Frontiers in Dentistry

The Effect of Dimethyl Sulfoxide on the Microtensile Bond Strength of Universal Adhesives to Dentin

Zahra Dadvar[1], Mohammad Esmaeel Ebrahimi Chaharom[1*], Soodabeh Kimyai[1], Mahmoud Bahari[1], Mehdi Daneshpooy[1]

1. Department of Esthetic and Restorative Dentistry, Faculty of Dentistry, Tabriz University of Medical Sciences, Tabriz, Iran

Article Info

Article type:
Original Article

Article History:
Received: 02 Sep 2023
Accepted: 10 Mar 2024
Published: 17 Sep 2024

**** Corresponding author:***
Department of Esthetic and Restorative Dentistry, Faculty of Dentistry, Tabriz University of Medical Sciences, Tabriz, Iran

Email: ebrahimimo@tbzmed.ac.ir

A B S T R A C T

Objectives: The goal of this investigation was to see how a dentin pretreatment with 5% DMSO affected the microtensile bond strength (μTBS) of universal adhesives.

Materials and Methods: In terms of adhesive kind and etching procedure, 32 healthy third human molars were randomly separated into eight groups. Three universal adhesives with etch-and-rinse and self-etch strategies (G-Premio Bond: GPB.ER/SE, All-Bond Universal: ABU.ER/SE, Prime & Bond Elect: PBE.ER/SE), one two-stage self-etch adhesive (Clearfil SE Bond: CSB), and one two-stage etch-and-rinse adhesive (Adper Single Bond 2: ASB) were employed in with and without DMSO modes (group/N=16). Dentin pretreatment was conducted with 50 μl of 5% DMSO, followed by the use of an adhesive. The μTBS of samples was tested. The influence of adhesive type and DMSO application on bond strength was evaluated using a two-way analysis of variance (ANOVA) (α=0.05).

Results: The dentin-adhesive μTBS was significantly affected by DMSO administration (P=0.003), type of adhesive (P=0.001), and the combination of DMSO application and type of adhesive (P=0.027). In the DMSO application mode, the average bond strength of universal adhesives with etch and rinse mode was significantly higher than in the non-application mode, but in the self-etch technique, there was no significant difference pattern between DMSO applications and non-application modes in terms of adhesive bond strength.

Conclusion: The use of DMSO in an etch-and-rinse technique can dramatically enhance the universal adhesive-dentin μTBS and has promise benefits for clinicians in terms of enhancing dentin bond performance.

Keywords: Dentin-Bonding Agents; Adhesives; Dimethyl Sulfoxide; Dental Bonding

➢ **Cite this article as:** Dadvar Z, Ebrahimi Chaharom ME, Kimyai S, Bahari M, Daneshpooy M. The Effect of Dimethyl Sulfoxide on the Microtensile Bond Strength of Universal Adhesives to Dentin. *Front Dent*. 2024:21:36.

INTRODUCTION

Dentin bonding has always been difficult due to the difficulty of adhering resin materials to the tooth structure. Dentin bonding is reduced, resulting in lower retention, restoration life, and resource and expense waste. As a result, efficient strategies for reducing dentin deterioration and increasing the longevity of adhesive restorations are beneficial [1].The major cause of dentin bond strength loss is hybrid layer degradation, which is caused by adhesive hydrolysis as well as enzymatic destruction of collagen fibers [1-3].Various approaches for preventing hybrid layer biodegradation have been proposed in earlier investigations, including the use of matrix metalloproteinase inhibitors and cathepsin cysteine [2-5].Despite encouraging laboratory outcomes, there are currently no clinically viable and widely acknowledged procedures [4]. In addition, current approaches do not prevent

the simultaneous breakdown of sticky resins and collagen fibers [2]. Ethanol wet bonding is one of the ways given in the articles, and it is advised for the mild replacement of free water in the dentin substrate prior to resin bonding. Despite the positive in vitro results, it has been demonstrated that this approach can be clinically particularly technique sensitive. After ethanol evaporation, the demineralized collagen matrix may collapse even further [1,6]. The growing demand for simple, user-friendly adhesive systems has resulted in the development of a new category of adhesives known as "universal adhesives." The word "universal" refers to the manufacturer's claims about the materials' usage in etch-and-rinse and self-etch processes, as well as their varied uses for a variety of direct and indirect restorative treatments. Although the endurance of these adhesives' bonds varies depending on the type of substance used, they are all susceptible to hydrolytic breakdown [7]. Overall, laboratory tests have revealed that selective enamel etching is required for a long-lasting bond in universal adhesives [7-10]. On the other hand, with etch-and-rinse adhesive systems, it has been noted that the adhesive may not reach the depth of demineralized dentin [11]. As a result, using a "penetration enhancer" improves adhesive infiltration to the depths of demineralized dentin [12]. The polar aprotic solvent dimethyl sulfoxide (DMSO; $(CH_3)_2SO$) may dissolve both polar and non-polar molecules, including numerous dental adhesive monomers. Because of its amphiphilic character, it might be a good material for increasing penetration for medical applications [1-4,6,12-16]. The interfibrillar gap can be altered by DMSO by reducing inter-peptide hydrogen interactions in the collagen matrix, resulting in the separation of densely intersecting dentinal collagen and its transformation into a separate fibrillar network [14]. Human gelatinase activity has been found to be inhibited by DMSO, which prevents the hydrolytic destruction of the exposed collagen network [1-4,6,12-15]. On the other hand, it appears that the presence of water is required for esterase hydrolysis of resin matrix and endogenous and exogenous collagenolytic and gelatinolytic techniques to hydrolyze collagen [17]. As a result, the interaction of DMSO with water can aid in preventing the hydrolytic destruction of the hybrid layer [17]. Furthermore, some studies have revealed that DMSO negative ions can create very strong ionic interactions with positive calcium ions in tooth structure. It appears that the material's comparatively high surface energy and the strong link produced between DMSO ions and Ca+2 ions can influence and strengthen the binding [4,5]. In both self-etch and etch-and-rinse procedures, better adhesive penetration into the exposed collagen network boosts the stability of immediate and long-term dentin bonding [1]. As a result, determining the impact of DMSO on dentin bonding will be a worthwhile research [1]. The goal of this study was to explore the impact of DMSO on microtensile bond strength (μTBS) of universal adhesives and compare it to conventional adhesives, due to the demanding dentin bond strength and the fact that few studies have been completed on the influence of DMSO on the bond strength of universal adhesives. The null hypotheses of this investigation were that adhesive type and etching strategy (i) and DMSO application (ii) have no effect on μTBS.

MATERIALS AND METHODS

The local ethics committee approved the current study (code: IR.TBZMED.REC.1400.109). A total of 32 healthy third molars were used in the study. To lower the risk of dentin sclerosis, caries-free teeth and individuals aged 20-35 years were utilized to replicate the influence of various variables on dentin samples. Only healthy teeth without caries, fractures, or cracks were chosen after a visual and an exploratory examination. The teeth were stored in a 0.5 percent T chloramine solution (Merck, Germany) after being cleaned with a brush and pumice until the test [5]. To remove occlusal enamel, the teeth were sliced perpendicular to the longitudinal axis and under water. To standardize the smear layer, the midcoronal dentin surfaces were polished for 60 seconds with grit 600 silicon carbide sandpaper under running water [6]. Samples (N=256) were randomly separated into two groups based on DMSO dentin pretreatment, with each group broken into eight subgroups based on various adhesives and etching strategies (N=16, Figure 1). Three universal adhesives, one

two-stage etch-and-rinse, and one two-stage self-etch adhesive were selected from this group:

Group 1: Adper Single Bond2 (3M Oral Care, St Paul, MN, USA) / ASB

Group 2: Clearfil SE Bond (Kuraray Noritake Dental Inc., Tokyo, Japan) / CSB

Group 3: All-Bond Universal (Bisco, Schaumburg IL, USA) in etch & rinse mode / ABU.ER

Group 4: All-Bond Universal (Bisco, Schaumburg IL, USA) in self etch mode / ABU.SE

Group 5: Prime and Bond Elect (Dentsply Sirona, York, PA, USA) in etch & rinse mode / PBE.ER

Group 6: Prime and Bond Elect (Dentsply Sirona, York, PA, USA) in self etch mode / PBE.SE

Group 7: G-premio Bond (GC Corp., Tokyo, Japan) in etch & rinse mode / GPB.ER

Group 8: G-premio Bond (GC Corp., Tokyo, Japan) in self etch mode / GPB.SE

In etch-and-rinse adhesives and universal adhesives, a 35 percent phosphoric acid gel (3M ESPE, St. Paul, MN, USA) was applied for 15 seconds using an etch-and-rinse approach, followed by dentin rinsing and blot drying. Dentin pretreatment consisted of circular scrubbing 50µL of 5% DMSO solution (Merck, Germany) for 60 seconds with a disposable brush, followed by blot drying until the moisture was absorbed by capillarity [1-6, 13-17]. The rationale for using 5% DMSO was based on previous studies that employed the same concentration [3, 14, 18]. Dentin pretreatment was performed on dentin surfaces covered with smear layer and prior to primer application in self-etch adhesives and universal adhesives with self-etch strategy by circular scrubbing of 50µL of 5% DMSO solution for 60 seconds with disposable brush on dentin surfaces covered with smear layer [2,13]. No dentin treatment was used in the control groups. The usage method, components, and manufacturers of adhesives are shown in Table 1. After bonding according to the manufacturer's instructions in each group, the entire dentin surface was restored with Valux Plus composite (3M ESPE, St Paul, MN, USA) up to a height of 6mm (in three 2-mm thick pieces) and the thickness of each layer was controlled [5]. Each layer was cured separately for 40 seconds by a Demetron A2 light curing unit (Kerr, Scafati, Italy) with an intensity of 530mW/cm^2 [5]. The samples were then sliced vertically into 1 mm^2 cross sections after undergoing a 500-cycle thermocycling procedure at 5±5/55 5°C. Each tooth yielded a minimum of 16 sticks. Bond strength was determined using µTBS tester (Bisco, Schaumburg, IL, USA) at a loading speed of 0.5mm/min. The failure pattern of the samples was assessed after µTBS testing using a stereomicroscope (Nikon SMZ800, Tokoyo, Japan) with a ×10 magnification and categorized in the following order: Type I: Cohesive failure in dentin, Type II: Cohesive failure in composite block, Type III: Adhesive failure, Type IV Mixed failure [5]. Data analysis was carried out using two-way ANOVA after validating the normality of data distribution (Kolmogorov-Smirnov Test, $P>0.05$) and homogeneity of variance (Levene's test, $P<0.05$). If there was a significant difference between the adhesives, the Games-Howell post-hoc test was used to compare them pairwise. The impact of DMSO administration or non-application on the mean µTBS was evaluated using an independent samples t-test. The statistical significance threshold was set at $P<0.05$.

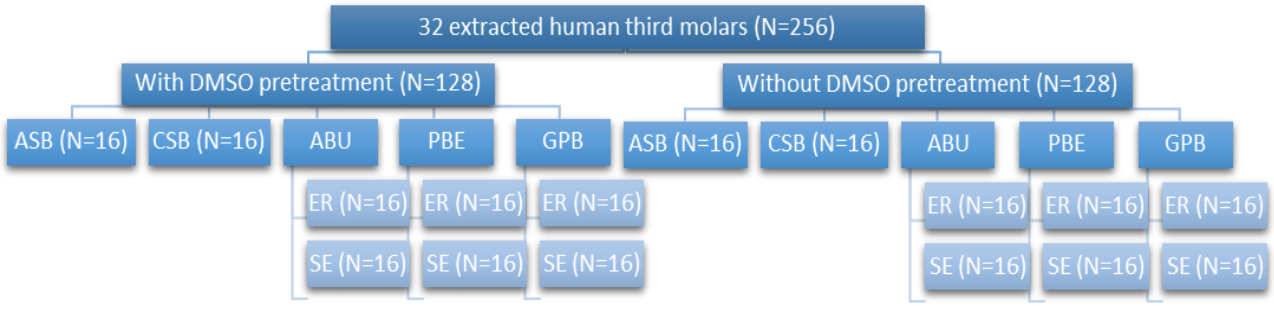


Fig. 1. Study design. ASB: Adper Single Bond2; CSB: Clearfil SE Bond; ABU.ER: All-Bond Universal in etch & rinse mode; ABU.SE: All-Bond Universal in self-etch mode; PBE.ER: Prime and Bond Elect in etch & rinse mode; PBE.SE Prime and Bond Elect in self-etch mode; GPB.ER: G-premio Bond in etch & rinse mode; GPB.SE: G-premio Bond in self-etch mode

Table 1. Adhesive systems, their main components and application modes

Adhesive systems	Components	Application mode (control/DMSO wet bonding)
Single Bond 2 (3M/ESPE)	Bis-GMA, HEMA, dimethacrylate, functional copolymer. Lot N:NC87572	1. Acid etching (15 seconds) 2. Rinsing (10 seconds) 3. Blot drying 4. Active application of 5% DMSO (60 seconds, DMSO wet-bonding) or no dentin treatment (control) 5. Blot drying 6. Application 2-3 successive layers (15 seconds) 7. Light curing (10 seconds)
Clearfil SE bond (Kuraray Noritake Dental Inc.) Primer/Adhesive	10-MDP; HEMA; CQ; hydrophilic dimethacrylate; water (pH =2.0). Lot N:8U0338 10-MDP; N,N-diethanol-p-toludine; HEMA; Bis-GMA; silanated colloidal silica; hydrophobic dimethacrylate; CQ Lot N:950584	1. Blot drying 2. Active application of 5% DMSO (60 seconds, DMSO wet-bonding) or no dentin treatment (control) 3. Blot drying 4. Primer application 5. Mild air (5 seconds) 6. Active adhesive application (20 seconds) 7. Gentle air stream 8. Light cure (10 seconds)
All-Bond Universal (Bisco Inc.)	2-HEMA, 10-MDP, Bis-GMA, ethanol, water, initiators (pH=3.2). lot N:2000000059	*Self-etch strategy:* 1. Blot drying 2. Active application of 5% DMSO (60 seconds, DMSO wet-bonding) or no dentin treatment (control) 3. Blot drying 4. Agitating 2 separate coatings of adhesive (10-15 seconds) 5. Air drying (10 seconds) 6. Light curing (10 seconds) *Etch-and-rinse strategy:* 1. Etching (15 seconds) 2. Rinsing. 3. Blot drying (1-2 seconds) 4. Appling adhesive in the same manner as in the self-etch mode.
Prime&Bond Elect (Dentsply Caulk)	Mono-, di- and trimethacrylate resins, PENTA, diketone, stabilisers organic phosphine oxide, cetylamine hydrofluoride, acetone, water, self-cure activator (pH=2.5). Lot N:1909000666	Self-etch strategy: 1. Blot drying 2. Active application of 5% DMSO (60 seconds, DMSO wet-bonding) or no dentin treatment (control) 3. Blot drying 4. Agitating one coatings of adhesive (20 seconds) & reappling to coat preparation. 5. Air drying (5 seconds) 6. Light curing (10 seconds) Etch-and-rinse strategy 1. Etching (15 seconds) 2. Rinsing (15 seconds) 3. Blot drying 4. Appling adhesive in the same manner as in the self-etch mode.
G-Premio Bond (GC Corp.)	10-MDP, 4-MET, MEPS, methacrylate monomer, acetone, water, silica, initiators (pH=1.5). Lot: 1909142	Self-etch strategy: 1. Blot drying 2. Active application of 5% DMSO (60 seconds, DMSO wet-bonding) or no dentin treatment (control) 3. Blot drying 4. Applying of adhesive (10 seconds) 5. Air drying (5 seconds) 6. Light curing (10 seconds) Etch-and-rinse strategy 1. Etching (15 seconds) 2. Rinsing (15 seconds) 3. Blot drying 4. Appling adhesive in the same manner as in the self-etch mode.

Bis-GMA: bis-phenol A diglycidylmethacrylate; HEMA: 2-hydroxyethyl methacrylate; 10-MDP: 10-methacryloxydecyl dihydro- gen phosphate; CQ: camphoroquinone; PENTA: dipentaerythritol pentacrylate phosphate; 4-MET: 4-Methacryloyloxyethyl trimellitate; MEPS: methacryloyloxyalkyl thiophosphate methylmethacrylate.

RESULTS

The mean and standard deviation of μTBS values in the studied groups are shown in Table 2. "Pretreatment procedure" (P=0.03) and "adhesive type" (P<0.001) both had a significant influence on μTBS, according to a two-way ANOVA.

Table 2. Means and standard deviations of Micro-tensile Bond Strength values in the study groups (MPa)

Adhesive System	Dentin Pretreatment	
	No DMSO	DMSO
Adper Single Bond2	34.69±16.66	36.36±7.06
Clearfil SE Bond	28.16±8.35	27.70±4.19
All-Bond Universal: ER	40.69±7.36	49.94±13.04
All-Bond Universal: SE	24.91±6.11	24.5±6.6
Prime & Bond Elect: ER	28.91±2.75	38.06±13.42
Prime & Bond Elect: SE	21.11±2.75	21.97±7.77
G-premio Bond: ER	25.09±7.04	34.47±6.82
G-premio Bond: SE	30.40±10.11	28.75±8.23

ER: etch-and-rinse; SE: self-etch; DMSO: dimethyl sulfoxide

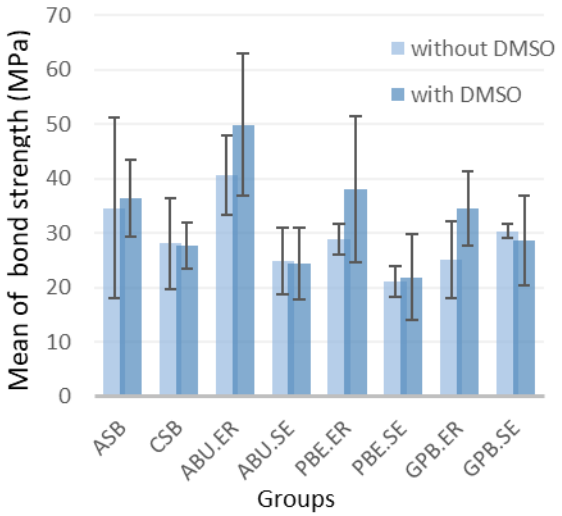


Fig. 2. Bar graph of microtensile bond strength values based on study groups

The use of DMSO and the researched groups exhibited an interaction (P=0.027); in other words, the studied groups with and without DMSO administration had distinct impacts on μTBS values (with a mean value of 32.70±12.19 in comparison to 29.42±10.11, respectively) (P=0.03). The average μTBS in the ABU.ER, PBE.ER, and GPB.ER groups with DMSO application mode was greater than the non-application mode (P<0.05), according to

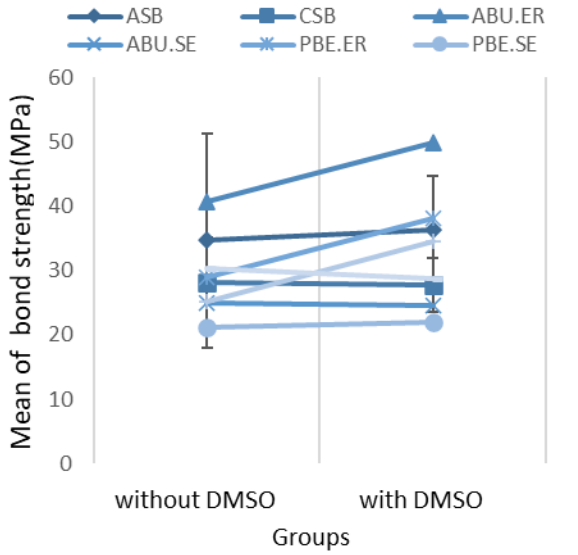


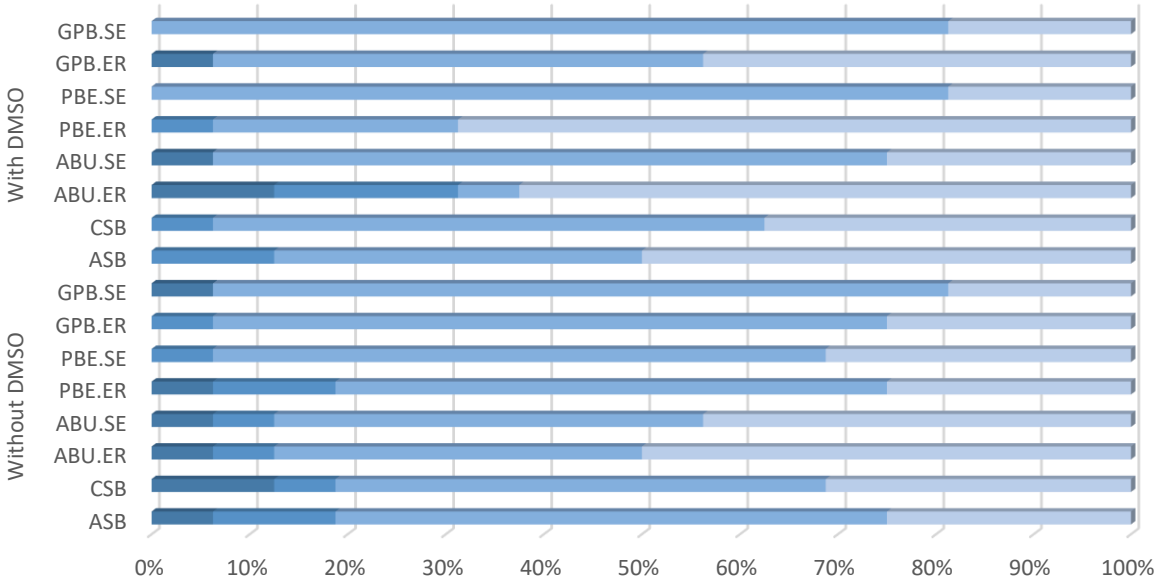
Fig. 3. Linear graph of microtensile bond strength values based on pretreatment method

the independent samples t-test findings. According to the results of the Games-Howell post hoc test for pairwise comparison, mean μTBS values were significantly higher in ABU.ER and PBE.ER groups compared to ABU.SE and PBE.SE groups with the DMSO non-application mode; however, there was no statistically significant difference between the GPB.ER and GPB.SE (Figures 2 and 3). According to the failure patterns of the samples, the adhesive type has the largest proportion of failure patterns, followed by the mixed type. Figure 4 depicts the sample frequency depending on the failure pattern in the investigated groups.

DISCUSSION

Due to the challenging nature of dentin bonding, several methods with the aim of improving the performance of dentin bonding agents have been presented, one of which is the DMSO wet-bonding technique. However, there are still limited studies on the effects of using this method on the dentin bond of universal adhesives as materials that are adaptable to different substrates and have components with the ability to bond chemically to the dentin [16].

The current research found that "adhesive type and approach" and "dentin DMSO pretreament," as well as their interactions, all had a substantial impact on μTBS, rejecting the



	Without DMSO								With DMSO							
	ASB	CSB	ABU.ER	ABU.SE	PBE.ER	PBE.SE	GPB.ER	GPB.SE	ASB	CSB	ABU.ER	ABU.SE	PBE.ER	PBE.SE	GPB.ER	GPB.SE
Type I	1	2	1	1	1	0	0	1	0	0	2	1	0	0	1	0
Type II	2	1	1	1	2	1	1	0	2	1	3	0	1	0	0	0
Type III	9	8	6	7	9	10	11	12	6	9	1	11	4	13	8	13
Type IV	4	5	8	7	4	5	4	3	8	6	10	4	11	3	7	3

Fig. 4. Frequency of the studied samples based on the failure pattern in the study groups

study's null hypothesis. The results of this study in DMSO non-application mode is consistent with previous studies that have shown that All Bond Universal Adhesives benefit from prior acid etching (pH=3.1, ultra mild). [19-23]. As a result, the rise in μTBS value of the PBE.ER group compared to the PBE-SE group in the current research may be explained (pH=2.5, ultra mild).

It has previously been shown that there is no significant difference between the self-etch and etch-and-rinse procedures in GPB adhesives in terms of μTBS (pH=1.5, intermediate strong), which is comparable to the findings of this investigation [7]. In comparison to the non-application mode, the 5 percent DMSO greatly raises the μTBS values in universal adhesives with etch-and-rinse technique (GPB.ER, PBE.ER, and ABU.ER). The application of DMSO, on the other hand had no significant effect on the bond strength of any of the universal adhesives in the self-etching strategy, as well as on the two-step etch and rinse ASB and the two-step self-etch CSB adhesive. Szesz et al. looked examined the effects of varied DMSO concentrations in two etch-and-rinse adhesives, Adper Single Bond2 and Prime & Bond 2.1, and found that DMSO helps to sustain dentinal bond strength over time [24]. Furthermore, Stape et al. examined the effects of using an aqueous or ethanolic DMSO solution to reduce the impacts of dentin moisture on the bonding of an etch-and-rinse adhesive, concluding that dry bonding procedures with DMSO increase bonding performance and hybrid layer homogeneity [25]. Another research looked at the effects of dry bonding in terms of shear bond strength, using a universal adhesive (Single Bond Universal), self-etch and etch-and-rinse techniques, and DMSO prepreparation. The use of DMSO has a substantial influence on

strengthening the bonding strength and durability of samples, according to the study's findings [26]. Furthermore, while employing etch and rinse (Scotch Bond Multi-Purpose) and Self-etch (Clearfil SE Bond) systems, Stape et al. studied the outcomes of wet bonding procedure with DMSO in dentin bond strength. In etch-and-rinse adhesive, they found a substantial increase in dentin bond strength in DMSO-pretreated samples, but these changes were not significant in the self-etch adhesive system [13], which is similar with the results of the current investigation on the CSB. DMSO is an aprotic and multifunctional polar molecular solvent that is used in biological tissues as an optical clearing agent (OCA) [4]. OCAs minimize light scattering and enable for higher-contrast imaging at longer depths than tissues that have not been treated with these agents [4]. Tjäderhane et al. were the first to show the action of OCAs on highly cross-linked and insoluble collagen of hard tissue such as dentin using DMSO [4]. The cause of the optical clearing effect is unknown; however, it is thought to be linked to DMSO's capacity to change the characteristics of water molecules [4]. The main structure of water supply hydration to biomolecules in biological structures is cyclic water pentamers (Figure 5), which is probable because the cyclic pentamer has the lowest energy across various water clusters (from dimer to hexamer) [4].

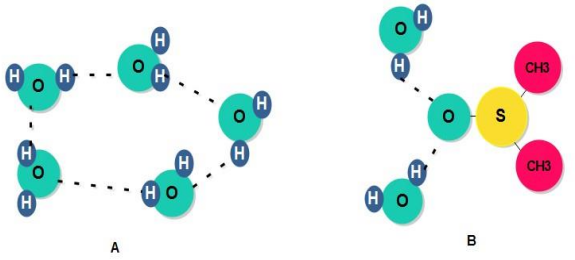


Fig. 5. A. The circular pentamer structure of water B. The combination of one DMSO molecule and two water molecules.

The DMSO molecule's relative negative charge on the oxygen atoms prefers to hydrogen bond with water, and DMSO normally attaches to two hydrogen bonds with two water molecules (1 DMSO: 2H2O), lowering the water's self-associative propensity and therefore stabilizing the water molecule in a smaller structure [4,27]. The fact that DMSO is a hydrogen bond acceptor rather than a donor, as well as the fact that the DMSO-water connection is four times stronger than the water-water interaction, contribute to this effect [4,28]. In hybrid layer, failure of water's self-associative tendency and a decrease in free water may improve bond strength and lower the pace of adhesive hydrolytic disintegration [4]. DMSO has been proven to improve the wettability of an organic acid-etched dentin matrix in studies [4,29]. Zhang et al. revealed a decreased universal adhesive contact angle with demineralized DMSO-pretreated dentin, as well as an increase in hydrophobic adhesive penetration in demineralized dentin [27]. DMSO improves the adhesive's dentin wetting property, allowing it to penetrate deeper into the exposed collagen matrix and improve collagen retention within the resin polymerized matrix [4]. Furthermore, DMSO's ability to inhibit hydrogen bonds between collagen fibrils disperses the collagen matrix and alters the organized structure of collagen fibrils, resulting in the separation and reversible destabilization of highly cross-linked collagen. This will also boost resin monomer infiltration and release [2,6,13]. One of the main reasons for improving the bond strength of DMSO in the etch-and-rinse approach is the possibility of changing the DMSO-dentin substrate interaction, which is a type of "biomodification" in dentin tissue [13]. Because the monomers have always had a hard time infiltrating the hybrid layer in etch-and-rinse bonding systems, total penetration of the monomers into the exposed collagen fibrils is always of interest. According to Guo et al., DMSO not only infiltrates and penetrates the monomers deep into the hybrid layer, but it also lowers exposed collagen [1]. Furthermore, in situ zymography revealed that DMSO inhibits the matrix metalloproteinase, including MMP 2 and 9, by interfering with the interactions between gelatinase and substrate at the end of the hybrid layer, where exposed collagen is

present due to incomplete infiltration [1,4]. Because the smear layer is removed and a suitable demineralized area is provided in the etch and rinse technique, and because DMSO increases the deep infiltration of the demineralized areas and causes better collagen preservation and proper encapsulation, as well as inhibition of proteolytic enzymes in the region, DMSO has significant effects in increasing the values of μTBS in the etch-and-rinse technique, which is consistent with the present study [1]. Under typical bonding circumstances, the difference in the ratio of hydrophilic-hydrophobic components of the adhesive, or the capacity to dissolve in water, plays a role in penetration of the adhesive system [13]. Because dentin is a moist substrate, the adhesive system's ability to release into the dentin substrate is hampered by the separation of hydrophilic and hydrophobic monomers [13]. The phenomenon of "phase separation" occurs when hydrophobic monomers, such as Bis-GMA, are released into locations where residual water is present [2]. Because phase separation in Bis-GMA/HEMA bonding resins prevents the release of relatively large molecules like Bis-GMA (molecular weight 512Da), the hybrid layer is frequently infiltrated by HEMA (molecular weight 130Da), which is then linearly polymerized as polyHEMA chains to form a resin-collagen biopolymer with reduced mechanical properties [13]. As a result of phase separation, monomer release is always reduced, resulting in low-quality hybrid layers [13]. Because DMSO is an effective penetration enhancer and reduces water accumulation between fibrils due to its reduced water self-associative properties, it can dissolve a large number of hydrophobic / hydrophilic resin monomers, including Bis-GMA, and can often increase Bis-GMA across the hybrid layer and improve the collagen resin coating in etch-and-rinse adhesives [13]. This minimizes the creation of the adhesive interface, which is weakly hybridized because of the hydrophobic Bis-GMA particles scattered in the hydrophilic HEMA matrix's phase separation [6,13]. Furthermore, because the vapour pressure of DMSO is lower than that of solvents like ethanol (0.6mmHg at 25°C) and is equivalent to 25% water vapour pressure at a concentration (50%) at 25°C, in the proposed DMSO-Wet bonding technique, fully demineralized dentin is saturated by this molecule after DMSO application, and DMSO remains partially within the collagen matrix during and after adhesive application [6]. This approach is expected to keep the interfibrillar space while preserving monomer conversion, and since bond strength varies with the width of the interfibrillar space inside the hybrid layer, it gives increased initial bond strength [2,6]. The assumption that self-etch adhesives may simultaneously etch and penetrate resin at full width of the bonded interface is no longer widely accepted, as the current work shows [13]. Although there is a decrease in collagen exposure and an increase in the degree of conversion of resin monomers when DMSO and then self-etch adhesive are applied to dentin, previous studies have shown that there is no significant difference in immediate bond strength between the control group and the DMSO group, which is consistent with the results of the current study [13]. Collagen exposure was reduced by 61.5 percent and 85.3 percent, respectively, in Clearfil SE bond and Scotch Bond multi-purpose adhesives, according to a research [13]. A smaller decrease in collagen exposure may explain the absence of notable improvement in μTBS. Furthermore, unlike etch-and-rinse mode, DMSO may not be able to fully permeate the exposed collagen because it is applied to smear-coated dentin and functional 10-MDP monomers and hydrophilic components concurrently breakdown the smear layer into a thin hybrid layer [13]. This might point to DMSO's limited ability to promote micro-mechanical retention in self-etch adhesives, which is in line with the findings of the current investigation [13]. In the self-etch mode, the etch pattern is comparable to that of 37 percent phosphoric acid in low-pH adhesive systems, but the dissolved calcium phosphate is not washed and is buried in the hybrid layer [30]. Furthermore, this calcium phosphate is unstable in aqueous environ-

ments, weakening the border zone's stability [30]. These findings may also be applied to the findings of the current GPB.SE research. In another experiment, scientists used a special tool called STD NMR spectroscopy to see how two different chemicals, MDP and 4-MET, interacted with atelocollagen. They found that when MDP was mixed with DMSO, it stayed connected to atelocollagen really well. But when 4-MET was mixed in, there wasn't as strong of a connection with atelocollagen. The involvement of the hydrophobic region of the aliphatic chain in MDP was highlighted in its interaction with atelocollagen. Conversely, the intensity of STD signals notably decreased when MDP was combined with HEMA. This NMR study presented evidence suggesting that HEMA in adhesives does not directly protect collagen fibrils [31]. We might highlight the influence of DMSO on water behaviour and the availability of hydrated collagen to hydrophobic monomers such as 10MDP, which really decreases water barriers to the polymerization process of hydrophobic monomers [2]. In reality, the water link surrounds collagen molecules, which are present in dentin as triple helical collagen, limiting the access of hydrophobic monomers to collagen and therefore limiting the chemical connection of collagen with 10MDP [6,27]. As a result, by interfering with the water-layer that is collecting surrounding the fibrillar layer, DMSO gives additional binding sites for 10MDP molecules to engage with collagen. This might explain why 10MDP universal adhesives have a higher bond strength in the etch-and-rinse procedure with DMSO than 10MDP-free ASBs in the two-stage etch-and-rinse approach (Table 1). GUO et al. investigated the effect of DMSO on TBS in Adper Single bond2, an etch-and-rinse adhesive, and found that while using this type of etch-and-rinse adhesive prevents the reduction of μTBS in the long run, it has no effect on the samples' immediate bond strength, which is consistent with the current study's findings [1]. The enhanced interaction of MDP-DMSO over MDP-HEMA is attributed to the fact that MDP molecules are surrounded by HEMA molecules with core hydrophobic areas, which lowers MDP's hydrophobic contact with the collagen molecule [2]. In the presence of MDP-DMSO and MDP-DMSO-HEMA, however, the collagen-MDP interaction is identical (Figure 6), showing that the enhanced interaction is related to the presence of DMSO rather than the lack of HEMA [2]. Despite the favorable outcomes of prior research, there remain concerns concerning DMSO-related toxicity; nevertheless, this toxicity has only been seen at high dosages [4]. As a medication carrier or therapeutic agent, DMSO has a wide range of uses today. DMSO, on the other hand, has been shown to have no impact on odontoblast-like cellular activity in vitro [32] and is also utilized as a solvent to test the cytotoxicity of adhesive monomers [33]. The bond stability of universal adhesives in DMSO-pretreated dentin will need more research. Furthermore, SEM and TEM examination are advised to better understand the resin penetration depth in both DMSO and non-DMSO modes.

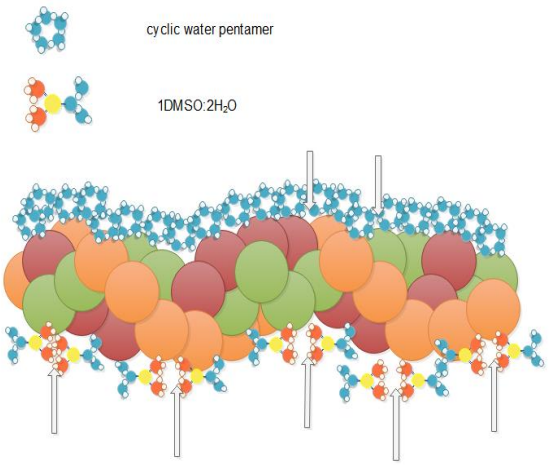


Fig. 6. A layer of water connected to a cyclic pentamer structure covers collagen molecules in a triple helix, preventing functional monomers from chemically connecting with collagen (upper molecule level in the figure). This water barrier may be disrupted by DMSO, which affords additional binding sites for 10MDP molecules (lower molecule level in the figure). This is true for MDP-DMSO and MDP-DMSO-HEMA molecules, while MDP-HEMA is less relevant. The exposed binding location for functional monomers is shown by arrows.

CONCLUSION

The findings revealed that DMSO application and non-application, adhesive type and strategy, and DMSO application and adhesive type interactions all had a substantial impact on μTBS. In the etch and rinse pattern, the bond strength of universal adhesives was significantly higher in the DMSO application mode than in the non-application mode, but there was no significant difference in adhesive bond strength in the self-etch pattern in the DMSO application mode versus the non-application mode.

ACKNOWLEDGMENTS

The authors extend their gratitude to the Vice Chancellor for Research at Tabriz University of Medical Sciences for their financial support.

CONFLICT OF INTEREST STATEMENT

None declared.

REFERENCES

1. Guo J, Lei W, Yang H, Zhang Y, Zhao S, Huang C. Dimethyl Sulfoxide Wet-bonding Technique May Improve the Quality of Dentin Bonding. J Adhes Dent. 2017 Jun 8:229-237.
2. Stape TH, Tjäderhane L, Tezvergil-Mutluay A, Yanikian CR, Szesz AL, Loguercio AD, Martins LR. Dentin bond optimization using the dimethyl sulfoxide-wet bonding strategy: A 2-year in vitro study. Dent Mater. 2016 Dec;32(12):1472-1481.
3. Salim Al-Ani AAS, Scarabello Stape TH, Mutluay M, Tjäderhane L, Tezvergil-Mutluay A. Incorporation of dimethyl sulfoxide to model adhesive resins with different hydrophilicities: Physico/mechanical properties. J Mech Behav Biomed Mater. 2019 May;93:143-150.
4. Tjäderhane L, Mehtälä P, Scaffa P, Vidal C, Pääkkönen V, Breschi L, Hebling J, Tay FR, Nascimento FD, Pashley DH, Carrilho MR. The effect of dimethyl sulfoxide (DMSO) on dentin bonding and nanoleakage of etch-and-rinse adhesives. Dent Mater. 2013 Oct;29(10):1055-62.
5. Chaharom ME, Bahari M, Rahbar M, Golbaz S. Effect of galardin and its solvents on the microtensile bond strength of different adhesive systems to dentin. Pesquisa Brasileira em Odontopediatria e Clínica Integrada. 2019 Sep 2;19:e4438.
6. Stape THS, Tjäderhane L, Abuna G, Sinhoreti MAC, Martins LRM, Tezvergil-Mutluay A. Optimization of the etch-and-rinse technique: New perspectives to improve resin-dentin bonding and hybrid layer integrity by reducing residual water using dimethyl sulfoxide pretreatments. Dent Mater. 2018 Jul;34(7):967-977.
7. Nagarkar S, Theis-Mahon N, Perdigão J. Universal dental adhesives: Current status, laboratory testing, and clinical performance. J Biomed Mater Res B Appl Biomater. 2019 Aug;107(6):2121-2131.
8. van Dijken JW, Pallesen U. Three-year Randomized Clinical Study of a One-step Universal Adhesive and a Two-step Self-etch Adhesive in Class II Composite Restorations. J Adhes Dent. 2017;19(4):287-294.
9. Oz FD, Kutuk ZB, Ozturk C, Soleimani R, Gurgan S. An 18-month clinical evaluation of three different universal adhesives used with a universal flowable composite resin in the restoration of non-carious cervical lesions. Clin Oral Investig. 2019 Mar;23(3):1443-1452.
10. Arbildo-Vega H, Lamas-Lara C, Cruzado-Oliva F, Rosas-Prado C, Gómez-Fuertes A, Vásquez-Rodrigo H. Comparison of the clinical effect of the adhesive strategies of universal adhesives in the treatment of non-carious cervical lesions. Systematic review and meta-analysis. J Oral Res. 2018 May 31;7(5):210-22.
11. Sharafeddin F, Nouri H, Koohpeima F. The Effect of Temperature on Shear Bond Strength of Clearfil SE Bond and Adper Single Bond Adhesive Systems to Dentin. J Dent (Shiraz). 2015 Mar;16(1):10-6.
12. Sharafeddin F, Salehi R, Feizi N. Effect of Dimethyl Sulfoxide on Bond Strength of a Self-Etch Primer and an Etch and Rinse Adhesive to Surface and Deep Dentin. J Dent (Shiraz). 2016 Sep;17(3 Suppl):242-249.
13. Stape TH, Tjäderhane L, Marques MR, Aguiar FH, Martins LR. Effect of dimethyl sulfoxide wet-bonding technique on hybrid layer quality and dentin bond strength. Dent Mater. 2015 Jun;31(6):676-83.
14. Shafiei F, Memarpour M, Sarafraz Z. Effect of dimethyl sulfoxide on bond durability of fiber posts cemented with etch-and-rinse adhesives. J Adv Prosthodont. 2016 Aug;8(4):251-8.
15. Stape TH, Tezvergil-Mutluay A, Mutluay MM, Martins LR, do Prado RL, Pizi EC, Tjäderhane L. Influence of dimethyl sulfoxide used as a solvent on the physical properties and long-term dentin bonding of hydrophilic resins. J Mech Behav Biomed Mater. 2016 Dec;64:220-8.
16. Nagpal R, Mehmood N, Singh U. Enhancing the resin-dentin bond with DMSO: A narrative review. Glob J Oral Sci. 2019;5:40-6.

17. Isolan CP, Valente LL, Münchow EA, Basso GR, Pimentel AH, Schwantz JK, et al. Bond strength of a universal bonding agent and other contemporary dental adhesives applied on enamel, dentin, composite, and porcelain. Applied Adhesion Science. 2014 Dec;2:1-0.
18. Mehtälä P, Pashley DH, Tjäderhane L. Effect of dimethyl sulfoxide on dentin collagen. Dent Mater. 2017 Aug;33(8):915-922.
19. Rosa WL, Piva E, Silva AF. Bond strength of universal adhesives: A systematic review and meta-analysis. J Dent. 2015 Jul;43(7):765-76.
20. Muñoz MA, Sezinando A, Luque-Martinez I, Szesz AL, Reis A, Loguercio AD, Bombarda NH, Perdigão J. Influence of a hydrophobic resin coating on the bonding efficacy of three universal adhesives. J Dent. 2014 May;42(5):595-602.
21. Wagner A, Wendler M, Petschelt A, Belli R, Lohbauer U. Bonding performance of universal adhesives in different etching modes. J Dent. 2014 Jul;42(7):800-7.
22. Muñoz MA, Luque I, Hass V, Reis A, Loguercio AD, Bombarda NH. Immediate bonding properties of universal adhesives to dentine. J Dent. 2013 May;41(5):404-11.
23. Luque-Martinez IV, Perdigão J, Muñoz MA, Sezinando A, Reis A, Loguercio AD. Effects of solvent evaporation time on immediate adhesive properties of universal adhesives to dentin. Dent Mater. 2014 Oct;30(10):1126-35.
24. Szesz AL, Pereira GMA, Siqueira FSF, Cardenas AFM, Bandeca MC, Armas-Vega A, Reis A, Loguercio AD. Effect of Addition of Dimethyl Sulfoxide to Simplified Adhesives on Dentin Bond Durability after Three Years of Water Storage. J Adhes Dent. 2021 Apr 7;23(2):159-165.
25. Stape THS, Uctasli M, Cibelik HS, Tjäderhane L, Tezvergil-Mutluay A. Dry bonding to dentin: Broadening the moisture spectrum and increasing wettability of etch-and-rinse adhesives. Dent Mater. 2021 Nov;37(11):1676-1687.
26. Sangavi Sithu Balakrishnan DS, Naik R. Influence of novel dry bonding approaches on the shear bond strength of a universal adhesive: An in vitro study. Int J Appl Dent Sci. 2021; 7(1): 241-4
27. Zhang Z, Yu J, Yao C, Yang H, Huang C. New perspective to improve dentin-adhesive interface stability by using dimethyl sulfoxide wet-bonding and epigallocatechin-3-gallate. Dent Mater. 2020 Nov;36(11):1452-1463.
28. Venkataramanan NS. Microsolvation of DMSO: Density functional study on the structure and polaraizabilities. Int J Quantum Chem. 2012 Jul 5;112(13):2599-606.
29. Mehtälä P, Agee K, Breschi L, Pashley DH, Tjäderhane L. Proprietary solvent enhances dentin wettability. Dent Mater. 2010(26):e12-3.
30. Tjäderhane L, Nascimento FD, Breschi L, Mazzoni A, Tersariol IL, Geraldeli S, Tezvergil-Mutluay A, Carrilho MR, Carvalho RM, Tay FR, Pashley DH. Optimizing dentin bond durability: control of collagen degradation by matrix metalloproteinases and cysteine cathepsins. Dent Mater. 2013 Jan;29(1):116-35.
31. Hiraishi N, Tochio N, Kigawa T, Otsuki M, Tagami J. Role of 2-hydroxyethyl methacrylate in the interaction of dental monomers with collagen studied by saturation transfer difference NMR. J Dent. 2014 Apr;42(4):484-9.
32. Hebling J, Bianchi L, Basso FG, Scheffel DL, Soares DG, Carrilho MR, Pashley DH, Tjäderhane L, de Souza Costa CA. Cytotoxicity of dimethyl sulfoxide (DMSO) in direct contact with odontoblast-like cells. Dent Mater. 2015 Apr;31(4):399-405.
33. Geurtsen W, Lehmann F, Spahl W, Leyhausen G. Cytotoxicity of 35 dental resin composite monomers/additives in permanent 3T3 and three human primary fibroblast cultures. J Biomed Mater Res. 1998 Sep 5;41(3):474-80.