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Research Article

Do universal adhesives promote bonding to dentin? A systematic review and meta-analysis

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No potential conflict of interest relevant to this article was reported.

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ABSTRACT

Objectives: The aims of this study were to conduct a systematic review of the microtensile bond strength (μTBS) of multi-mode adhesives to dentin and to perform a meta-analysis to assess the significance of differences in the μTBS of one of the most commonly used universal adhesives (Scotchbond Universal, 3M ESPE) depending on whether the etch-and-rinse or self-etch mode was used.
Materials and Methods: An electronic search was performed of MEDLINE/PubMed, ScienceDirect, and EBSCOhost. Laboratory studies that evaluated the μTBS of multi-mode adhesives to dentin using either the etch-and-rinse or self-etch mode were selected. A meta-analysis was conducted of the reviewed studies to quantify the differences in the μTBS of Scotchbond Universal adhesive.
Results: Only 10 studies fulfilled the inclusion criteria for the systematic review. Extensive variation was found in the restorative materials, testing methodologies, and failure mode in the reviewed articles. Furthermore, variation was also observed in the dimensions of the microtensile testing beams. The meta-analysis showed no statistically significant difference between the etch-and-rinse and self-etch modes for Scotchbond Universal adhesive ($p > 0.05$).
Conclusions: Multi-mode 'universal' adhesives can achieve substantial bonding to dentin, regardless of the used modes (either etch-and-rinse or self-etch).

Keywords: Dentin bonding agents; Multi-mode adhesives; Systematic review; Universal adhesives

INTRODUCTION

Evidence-based dentistry is an approach to oral health care requiring the judicious integration of systematic assessments of clinically relevant scientific evidence [1]. In routine dental practice, clinicians are committed to providing the best possible dental care for patients. Nowadays, clinical decision-making procedure becomes more sophisticated due to the huge amount of scientific information that is continually published on new therapies, techniques, and restorative materials, which underscores the importance of an evidence-based approach in the field of dentistry. Systematic reviews and meta-analyses are considered to be the highest level of evidence supporting evidence-based decision-making [2].

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The preliminary results of this study were presented at the International Association for Dental Research (IADR) general meeting held in South Korea (June 2016).

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Adhesive dentistry has advanced rapidly in the past 10 years. Three main strategies are used. The first is based on the total removal of the smear layer, and is referred to as the 'etch-and-rinse' approach [3]. Conversely, the second strategy depends on modifying the smear layer, aiming to incorporate it into the adhesive layer; this is referred to as the 'self-etch' approach. Additionally, the multi-mode strategy is a combination of the etch-and-rinse and self-etch approaches [4].

In the late 1990s, the chronological 'generation'-based classification of adhesives was widely used. In this classification, adhesives are classified into 7 generations, according to the chronology of their development. The fourth generation of adhesives was the most famous, to the point that they were referred to as the 'gold standard' or 'classic' adhesives, in addition to the more descriptive term of 'three-step etch-and-rinse' adhesives. Subsequent generations were introduced to simplify the clinical use of adhesives, up to the seventh generation, which comprises 'all-in-one' adhesives. Due to the many overlaps and unclear boundaries between the generations, this classification has almost disappeared from regular use, and a new classification was introduced by Van Meerbeek in the early 2000s [4]. According to Van Meerbeek's classification, contemporary dental adhesives are categorized into 3 main groups based on the smear layer treatment strategy: etch-and-rinse, self-etch, and the resin-modified glass-ionomer approach. Then, according to the number of clinical application steps, etch-and-rinse adhesives are further divided into 2 groups: 2- or 3-step etch-and-rinse adhesives. Similarly, self-etch adhesives are further divided into one-step ('all-in-one') or two-step self-etch adhesives. Recently, another group, known as universal or multi-mode adhesives, was added to the previous classification [5].

These novel multi-mode adhesives reduce the complexity of clinical application procedures. Adhesives in this category may be used as etch-and-rinse adhesives, self-etch adhesives, or as self-etch adhesives on dentin and etch-and-rinse adhesives on enamel (a technique commonly referred to as 'selective enamel etching') [6]. Functional monomers are the principal ingredient of recently developed multi-mode adhesives [7,8], as they play a major role in chemical adhesion to dentin. Thirty years ago, a dental manufacturer (Kuraray Noritake Dental Inc., Tokyo, Japan) incorporated 10-methacryloyloxydecyl dihydrogen phosphate (10-MDP) as a functional monomer in their dental adhesives. The phosphate group of the MDP interacts with the hydroxyapatite and significantly contributes to the long-term durability of the resin-dentin interface [9].

MDP-based adhesives can chemically bond to the hydroxyapatite crystals of dentin via the electrostatic interactions of ionic bonds formed with the calcium ions of the hydroxyapatite crystals, resulting in an insoluble MDP-calcium salt. Moreover, the phosphate groups in MDP form covalent bonds with the corresponding phosphate groups of hydroxyapatite crystals to form insoluble salts [10,11]. The continual deposition of successive coats of these salts on the outer surface of the hydroxyapatite crystal is a process known as 'nanolayering' [12,13]. Laboratory bond strength tests can provide important insights into the clinical performance of an adhesive under different dislodging forces [14].

The outcomes of previous studies regarding this particular point are unclear and sometimes conflicting. Wagner *et al.* [15] evaluated the microtensile bond strength of 3 different multi-mode adhesives applied in 2 different modes, self-etch or etch-and-rinse. Their results revealed that the separate etching step did not improve the microtensile bond strength of the multi-mode adhesives when compared to the self-etch application mode. Additionally, the study by Chen *et al.* [16] showed no significant difference in the bonding of multi-mode adhesive to dentin between the etch-and-rinse and self-etch application modes. Conversely, the study of Muñoz *et al.* [17] reported that this new category of adhesives exhibited inferior microtensile bond strength values compared to the control 'conventional' adhesives.

The key question of this review was "Do multi-mode adhesives provide adequate bonding to dentin when used in either the etch-and-rinse or self-etch mode?" This question cannot be answered in light of the currently available scientific evidence, which is weak. Therefore, this review was designed to assess and analyze the currently available published studies evaluating the bond strength of multi-mode adhesives to dentin. The null hypothesis tested was that there is no difference in the bond strength of multi-mode adhesives to dentin between the etch-and-rinse and self-etch modes.

MATERIALS AND METHODS

Search strategy

In the current review, 3 databases were searched: the National Library of Medicine (MEDLINE/PubMed), ScienceDirect, and EBSCOhost. Studies published after 2005 were included in this review. The keywords used when searching the databases were ('multi-mode' or 'universal' or 'multi-purpose' or 'bonding strategies' or 'multi-mode adhesive' or 'universal adhesive') and ('microtensile' or 'bond strength') and ('micromorphology' or 'ultramorphology').

Inclusion/exclusion criteria

Only laboratory studies and manuscripts written in English were included in this structured review. The following studies were excluded: non-English manuscripts, studies published before 2005 (only studies from 2005 until 2016 were included), *in vitro* studies using animal teeth, review articles, and clinical trials and case reports. Moreover, studies used that multi-mode adhesives for other purposes were excluded. The initial search of the PubMed database identified 542 articles, and was then followed by a subsequent search of the other 2 databases in addition to a manual search.

Eight manuscripts were excluded because they were not written in English, and 181 studies were excluded because they were published before 2005. A further 173 *in vitro* studies using animal teeth were excluded. Of the remaining 180 manuscripts, 57 clinical trials and 6 review articles were excluded, and 105 other studies were excluded because they utilized universal adhesives for other purposes, such as enamel bonding, bonding to primary teeth, bonding to anterior teeth, orthodontic bracket adhesion, prosthodontics, and endodontics. The detailed study selection procedures are illustrated in a flowchart (**Figure 1**).

Two authors of this review independently assessed the titles and abstracts of all the studies. Studies were included if they were conducted to evaluate the bonding of multi-mode adhesives to dentin using either the self-etch or etch-and-rinse mode. Studies in which the secondary outcome was the bond strength of multi-mode adhesives to enamel and dentin were also included. The full-text papers were independently assessed in duplicate by the 3 authors. In this review, a study was included if at least 2 of the reviewers (authors) agreed that it was suitable. The reviewed studies were subjected to meta-analysis to quantify the

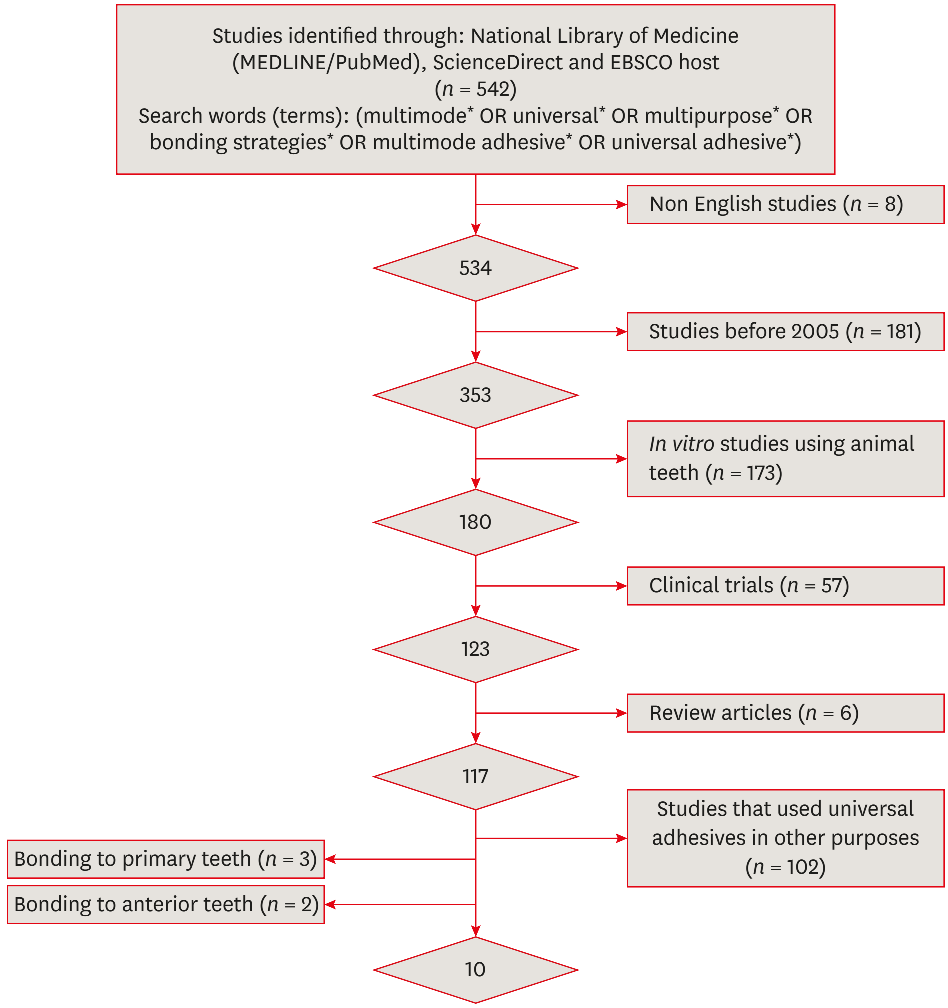

Figure 1. Flowchart of the study selection procedure.

differences in the mean microtensile bond strength of Scotchbond Universal adhesive using Comprehensive Meta-Analysis software, version 2 (Biostat, Englewood, NJ, USA), with 95% confidence intervals.

RESULTS

The current review evaluated 10 studies [15-24] that were conducted to evaluate the bond strength of 6 different brands of multi-mode adhesives to dentin. Seven of them (70%) evaluated the bond strength of the Scotchbond Universal adhesive (3M ESPE, St. Paul, MN, USA) [15-21]. Six studies (60%) evaluated the bond strength of All-Bond Universal (Bisco, Schaumburg, IL, USA) [15-18,20,21], and 4 studies (40%) evaluated the bond strength of G-bond Plus (GC, Tokyo, Japan) [18,22-24]. The remaining studies evaluated other universal adhesives: Prime & Bond Elect (Dentsply Caulk, Milford, DE, USA; 20%) [16,20], Futurabond Universal (Voco, Cuxhaven, Germany; 20%) [15,16], Peak Universal Adhesive (Ultradent, South Jordan, UT, USA; 20%) [17,21], and Clearfil Universal Bond (Kuraray Noritake Dental Inc.; 10%) [16].

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In addition, different types of restorative materials were used, as some studies used the nanocomposite Filtek Z350 (3M ESPE; 30%) [18,20,24], while other studies used Opallis (FGM, Joinville, SC, Brazil; 20%) [17,21]. Additionally, microhybrid composites were used in the studies, such as Filtek Z250 (3M ESPE; 10%) [19], Clearfil AP-X (Kuraray Noritake Dental Inc.; 10%) [22], Venus (Heraeus Kulzer, Hanau, Germany; 10%) [23], and TPH Spectra (Dentsply Caulk; 10%) [16]. The other restorative material used was a nanohybrid composite (GrandioSO, Voco; 10%) [15]. The geographical distribution of the reviewed manuscripts was as follows: 4 studies in South America (40%) [17,18,20,21], 3 in Europe (30%) [15,22,23], 2 in North America (20%) [19,24], and only one study in Asia (10%) [16].

Most of the reviewed articles were recently published. Four studies were published in 2014 (40%) [15,18,20,21], 2 were published in 2013 (20%) [17,24], 3 were published in 2012 (30%) [19,22,23], and only one study was published in 2015 (10%) [16]. All the reviewed studies (100%) used the microtensile bond strength testing method to determine the bond strength as the primary testing method [15-24]. However, they showed considerable variation in the secondary testing methods: 4 studies (40%) evaluated interfacial nanoleakage [17,18,20,21], 3 studies (30%) evaluated the degree of conversion [17,18,24], and the remaining studies (40%) evaluated the ultra-morphology of the resin-dentin interface using scanning electron microscopy or transmission electron microscopy [15,16,19,22]. Additionally, 2 studies (20%) evaluated the enamel microtensile bond strength [22,24] and one study (10%) evaluated the dentin microshear bond strength [23]. The summary findings, testing methods, and materials of the included studies are presented in **Tables 1** and **2**.

The predominant failure mode in the reviewed studies varied widely. The predominant failure mode was adhesive/mixed in 4 studies (40%) [17,18,21,24], adhesive in 3 studies (30%) [15,17,20], and mixed in 2 studies (20%) [15,16]. Moreover, all the authors clearly stated that the teeth were randomly selected. Furthermore, all the reviewed studies included a control group and were conducted on caries-free molars. The testing cross-head speed of the universal testing machine varied among the studies, as did the microtensile beam dimension. The majority of the studies (80%) used a cross-head speed of 0.5 mm/min [15,17-22,24]; however, 2 studies (20%) used a cross-head speed of 1 mm/min [16,22]. Six studies (60%) used beam dimensions of 0.8 × 0.8 mm [17-21,24], 2 studies (20%) used beam dimensions of 1 × 1 mm [15,22], 1 study (10%) [16] used beam dimensions of 0.9 × 0.9 mm, and another study (10%) [23] used sample dimensions of 0.7 × 0.7 mm. The examiner was blinded in only 3 studies (30%) [17,18,21].

Regarding the quality of the studies included, 8 presented a medium risk of bias, while 2 studies showed a low risk of bias. These results are presented in **Table 3**, according to the parameters considered in the analysis. The studies scored particularly poorly on the following items: description of the coefficient of variation, sample size calculation, and blinding of the examiner.

The outcomes of the microtensile bond strength testing of the multi-mode adhesives used in the reviewed articles are shown in **Table 4**. After carefully reviewing the selected articles, it was found that 70% evaluated the microtensile bond strength of Scotchbond Universal in both etching modes; therefore, a meta-analysis was conducted. The meta-analysis was performed by combining all the data concerning the microtensile bond strength of Scotchbond Universal in both etching modes with the related number of teeth per group used in the corresponding study (**Table 5**). The results of the meta-analysis of the microtensile bond strength for Scotchbond Universal were 37.07 ± 2.12 MPa for the etch-and-rinse mode

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Table 1. Summary of the studies included in this systematic review

Study	Predominant failure mode	No. of teeth (per group)	Objective	Conclusion
Chen *et al.* [16]	Mixed	200 (10)	To examine the short-term *in vitro* performance of 5 universal adhesives bonded to human coronal dentin	The increase in the versatility of universal adhesives was not accompanied by technological advances for overcoming the challenges associated with previous generations of adhesives.
Wagner *et al.* [15]	Adhesive	72 (12)	To compare the μTBS and resin penetration into dentin of 3 universal adhesives applied in 2 different etching modes	Application of an etching step prior to applying universal adhesives improved their dentin penetration, but did not affect bond strength to dentin.
Luque-Martinez *et al.* [20]	Adhesive	140 (7)	To evaluate the μTBS and nanoleakage of 3 universal adhesives, applied with increasing solvent evaporation time	An extended solvent evaporation time may improve the bonding effectiveness for specific universal adhesives depending on the adhesive strategy used.
Muñoz *et al.* [18]	Adhesive/mixed	60 (5)	To evaluate the effect of an additional hydrophobic resin coating on the μTBS, nanoleakage, and degree of conversion of 3 universal adhesives	The use of an additional hydrophobic resin coating improved the adhesive performance in terms of resin-dentin bond strengths of new universal adhesives when used with the self-etch strategy. The additional hydrophobic resin coating also improved the degree of conversion for both the etch-and-rinse and the self-etch strategies.
Muñoz *et al.* [21]	Adhesive/mixed	40 (5)	To evaluate the μTBS and nanoleakage of universal adhesives that did or did not contain MDP applied in 2 different etching modes	Universal adhesives that contained MDP showed higher and more stable μTBS with reduced nanoleakage at the interfaces after 6 months of water storage.
Perdigão *et al.* [24]	Adhesive/mixed	60 (5)	To evaluate the effect of acid etching and application of a hydrophobic resin coat on the enamel/dentin bond strengths and degree of conversion of a universal adhesive system	The use of a hydrophobic resin coat may be beneficial for the selective enamel etching technique, because it improved bond strengths to enamel when applied with the etch-and-rinse strategy and to dentin when used with the self-etch adhesion strategy.
Muñoz *et al.* [17]	Adhesive/mixed	40 (5)	To evaluate μTBS, nanoleakage, and degree of conversion of universal simplified adhesive systems	This new category of universal adhesives used on dentin was inferior as regards at least one of the properties evaluated compared to the control adhesives.
Hanabusa *et al.* [22]	Mixed	25 (5)	To test whether a new one-step adhesive could be applied in a multi-mode manner, either 'full' or 'selective,' self-etch, and etch-and-rinse approaches	Phosphoric-acid etching definitely improved bonding of the one-step self-etch adhesive to enamel, so one should be more careful with additional phosphoric-acid etching of dentin. Although the bond strength was not reduced, the resultant adhesive interface appeared ultra-structurally more vulnerable to biodegradation.
Perdigão *et al.* [19]	Adhesive	36 (6)	To evaluate the laboratory dentin and enamel μTBS and ultra-morphology of a new multi-purpose adhesive	This new category of universal adhesives used on dentin was superior as regards to the properties evaluated compared to the control adhesives.
Eren *et al.* [23]	-	75 (15-15-45)	To evaluate the microtensile, microshear, and shear bond strength test methods to assess the bond strength of 2 self-etch adhesives and one etch-and-rinse adhesive on dentin	Bond strength to dentin depended on the material and the test method used.

μTBS, microtensile bond strength; MDP, methacryloyloxydecyl dihydrogen phosphate.

(**Figure 2**) and 35.81 ± 2.64 MPa for the self-etch mode (**Figure 3**). According to the statistical model presented by Borenstein *et al.* [25], there was no significant difference between the etching modes (**Table 6**).

Assessment of risk of bias

Risk of bias was evaluated according to the following parameters: randomization, blinding of the examiner, the presence of a control group, samples with similar dimensions, cross-head speed, evaluation of the failure mode, analysis by a single observer, description of the coefficient of variation, and sample size calculation. If the authors reported the parameter, the article received a 'Yes' for that parameter; if it was not possible to find the information, the article received a 'No'. Articles that reported one to 3 items were classified as having a high risk of bias, those that reported 4 or 5 items were considered to have a medium risk of bias, and those that reported 6 to 8 items were classified as having a low risk of bias (**Table 3**).

Table 2. Testing methods and materials used in the included studies

Study	Year	Country	Primary testing method	Secondary testing method	Universal adhesives used	Type of composite
Chen *et al.* [16]	2015	China	Dentin μTBS	TEM of resin-dentin interface SEM of tracer-infused water rich zone	Prime&Bond Elect (Dentsply Caulk, Milford, DE, USA); Scotchbond Universal (3M ESPE, St. Paul, MN, USA), All-Bond Universal (Bisco Inc., Schaumburg, IL, USA); Futurabond U (Voco, Cuxhaven, Germany); Clearfil Universal Bond (Kuraray Noritake Dental Inc., Tokyo, Japan)	Microhybrid composite (TPH Spectra, Dentsply Caulk, Milford, DE, USA)
Wagner *et al.* [15]	2014	Germany	Dentin μTBS	Semi-quantitative analysis of penetration depth by confocal light scanning microscopy	Futurabond U (Voco, Cuxhaven, Germany); All-Bond Universal Bisco Inc., Schaumburg, IL, USA); Scotchbond Universal (3M ESPE, St. Paul, MN, USA)	Nanohybrid composite (GrandioSO, Voco, Cuxhaven, Germany)
Luque-Martinez *et al.* [20]	2014	Brazil	Dentin μTBS	Interfacial nanoleakage	All-Bond Universal (Bisco Inc., Schaumburg, IL, USA); Prime&Bond Elect (Dentsply Caulk, Milford, DE, USA); Scotchbond Universal (3M ESPE, St. Paul, MN, USA)	Nanocomposite (Filtek Z350, 3M ESPE, St. Paul, MN, USA)
Muñoz *et al.* [18]	2014	Brazil	Dentin μTBS	Interfacial nanoleakage and degree of conversion	Scotchbond Universal (3M ESPE, St. Paul, MN, USA); All-Bond Universal (Bisco Inc., Schaumburg, IL, USA); G-Bond Plus (GC, Tokyo, Japan)	Nanocomposite (Filtek Z350, 3M ESPE, St. Paul, MN, USA)
Muñoz *et al.* [21]	2014	Brazil	Dentin μTBS	Interfacial nanoleakage	Scotchbond Universal (3M ESPE, St. Paul, MN, USA); All-Bond Universal (Bisco Inc., Schaumburg, IL, USA); Peak Universal Adhesive (Ultradent, South Jordan, UT, USA)	Microhybrid composite (Opallis, FGM, Joinville, SC, Brazil)
Perdigão *et al.* [24]	2013	USA	Dentin μTBS	Enamel μSBS and degree of conversion	G-Bond Plus (GC, Tokyo, Japan)	Nanocomposite (Filtek Z350, 3M ESPE, St. Paul, MN, USA)
Muñoz *et al.* [17]	2013	Brazil	Dentin μTBS	Interfacial nanoleakage and degree of conversion	Scotchbond Universal (3M ESPE, St. Paul, MN, USA); All-Bond Universal (Bisco Inc., Schaumburg, IL, USA); Peak Universal Adhesive (Ultradent, South Jordan, UT, USA)	Microhybrid composite (Opallis, FGM, Joinville, SC, Brazil)
Hanabusa *et al.* [22]	2012	Belgium	Dentin μTBS	Enamel μSBS and ultra-structural analysis TEM	G-Bond Plus (GC, Tokyo, Japan)	Microhybrid composite (Clearfil AP-X, Kuraray Noritake Dental Inc., Tokyo, Japan)
Perdigão *et al.* [19]	2012	USA	Dentin μTBS	Ultra-structural analysis	Scotchbond Universal (3M ESPE, St. Paul, MN, USA)	Microhybrid composite (Filtek Z250, 3M ESPE, St. Paul, MN, USA)
Eren *et al.* [23]	2013	Turkey	Dentin μTBS	Dentin μSBS and shear test	G-Bond Plus (GC, Tokyo, Japan)	Microhybrid composite (Venus, Heraeus Kulzer, Hanau, Germany)

μTBS, microtensile bond strength; TEM, transmission electron microscopy; SEM, scanning electron microscopy.

DISCUSSION

Systematic reviews are a useful tool for clinical practitioners, as they provide accurate evidence-based answers to relevant questions in light of the best available scientific knowledge. Furthermore, systematic reviews can recommend new standardized research protocols and methodologies [26,27].

The outcomes of laboratory studies that evaluate the bonding of multi-mode adhesives to dentin are highly dependent on the dentin surface treatment protocol. The majority of new adhesive systems exhibit the versatility of being able to be used in both the etch-and-rinse and self-etch modes; however, the variation in the results may be attributed to the difference in chemical composition among these adhesives. Perdigão *et al.* [19] reported the presence of MDP in the composition of the multi-mode adhesive Scotchbond Universal (3M ESPE), which can bond chemically to dentin by the formation of stable nanolayer coats around dentinal hydroxyapatites [28,29].

Table 3. Criteria used in quality assessment and the determination of risk of bias

Study	Teeth randomization	Control group	Teeth free of caries	Samples with similar dimension	Evaluation of failure mode	Sample size calculation	Description of coefficient of variation	Universal testing machine cross-head speed	Blinding of the examiner	Risk of bias
Chen *et al.* [16]	Yes	Yes	Yes	0.9 × 0.9 mm Yes	Yes	No	No	1 mm/min Yes	No	Medium
Wagner *et al.* [15]	Yes	Yes	Yes	1 × 1 mm Yes	Yes	No	No	0.5 mm/min Yes	No	Medium
Luque-Martinez *et al.* [20]	Yes	Yes	Yes	0.8 × 0.8 mm Yes	Yes	No	No	0.5 mm/min Yes	No	Medium
Muñoz *et al.* [18]	Yes	Yes	Yes	0.8 × 0.8 mm Yes	Yes	No	No	0.5 mm/min Yes	Yes	Low
Muñoz *et al.* [21]	Yes	Yes	Yes	0.8 × 0.8 mm Yes	Yes	No	No	0.5 mm/min Yes	Yes	Low
Perdigão *et al.* [24]	Yes	Yes	Yes	0.8 × 0.8 mm Yes	Yes	No	No	0.5 mm/min Yes	No	Medium
Muñoz *et al.* [17]	Yes	Yes	Yes	0.8 × 0.8 mm Yes	Yes	No	No	0.5 mm/min Yes	Yes	Low
Hanabusa *et al.* [22]	Yes	Yes	Yes	1 × 1 mm Yes	Yes	No	No	1 mm/min Yes	No	Medium
Perdigão *et al.* [19]	Yes	Yes	Yes	0.8 × 0.8 mm Yes	Yes	No	No	0.5 mm/min Yes	No	Medium
Eren *et al.* [23]	Yes	Yes	Yes	0.7 × 0.7 mm Yes	Yes	No	No	0.5 mm/min Yes	No	Medium

Yes, parameter present; No, parameter not present.

Table 4. Dentin microtensile bond strength (μTBS) of Scotchbond Universal in both etching modes with the number of teeth per group used in the corresponding studies

Study	Adhesive system and No. of teeth (per group)	Dentin μTBS (MPa)	
		Etch-and-rinse	Self-etch
Chen *et al.* [16]	Scotchbond Universal 200 (10)	55.7 ± 10.7	59.9 ± 11.8
Wagner *et al.* [15]	Scotchbond Universal 72 (12)	49.1 ± 11.1	44.0 ± 21.9
Luque-Martinez *et al.* [20]	Scotchbond Universal 140 (7)	36.2 ± 3.3	32.3 ± 4.8
Muñoz *et al.* [18]	Scotchbond Universal 60 (5)	32.3 ± 3.7	34.7 ± 5.8
Muñoz *et al.* [21]	Scotchbond Universal 40 (5)	34.7 ± 4.6	33.3 ± 3.2
Muñoz *et al.* [17]	Scotchbond Universal 40 (5)	35.1 ± 6.6	32.4 ± 4.5
Perdigão *et al.* [19]	Scotchbond Universal 36 (6)	54.0 ± 18.8	54.4 ± 18.8

The values are shown as mean ± standard deviation.

Study name	Statistics for each study					
	Mean	Standard error	Variance	Lower limit	Upper limit	Sample size
Chen *et al.* [16]	55.700	3.384	11.449	49.068	62.332	10
Luque-martinez *et al.* [20]	36.200	1.247	1.556	33.755	38.645	7
Muñoz *et al.* [18]	32.300	1.655	2.738	29.057	35.543	5
Muñoz *et al.* [18]	34.700	2.057	4.232	30.668	38.732	5
Wagner *et al.* [15]	49.100	3.204	10.268	42.820	55.380	12
Muñoz *et al.* [21]	35.100	2.952	8.712	29.315	40.885	5
Perdigão *et al.* [19]	54.000	7.675	58.907	38.957	69.043	6
	37.069	0.800	0.641	35.500	38.638	

Mean and 95% CI

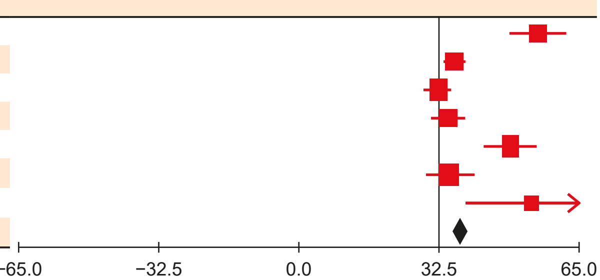

Figure 2. Results of the meta-analysis of microtensile bond strength for Scotchbond Universal in etch-and-rinse mode.
CI, confidence interval.

Table 5. Dentin microtensile bond strength (μTBS) of different universal adhesives used in the included studies

Study	Adhesive system	Dentin μTBS (MPa)	
		Etch-and-rinse	Self-etch
Chen *et al.* [16]	Prime&Bond Elect	57.8 ± 9.1	56.3 ± 10.2
	Scotchbond Universal	55.7 ± 10.7	59.9 ± 11.8
	All-Bond Universal	54.6 ± 8.3	50.1 ± 6.8
	Clearfil Universal Bond	49.1 ± 4.2	48.0 ± 7.4
	Futurabond Universal	46.5 ± 7.2	48.2 ± 9.7
Wagner *et al.* [15]	Futurabond Universal	41.2 ± 10.7	37.9 ± 14.0
	All-Bond Universal	44.8 ± 10.8	52.6 ± 12.7
	Scotchbond Universal	49.1 ± 11.1	44.0 ± 21.9
Luque-Martinez *et al.* [20]	All-Bond Universal	40.8 ± 5.0	22.0 ± 5.1
	Prime&Bond Elect	16.8 ± 2.4	18.9 ± 2.6
	Scotchbond Universal	36.2 ± 3.3	32.3 ± 4.8
Muñoz *et al.* [18]	Scotchbond Universal	32.3 ± 3.7	34.7 ± 5.8
	All-Bond Universal	40.8 ± 5.0	22.0 ± 5.1
	G-Bond Plus	20.5 ± 3.2	11.5 ± 3.3
Muñoz *et al.* [21]	All-Bond Universal	38.5 ± 4.0	20.9 ± 4.1
	Scotchbond Universal	34.7 ± 4.6	33.3 ± 3.2
	Peak Universal Adhesive	44.3 ± 1.6	39.5 ± 5.1
Perdigão *et al.* [24]	G-Bond Plus	19.1 ± 0.7	13.4 ± 1.3
Muñoz *et al.* [17]	Peak Universal Adhesive	43.6 ± 4.6	39.9 ± 4.5
	Scotchbond Universal	35.1 ± 6.6	32.4 ± 4.5
	All-Bond Universal	39.3 ± 3.7	13.4 ± 1.9
Hanabusa *et al.* [22]	G-Bond Plus	29.4 ± 8.2	30.5 ± 7.6
Perdigão *et al.* [19]	Scotchbond Universal	54.0 ± 18.8	54.4 ± 18.8
Eren *et al.* [23]	G-Bond Plus	-	26.4 ± 8.0

The values are shown as mean ± standard deviation.

Study name	Statistics for each study					
	Mean	Standard error	Variance	Lower limit	Upper limit	Sample size
Chen *et al.* [16]	59.900	3.731	13.924	52.586	67.214	10
Luque-martinez *et al.* [20]	32.300	15.421	237.80	2.075	62.525	7
Muñoz *et al.* [18]	34.700	2.594	6.728	29.616	39.784	5
Muñoz *et al.* [18]	33.300	1.431	2.048	30.495	36.105	5
Wagner *et al.* [15]	44.000	6.322	39.968	31.609	56.391	12
Muñoz *et al.* [21]	32.400	2.012	4.050	28.456	36.344	5
Perdigão *et al.* [19]	54.400	7.675	58.907	39.357	69.443	6
	35.813	0.999	0.998	33.855	37.771	

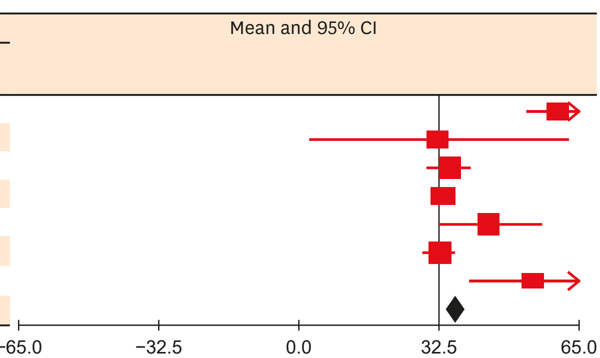

Figure 3. Results of the meta-analysis of microtensile bond strength for Scotchbond Universal in self-etch mode.
CI, confidence interval.

Scotchbond Universal also contains polyalkenoic acid copolymer (PAC; Vitrebond copolymer), which in combination with MDP enhances the bonding to dentin in comparison to corresponding PAC-free adhesives. In contrast, Muñoz *et al.* [17] reported that PAC might compete with the MDP monomer for calcium-binding sites in hydroxyapatite crystals, and due to its high molecular weight, could even prevent monomer approximation during

Table 6. Comparison of microtensile bond strength (μTBS) values obtained using the etch-and-rinse and self-etch modes

Adhesive strategy	No. of studies	μTBS (MPa)
Etch-and-rinse mode	7	37.07 ± 2.12
Self-etch mode	7	35.81 ± 2.64

Results are based on the *t*-test of the meta-analysis data following the statistical model of Borenstein *et al.* [25], which was applied in the earlier evidence-based study of Hamama *et al.* [38]. The values are shown as mean ± standard deviation.

polymerization, harming the chemical bond of MDP to dentin and adversely affecting bond strength. Moreover, it was demonstrated that 2-hydroxyethyl methacrylate competed with MDP by binding to the calcium of hydroxyapatite, decreasing the bond strength to dentin [30,31]. The majority of the included studies utilized the Scotchbond Universal (3M ESPE) multi-mode adhesive system. Therefore, it was beneficial to conduct a meta-analysis of these studies. The meta-analysis revealed no significant differences in the microtensile bond strength of Scotchbond multi-mode adhesive between the surface treatment modes.

Theoretically, in the etch-and-rinse mode, the phosphoric acid etching of dentin results in superficial dentin demineralization and total removal of the smear layer, consequently leading to the exposure of dentinal collagen fibrils and promoting the impregnation of monomers [32,33]. Many authors have explained the positive results that they obtained from laboratory bond testing within this theoretical framework. However, Pashley *et al.* [33] showed that the etching procedure reduced the amount of calcium and phosphate ions, as the hydroxyapatite crystals were nearly totally removed after the etching process, which may adversely affect the chemical bonding of MDP to hydroxyapatites.

Recently, it was found that the bonding of multi-mode adhesives to dentin in the etch-and-rinse mode relies on the infiltration of resin into exposed collagen fibril scaffolds, in a process known as 'micro-mechanical interlocking.' Furthermore, a true chemical bond was found to have formed due to the presence of functional monomer groups (MDP). This functional group has weak bonding affinity to hydroxyapatite-depleted collagen (etched dentin). This might explain the relatively low bond strength of multi-mode adhesives to dentin when used in the etch-and-rinse mode. Despite the presence of long funnel-shaped resin tags in the etch-and-rinse mode, recent studies showed that these resin tags did not contribute significantly to tensile bond strength [34,35].

In contrast, in the self-etch mode, the acidulated monomers simultaneously condition and prime the dentin surface by dissolving the smear layer, with a minimal adverse effect on dentinal calcium and phosphate levels. This might promote chemical interactions of hydroxyapatite crystals with the functional groups of MDP monomers, enhancing the chemical bond between the adhesive and the dentin substrate. However, the amount of resin impregnation during micro-mechanical interlocking in the self-etch mode was affected by the production of a hybrid layer that was thinner than that produced by the etch-and-rinse mode [36]. Moreover, Peumans *et al.* [37] reported that the thickness of the hybrid layer did not have a major influence on bonding to dentin.

Some variation was observed among the reviewed studies, particularly in the cross-head speed of the universal testing machine and the dimensions of the beams for microtensile bond strength tests. These variations in the methodological setup may have a major influence on the distribution of stresses along the resin/dentin interface. Despite these variations, the loading rate did not significantly influence the bond strength values due to the reduced dimensions of the specimens and the homogeneity of the adhesive interface. Sano *et al.* [14] reported that the tensile bond strength was inversely related to the surface area of the bonded interface. They attributed this phenomenon to the development of defects and/or stress raisers at the interface [14].

Evaluating the fracture pattern helps to explain the variation in bond strength across different multi-mode adhesive systems. Nevertheless, the results regarding failure patterns in the

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reviewed studies showed extensive variation, but the adhesive/mixed failure pattern was still the predominant failure mode in the plurality of the studies. Mixed failure was common when microtensile tests were performed under higher testing speeds. In the laboratory studies of Chen *et al.* [16] and Hanabusa *et al.* [22], increasing the cross-head speed from 0.5 to 1.0 mm/min resulted in a high frequency of mixed failure. Perdigão *et al.* [19] and Wagner *et al.* [15] concluded that adhesive failure patterns were associated with high bond strength values. It is well known that self-etch adhesives exhibit lower bond strength than etch-and-rinse adhesives; however, according the results of this evidence-based review, it seems that the MDP group enhances the bonding of self-etch adhesives to dentin.

Furthermore, most of the studies showed a medium risk of bias. Accordingly, it would be too difficult to control for all the variables that may have influenced the outcomes of the studies.

CONCLUSIONS

Although the reviewed studies showed great variability, sufficient scientific evidence was found to support the hypothesis that the bonding of multi-mode adhesives to dentin does not significantly vary depending on whether the etch-and-rinse or self-etch mode is used.

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