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

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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].
Conference meetings
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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
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].

Figure 1. Flowchart of the study selection procedure.
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%) [17,18,20,24], 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.
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).
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 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 (THP 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) | Nano hybrid 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 Z550, 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 Z550, 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 Z550, 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 Z550, 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.
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                       | No                     | No                                       | 1 mm/min                                  | Yes                      | Medium       |
| Wagner et al. [15]  | Yes                 | Yes           | Yes                  | 1 × 1 mm                      | Yes                       | No                     | No                                       | 0.5 mm/min                                | Yes                      | Medium       |
| Luque-Martinez et al. [20] | Yes | Yes | Yes | 0.8 × 0.8 mm | Yes | No | No | 0.5 mm/min | Yes | Medium |
| Muñoz et al. [18]   | Yes                 | Yes           | Yes                  | 0.8 × 0.8 mm                  | Yes                       | No                     | No                                       | 0.5 mm/min                                | Yes                      | Low          |
| Muñoz et al. [21]   | Yes                 | Yes           | Yes                  | 0.8 × 0.8 mm                  | Yes                       | No                     | No                                       | 0.5 mm/min                                | Yes                      | Low          |
| Perdigão et al. [24] | Yes | Yes | Yes | 0.8 × 0.8 mm | Yes | No | No | 0.5 mm/min | Yes | Medium |
| Muñoz et al. [17]   | Yes                 | Yes           | Yes                  | 0.8 × 0.8 mm                  | Yes                       | No                     | No                                       | 0.5 mm/min                                | Yes                      | Low          |
| Hanabusa et al. [22] | Yes | Yes | Yes | 1 × 1 mm | Yes | No | No | 1 mm/min | Yes | Medium |
| Perdigão et al. [19] | Yes | Yes | Yes | 0.8 × 0.8 mm | Yes | No | No | 0.5 mm/min | Yes | Medium |
| Eren et al. [23]    | Yes                 | Yes           | Yes                  | 0.7 × 0.7 mm                  | Yes                       | No                     | No                                       | 0.5 mm/min                                | Yes                      | Low          |

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.

Figure 2. Results of the meta-analysis of microtensile bond strength for Scotchbond Universal in etch-and-rinse 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 bonding.

### 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  | 43.8 ± 4.6        | 39.9 ± 4.5     |           |
|                        | Scotchbond Universal     | 35.1 ± 6.6        | 32.4 ± 4.5     |           |
|                        | All-Bond Universal       | 39.3 ± 3.7        | 33.4 ± 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.

### Figure 3. Results of the meta-analysis of microtensile bond strength for Scotchbond Universal in self-etch mode.

The 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 bonding.

### 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
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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