Antunes, A.; Pereira, P.N. Effect of dentin biomodification using naturally derived collagen cross-linkers: One-year bond strength study. *Int. J. Dent.* **2013**, *2013*, 918010. [CrossRef]
97. Monteiro, T.M.A.; Basting, R.T.; Turssi, C.P.; França, F.M.G.; Amaral, F.L.B. Influence of natural and synthetic metalloproteinase inhibitors on bonding durability of an etch-and-rinse adhesive to dentin. *Int. J. Adhes. Adhes.* **2013**, *47*, 83–88. [CrossRef]
98. Abu Nawareg, M.; Elkassas, D.; Zidan, A.; Abuelenain, D.; Abu Haimed, T.; Hassan, A.H.; Chiba, A.; Bock, T.; Agee, K.; Pashley, D.H. Is chlorhexidine-methacrylate as effective as chlorhexidine digluconate in preserving resin dentin interfaces? *J. Dent.* **2016**, *45*, 7–13. [CrossRef]
99. Lee, J.; Sabatini, C. Glutaraldehyde collagen cross-linking stabilizes resin-dentin interfaces and reduces bond degradation. *Eur. J. Oral Sci.* **2017**, *125*, 63–71. [CrossRef]
100. Prasansuttiporn, T.; Thanatvarakorn, O.; Tagami, J.; Foxton, R.M.; Nakajima, M. Bonding Durability of a Self-etch Adhesive to Normal Versus Smear-layer Deproteinized Dentin: Effect of a Reducing Agent and Plant-extract Antioxidant. *J. Adhes. Dent.* **2017**, *19*, 253–258.
101. Ramezanian Nik, I.; Baradaran Naseri, E.; Majidinia, S.; Ramezanian Nik, S.; Jafari Giv, M. Effect of Chlorhexidine and Ethanol on Microleakage of Composite Resin Restoration to Dentine. *Chin. J. Dent. Res.* **2017**, *20*, 161–168.
102. Costa, C.A.G.; Passos, V.F.; Neri, J.R.; Mendonca, J.S.; Santiago, S.L. Effect of Metalloproteinase Inhibitors on Bond Strength of a Self-etching Adhesive on Erosively Demineralized Dentin. *J. Adhes. Dent.* **2019**, *21*, 337–344.
103. Fialho, M.P.N.; Hass, V.; Nogueira, R.P.; Franca, F.M.G.; Turssi, C.P.; Basting, R.T.; Amaral, F.L.B. Effect of epigallocatechin-3-gallate solutions on bond durability at the adhesive interface in caries-affected dentin. *J. Mech. Behav. Biomed. Mater.* **2019**, *91*, 398–405. [CrossRef] [PubMed]
104. Landmayer, K.; Liberatti, G.A.; Farias-Neto, A.M.; Wang, L.; Honorio, H.M.; Francisconi-Dos-Rios, L.F. Could applying gels containing chlorhexidine, epigallocatechin-3-gallate, or proanthocyanidin to control tooth wear progression improve bond strength to eroded dentin? *J. Prosthet. Dent.* **2020**, *124*, 798.e1–798.e7. [CrossRef] [PubMed]
105. Costa, A.R.; Naves, L.Z.; Garcia-Godoy, F.; Tsuzuki, F.M.; Correr, A.B.; Correr-Sobrinho, L.; Puppin-Rontani, R.M. CHX Stabilizes the Resin-demineralized Dentin Interface. *Braz. Dent. J.* **2021**, *32*, 106–115. [CrossRef] [PubMed]
106. Giacomini, M.C.; Candia Scaffa, P.M.; Goncalves, R.S.; Jacomine, J.C.; Zabeu, G.S.; Carrilho, M.R.O.; Honorio, H.M.; Wang, L. Performance of MDP-based system in eroded and carious dentin associated with proteolytic inhibitors: 18-Month exploratory study. *J. Mech. Behav. Biomed. Mater.* **2021**, *114*, 104177. [CrossRef]
107. Shioya, Y.; Tichy, A.; Yonekura, K.; Hasegawa, M.; Hatayama, T.; Ikeda, M.; Tagami, J.; Nakajima, M.; Hosaka, K. Sodium p-Toluenesulfinate Enhances the Bonding Durability of Universal Adhesives on Deproteinized Eroded Dentin. *Polymers* **2021**, *13*, 3901. [CrossRef]
108. Xu, J.; Chen, Y.; Li, X.; Lei, Y.; Shu, C.; Luo, Q.; Chen, L.; Li, X. Reconstruction of a Demineralized Dentin Matrix via Rapid Deposition of CaF_2 Nanoparticles In Situ Promotes Dentin Bonding. *ACS Appl. Mater. Interfaces* **2021**, *13*, 51775–51789. [CrossRef]

109. Tekbas Atay, M.; Seseogullari-Dirihan, R.; Mutluay, M.M.; Tezvergil-Mutluay, A. Long-term effect of curcuminoid treatment on resin-to-dentin bond strength. *Eur. J. Oral. Sci.* **2022**, *130*, e12837. [CrossRef]
110. Lemos, M.; Araujo-Neto, V.G.; Lomonaco, D.; Mazzetto, S.E.; Feitosa, V.P.; Santiago, S.L. Evaluation of Novel Plant-derived Monomers-based Pretreatment on Bonding to Sound and Caries-affected Dentin. *Oper. Dent.* **2022**, *47*, E12–E21. [CrossRef]
111. Zhang, Y.; Liu, Y.H.; Zhou, Y.S.; Chung, K.H. Influence of carbodiimide-ethanol solution surface treatment on dentin microtensile bond strength. *Beijing Da Xue Xue Bao Yi Xue Ban* **2015**, *47*, 825–828.
112. Wang, H.; Xiao, Z.; Yang, J.; Lu, D.; Kishen, A.; Li, Y.; Chen, Z.; Que, K.; Zhang, Q.; Deng, X.; et al. Oriented and Ordered Biomimetic Remineralization of the Surface of Demineralized Dental Enamel Using HAP@ACP Nanoparticles Guided by Glycine. *Sci. Rep.* **2017**, *7*, 40701. [CrossRef]
113. Meng, Y.C.; Huang, F.; Wang, S.L.; Li, M.W.; Lu, Y.; Pei, D.D. [Effect of hydroxyapatite based agents on the bonding properties of universal adhesives]. *Zhonghua Kou Qiang Yi Xue Za Zhi* **2022**, *57*, 173–181.