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Original Article

In Vitro Evaluation of the Effects of Different Chemical Solvent Agents on Shear Bond Strength of Ceramic Orthodontic Brackets

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Main Points

- Ceramic bracket pieces remained on the tooth surface and enamel cracks occured during debonding process.
- The ethanol 5 min and 15 min groups had the highest SBS values and most damaged SEM images of the enamel.
- The lowest SBS values were observed in the acetone 5 min and 15 min groups.
- The acetone application can be considered an effective clinical method for the future.

ABSTRACT

Objective: In this study, the effects of different chemical solvents such as acetone, ethanol, dimethyl sulfoxide (DMSO), peppermint oil, and hot water on the shear bond strength (SBS) of mechanically and chemically bonded ceramic brackets were examined. Their use for facilitation of the debonding process in practice was evaluated regarding the purposes of this study.

Methods: One hundred and thirty-two human premolar teeth extracted for orthodontic purposes were randomly divided into 11 groups. SBS were applied using a universal test machine. The amount of residual adhesives was determined through adhesive remnant index scoring. Scanning electron microscopy (SEM) images were examined to determine the effects of solvents on the enamel surface.

Results: In all test groups, the highest SBS values were found in the ethanol 5- and 15-minutes groups. SEM examination showed micro-cracks in all groups. Increased SBS values were also found in 5- and 15-minutes groups of hot water and DMSO, while both peppermint oil groups had similar SBS values as the control group. SBS values of both acetone 5- and 15-minutes groups were found to be lower than the control and other groups.

Conclusion: Acetone application for 5 or 15 minutes before debonding of ceramic brackets could be an alternative clinical approach to prevent enamel damage and facilitate debonding.

Keywords: Acetone, ceramic bracket, ethanol, organic chemical solvent, shear bond strength

INTRODUCTION

During the entire treatment period, orthodontic brackets must resist mechanical and masticatory forces and have a bond strength of at least 6-8 megapascal (MPa).[1] However, this desired bond strength should not exceed approximately 13.75 MPa, which is the cohesive internal strength of the enamel, in order not to damage the tooth enamel during the debonding of the brackets.[2] However, since ceramic brackets do not have the flexibility to stretch as much as stainless steel brackets, they cannot be removed by deforming at the end of orthodontic treatment.[3,4] According to *in vitro* bond strength tests performed with ceramic brackets, it was observed that the fracture occurred frequently at the enamel-adhesive interface, and it was found that these forces could reach up to 28.3 MPa.[5] Depending on this situation, the integrity of the tooth enamel may be disrupted during the debonding process of the ceramic brackets, ceramic bracket pieces may remain on the tooth surface, and

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sometimes permanent damages such as enamel cracks and failures may occur as malpractice.[6-9] Residual composites and bracket remnants may cause rough surfaces and be a risk factor for maintaining oral hygiene after the debonding process so the ceramic brackets are often not indicated in children because of the less treatment compliance and the poor oral hygiene of these patients.[10-12] In addition, the use of ceramic brackets is contraindicated in syndromic patients with hypoplastic and hypocalcific enamel such as oral-facial-digital syndrome.[13,14] Also the risk of enamel fracture during debonding is high in teeth with endodontic treatment and large restorations.[15] Enamel tissue loss occurs at a depth of 5-50 µm due to the roughening of the tooth surface with acid during the bonding of the brackets, and irreversible hard tissue losses of around 100-150 µm occur with the effect of composite remnant removal procedures.[3,4] Different techniques such as electrothermal, laser and ultrasonic debonding have been tried supporting the mechanical removal of the brackets to prevent such problems during the removal of ceramic brackets.[2,16] Due to the irreversible pulp damage and the gingival irritation risks that can be caused by these techniques, it has become necessary to try alternative methods for the debonding of ceramic brackets.

In our study, it was aimed to reduce the debonding force required during the debonding process of ceramic brackets and to reach the range of 12.75-13.75 MPa, which is considered the safe limit for the integrity of the tooth enamel as stated in the literature.[2] The purpose of this study was to evaluate the effects of different chemical agents that were predicted to dissolve the organic matrix of orthodontic adhesive. Under in vitro conditions, different chemical solvents were applied to the enamel-adhesive and adhesive-bracket interfaces to develop a new technique that can be used in orthodontic clinics to protect the enamel.

METHODS

This research was conducted in compliance with the Helsinki Declaration, and the protocol was authorized by the University of Istanbul Ethics Committee in Istanbul, Turkey (Protocol number: 2019/11).

An initial statistical evaluation for sample size calculation was performed considering a power of 90% (α=0.05, 1- β=90%). This analysis suggested a minimum sample size of 12 teeth.

In our study, there are 11 groups, each consisting of 12 teeth, and 132 mandibular and maxillary human premolar teeth extracted for orthodontic purposes. The teeth that were found to have cavity, crack, filling, or dental extracting forceps damage because of the examination under light were excluded from the study. It was prioritized that the tooth surfaces had not been treated with any chemical agent before and that the buccal surfaces were smooth.

After the periodontal ligament remnants on the root surfaces of the extracted teeth were debrided with a periodontal curette, the extracted teeth were kept in distilled water renewed twice a week at room temperature until the experiments were started. The enamel surfaces of all teeth were cleaned with a fluoride free paste and polishing brush using a low-speed air-cooled micromotor and contra-angle handpiece without using any abrasive agents, then washed with air-water spray and dried.

Ceramic 0.018"x0.022" slot orthodontic brackets (Ortho Technology, PURE Sapphire Bracket System, Opal Orthodontics, South Jordan, UT, USA) were bonded to the tooth surface using 37% orthophosphoric acid, primer (Transbond XT, 3M Unitek, Monrovia, CA, USA) and adhesive (Transbond XT, 3M Unitek, Monrovia, CA, USA). Guide labels were used to ensure that the brackets were in the middle 1/3 area in the mesiodistal and occlusogingival directions and parallel to the long axis of the tooth. To standardize the applied force, heavy elastic of 6 1⁄2 ounce, 1/8 size was placed on the tooth in such a way that it would surround the equatorial line of the tooth and include the bracket. A new elastic was used for each sample and to prevent different forces that may occur due to the dimensional differences among the premolar teeth, 200 g force was measured each time with a dynamometer and the resin remnants around the bracket were cleaned with the help of a probe. Afterwards, the adhesive was polymerized with an LED light device (3M Elipar-S10, 3M ESPE, St. Paul, MN, USA) emitting light at a wavelength of 430-480 nanometer for 20 seconds.

The prepared samples were immersed in water baths at 5 °C and 55 °C, respectively, 1000 times each, resulting in thermal stress. The waiting time for each bath was set to be 20 seconds and the transfer time between the baths to be 10 seconds. The sample teeth were placed vertically on the acrylic blocks with the help of a reference wire, with all of their crowns exposed and their roots in the acrylic.

In our study, there are 11 groups, each consisting of 12 teeth, formed by applying 5 different organic chemical solvents [acetone, ethanol, dimethyl sulfoxide (DMSO), peppermint oil, hot water] to the teeth before debonding for two different durations (5 min and 15 min), with the control group. 99.8% acetone, 99.5% ethanol, 99.9% DMSO, 100% pure peppermint oil and 60 °C hot water were used in this regard.

The solutions poured into a 250 milliliter beaker were divided into 12 glass beakers with a depth of 40 millimeter (mm) and an inner diameter of 15 mm, separate one for each sample, using a pasteur pipette. The samples were placed in glass beakers so that the tooth surface with the brackets remained in the solution, and they were kept waiting until the time elapsed using a chronometer. Since the samples prepared in steel molds with an inner diameter of 18 mm were placed in glass test beakers with an inner diameter of 15 mm, only the tooth crowns were kept in solution, and by preventing the contact of acrylic with the solution, the release of chemicals from the acrylic to the solution was prevented (Figure 1a).

Debonding test was applied to each sample, which was kept in chemical solutions, immediately after 5-minute and 15-minute durations, and the samples were kept in the biopsy container with the stripped bracket to measure the failure force and measure adhesive remnant index (ARI) scoring. For the control group, after the brackets adhered to the tooth surface, the teeth were embedded in the acrylic base following the thermal cycle process and the failure forces were measured with a (Buehler Instron, Buehler United Kingdom Warwick Manufacturing Group, Coventry, United Kingdom) without being kept in any solution (Figure 1b). The speed of the movable top plate of the test machine was set to 1 mm/minute, the maximum force to be applied by the machine was set to 500 N, and the measurements were performed with an accuracy of 0.2 N. The measured forces (Newton) were divided by the base surface areas of the brackets, and the amount of force per unit area was converted into MPa ($MPa=N/mm^2$). The base surface area of the bracket used was determined by contacting the manufacturer and was taken as 13.12 mm^2.

After the debonding tests, the tooth surfaces were examined under x15 zoom and bracket bases x25 zoom with a double-ocular stereomicroscope device (Nikon SMZ 1000) and the images were recorded one by one with the "Camera" computer program.

Since we used ceramic brackets in our study, the amount of residual adhesive on the tooth surface was determined by the modified version by Bishara and Trulove[7,8] in 1990 of the ARI defined by Artun and Bergland.

To evaluate the effects of the applied solutions on both enamel and adhesive, samples with an ARI score of 2 or 3 were selected and images at ×40, ×100, ×500 and ×1000 zoom were photographed with the scanning electron microscopy (SEM) device (JEOL JSM 6510-LV). The images of the enamel surfaces were evaluated according to the ARI system.

Statistical Analysis

SPSS (version 22.0;SPSS,Chicago,Il, USA), was used for statistical analysis. The ANOVA test was used to compare more than two independent groups and the homogeneity of variances assumption is provided in the comparison of the variables, and the double-sided Dunnett t-test was used as the post-hoc test for the comparison of the variables that were found to be statistically significant with the control group. Welch ANOVA test was used to compare the variables with normal distribution but not with the homogeneity of variances assumption, and Dunnett t3 test was used for pairwise comparison of statistically significant results between groups. The p value of .05 was considered as the level of significance. The ARI score values of the samples were determined as percentage distributions according to the groups.

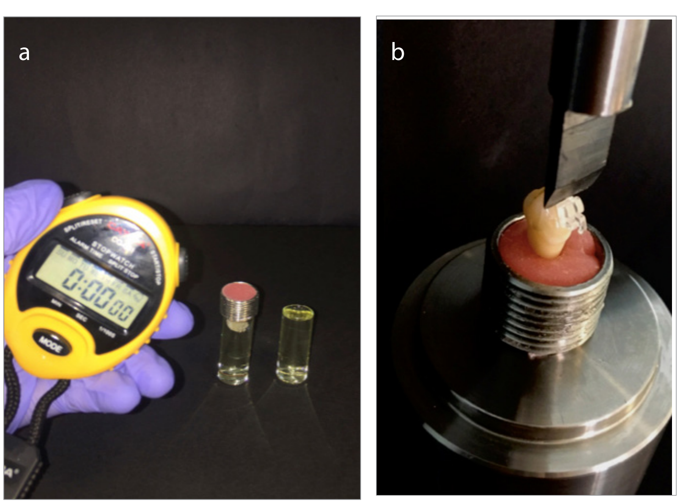

Figure 1. (a) Application of the solvents, (b) Shear force applied with the Universal Test Machine.

RESULTS

Comparison of the control group with all of the other groups is listed in Table 1. Pairwise comparison of the control group with the other groups is described in Table 2. Comparison of the SBS values of the 5 min groups within themselves is shown in Table 3, whereas comparison of the SBS values of the 15 min groups within themselves is shown in Table 4. Table 5 compares the SBS values of samples kept in the same solution for short (5 min) and long (15 min) durations. The ARI score distributions of the samples are shown in Table 6.

It was observed that hot water and DMSO did not soften the composite; in contrast, they increased the shear bond strength value by hardening, while peppermint oil did not have any effect on softening or hardening of the composite (Table 1).

Table 1. Comparison of SBS values between groups

	N	SBS value Mean ± SD		p value
Control group	12	18.86	3.99	
Acetone 5 min	12	13.99	1.41	
Acetone 15 min	12	11.66	1.20	
Ethanol 5 min	12	32.53	7.31	
Ethanol 15 min	12	30.83	6.84	
DMSO 5 min	12	24.83	4.19	0.000*
DMSO 15 min	12	22.88	3.05	
Peppermint oil 5 min	12	19.25	3.79	
Peppermint oil 15 min	12	17.18	3.67	
Hot water 5 min	12	24.93	4.86	
Hot water 15 min	12	25.17	5.76	

ANOVA test; *p<0.05; SBS, shear bond strength; SD, standard deviation

The shear bond strength value of the acetone 5-minute and acetone 15-minute groups was found to be significantly lower than that of the control group and the other chemical solutions with the same duration (Table 2, Table 3 and Table 4).

The mean of the SBS values for the acetone 15 min group is statistically significantly lower than that of the acetone 5 min group (Table 5).

Considering the ARI scores, adhesive fracture (at the enamel-adhesive interface) was observed for a large percentage of samples. Enamel fractures (ARI score 4) (Figure 2a) and bracket fractures (ARI score 5) (Figure 2b) were observed as well (Table 6).

Table 2. Pairwise comparison of the SBS values between control group and other groups

Group (I)	Group (J)	Mean difference (I-J)	SE	p value
Acetone 5 min	Control	- 4.88	1.87	0.003*
Acetone 15 min	Control	-7.20	1.87	0.002*
Ethanol 5 min	Control	13.67	1.87	0.001*
Ethanol 15 min	Control	11.97	1.87	0.001*
DMSO 5 min	Control	5.96	1.87	0.06
DMSO 15 min	Control	4.01	1.87	0.207
Peppermint oil 5 min	Control	0.39	1.87	1.000
Peppermint oil 15 min	Control	-1.69	1.87	0.958
Hot water 5 min	Control	6.07	1.87	0.013*
Hot water 15 min	Control	6.30	1.87	0.009*

Dunnett t-test (double-sided); *p<0.05; SE, standard error

Table 3. Comparison of SBS values of 5 min groups within themselves

5 min group (I)	5 min groups (J)	Mean difference (I-J)	SE	p value
Acetone	Ethanol	-18.55	2.15	0.000*
	DMSO	-10.84	1.28	0.000*
	Peppermint oil	-5.26	1.17	0.005*
	Hot water	-10.94	1.46	0.000*
Ethanol	DMSO	7.70	2.43	0.049*
	Peppermint oil	13.28	2.37	0.000*
	Hot water	7.60	2.53	0.066
DMSO	Peppermint oil	5.58	1.63	0.023*
	Hot water	-0.10	1.85	1.000
Peppermint oil	Hot water	-5.68	1.78	0.041*

Dunnett t3-test; *p<0.05; SE, standard error

A rougher surface was observed for the acetone, peppermint oil, and hot water groups compared to the control group when SEM images were examined. Among all these groups, the enamel surface exhibited a more irregular structure for the DMSO-applied groups (Figure 3), and it was observed that ethanol was the most damaging solution to the enamel surface.

DISCUSSION

In our study, to prevent the side effects that may occur during the removal of ceramic brackets with different techniques such as

Table 4. Comparison SBS values of the 15 min groups within themselves

15 min group (I)	15 min groups (J)	Mean difference (I-J)	SE	p value
Acetone	Ethanol	-19.16	2.01	0.000*
	DMSO	-11.21	0.95	0.000*
	Peppermint oil	-5.52	1.12	0.002*
	Hot water	-13.51	1.70	0.000*
Ethanol	DMSO	7.96	2.16	0.020*
	Peppermint oil	13.65	2.24	0.000*
	Hot water	5.67	2.58	0.302
DMSO	Peppermint oil	5.70	1.38	0.004*
	Hot water	-2.29	1.88	0.903
Peppermint oil	Hot water	-7.99	1.97	0.007*

Dunnett t3-test; *p<0.05; SE, standard error

Table 5. Comparison of groups in the same chemical solution at different durations

	N	SBS value (Mean ± SD)	SE	p value
Acetone 5 min	12	13.98 ± 1.41	0.41	0.001*
Acetone 15 min	12	11.66 ± 1.20	0.35	
Ethanol 5 min	12	32.53 ± 7.31	2.11	0.563
Ethanol 15 min	12	30.83 ± 6.84	1.98	
DMSO 5 min	12	24.83 ± 4.19	1.21	0.206
DMSO 15 min	12	22.88 ± 3.05	0.88	
Peppermint oil 5 min	12	19.25 ± 3.79	1.09	0.187
Peppermint oil 15 min	12	17.18 ± 3.67	1.06	
Hot water 5 min	12	24.93 ± 4.86	1.40	0.914
Hot water 15 min	12	25.17 ± 5.76	1.66	

ANOVA test; *p<0.05; SBS, shear bond strength; SD, standard deviation; SE, standard error electrothermal, laser and ultrasonic debonding; organic chemical solvent agents such as acetone, ethanol, DMSO, peppermint oil and hot water were considered to be applied as an alternative to these techniques during the debonding stage.[2,16] It was hypothesized that the application of these chemical dissolving agents to the tooth surface before debonding could achieve failure with the least damage and with the lowest forces, and the highest concentrations of these chemical dissolving agents were used to see the maximum effect. DMSO was preferred in our study considering its ability to dissolve many substances better than water and its antimicrobial, anti-inflammatory and analgesic effects. In the literature, studies have supported that peppermint oil softens the adhesive and reduces the shear bond strength (SBS) of the ceramic brackets, but there are also studies stating that this agent is effective only when applied for a long duration.[17-19] In our study, the effect of ceramic brackets on the debonding test was evaluated comparatively by applying the same agent for both short and long durations. In the orthodontic literature, there is only one study sharing clinical experience on the effect of hot water on the removal of ceramic brackets.[20] Regarding the determination of the temperature of hot water included in our study, hot water was applied by determining a safe temperature (60 °C) level that would not damage the oral tissues and pulp but would soften the composite "if it had any effect".

Although all teeth can be used in the *in vitro* studies[21], generally, premolar teeth extracted for orthodontic purposes are used for shear or tensile tests.[6,22,23] The lower and upper human premolar teeth with complete root development and extracted for orthodontic treatment from individuals aged 12-17 years were used in our study. The use of premolar teeth of individuals in the

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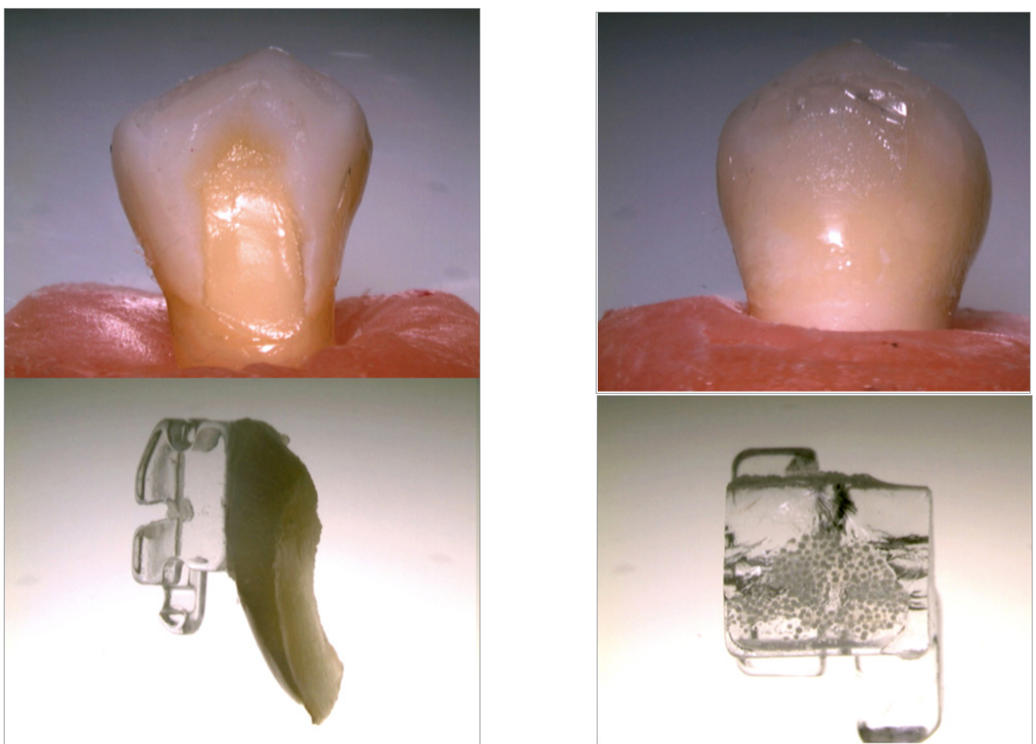

Figure 2. (a) Enamel fracture (ARI score 4), (b) Bracket fracture (ARI score 5)
ARI, adhesive remnant index

Table 6. Distribution of the samples according to ARI score

	Control group	Acetone 5 min	Acetone 15 min	Ethanol 5 min	Ethanol 15 min	DMSO 5 min	DMSO 15 min	Peppermint oil 5 min	Peppermint oil 15 min	Hot water 5 min	Hot water 15 min	N (%)
ARI 0	1	5	5	5	2	6	7	2	7	10	8	58 (44%)
ARI 1	6	2	3	3	5	5	1	2	4	1	2	34 (25.8%)
ARI 2	2	0	2	1	1	0	0	3	0	0	1	10 (7.6%)
ARI 3	0	1	0	0	2	1	1	3	1	1	0	10 (7.6%)
ARI 4	0	1	1	0	2	0	2	2	0	0	0	8 (6%)
ARI 5	3	3	1	3	0	0	1	0	0	0	1	12 (9%)
N	12	12	12	12	12	12	12	12	12	12	12	132 (100%)

ARI, adhesive remnant index; DMSO, dimethyl sulfoxide

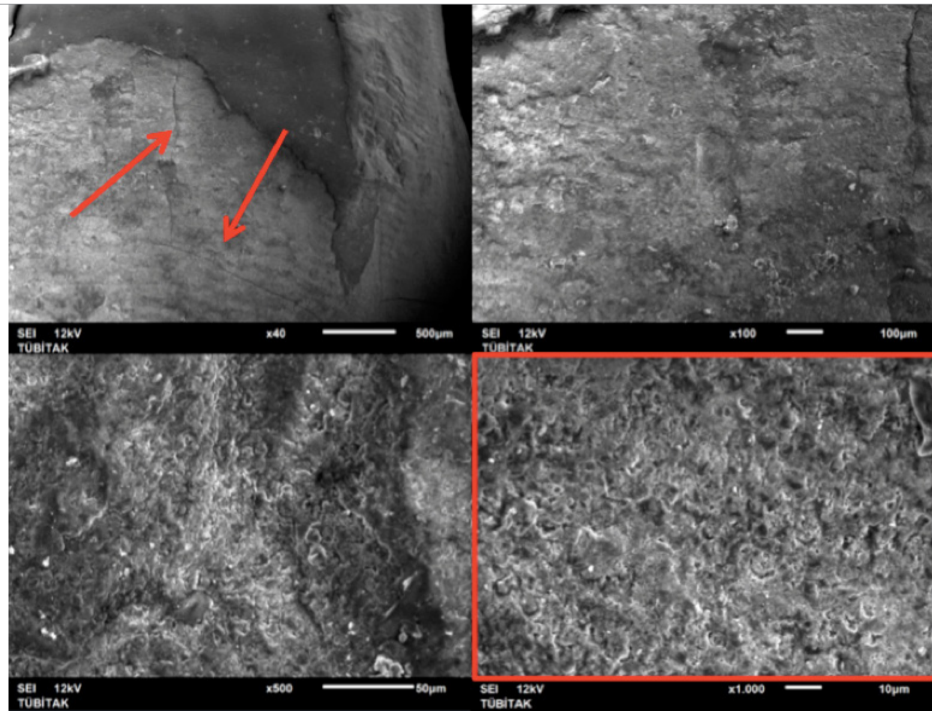

Figure 3. SEM image of group DMSO 15-minutes.
SEM, scanning electron microscopy; DMSO, dimethyl sulfoxide

same age range in the study is important for ensuring that the structures of enamel prisms are similar. It has been reported in the literature that monocrystalline ceramic brackets cause more damage to the enamel than polycrystalline ceramic brackets during the debonding phase.[24] Regarding the bonding types of ceramic brackets, it has been reported that the risk of enamel damage is higher for chemically bonded ceramic brackets.[25,26] In our study, to see the effects of the solutions to be applied clearly, a monocrystalline ceramic bracket type (Pure Sapphire Bracket System, Ortho Technology, West Columbia, US), which can bond to the tooth both chemically and mechanically was preferred. Since we used ceramic brackets in our study, the residual adhesive amount was determined by the modification of ARI scoring.[7,8] For the modification of the ARI scoring, bracket fracture scoring, and enamel fracture scoring was added to the original scoring. In previous studies on the reliability of ARI scoring, it was reported that ARI scores could be evaluated differently for different zoom magnitudes.[27] Therefore, in our study, ARI scoring evaluation was performed twice, with an interval of fifteen days, by the same researcher.

In our study, although the SBS value of the acetone 5-minute and 15-minute groups were lower than that of the control group, the decrease in the group in which only acetone was applied for a long duration (15 min) was found to be statistically significant. Thus, the findings support the hypothesis suggesting that the longer application time of chemical solutions, amplifies their effectiveness. It was found that acetone was the solution that showed the most softening effect on the composite, since the reduction in SBS was lower for acetone groups compared to other chemical solution groups, and this difference was statistically significant. According to the results of our study, we believe that the SBS can be reduced by applying acetone before the debonding of ceramic brackets and it can be an alternative method that will cause less damage to the enamel surface.

In the study of Santana et al.[28], it was reported that the application of acetone and ethanol in addition to the ultrasonic debonding technique did not cause any decrease in the SBS. In the study of Cruickshank and Chadwick[29], ethanol, polyacrylic acid, acetone and acetic acid were applied to anterior composite restorations for 3 min, but the hypothesis that chemical solvents soften the composite was not accepted. However, Wu and McKinney[30] reported that ethanol-dissolved bisphenol a-glycidyl methacrylate was much better than distilled water, and the softening effect of the adhesive increased as the concentration increased. In the literature, it has been stated that polymers with involving more crosslinks can be softened more difficult than polymers with linear structure.[31,32] Depending on the concentration of ethanol and the crosslink densities of the composites, the amount of softening of the adhesive may vary. The hypothesis in the literature that ethanol softens the composite is inconsistent with our results. The highest SBS was observed in the ethanol 5-minute and ethanol 15-minute groups among all groups. No statistically significant difference was found between the short duration and long duration applications of ethanol in terms of softening the composite and reducing the SBS. We believe that this is because the concentration of the agent used, and the application durations are different from those used in other studies.

We observed that the application of DMSO for a short duration (5 min) increased the SBS statistically significantly compared to the SBS of the control group. Thus, it can be said that DMSO is a more effective solvent than ethanol, and less effective than acetone and peppermint oil. We think that due to the high affinity of DMSO to water, the adhesive may harden after application. Although we thought that DMSO would soften the adhesive because it is a good organic solvent while planning our study, it seems that it cannot be a new and alternative method that we can use in the clinic based on the findings we have obtained.

Although Gustiana et al.[19] stated that the solutions should be kept for a long duration, such as 60 min, to observe their full effect, they also reported that short duration applications would be more practical in terms of applications in clinical work practices. In the study of Larmour and Chadwick[17], it was reported that peppermint oil could not be effective for the short duration applications of 1-2 minutes. For this reason, we observed the maximum effects of the solutions by forming groups of short (5 min) and long (15 min) durations in our study. Although there was no statistically significant difference between the short duration and long-duration applications of peppermint oil, its SBS was similar to that of the control group. When compared with other solvents, peppermint oil appears to have the least effect on softening or hardening of the composite. Although we applied each solution for 15 min at the longest to ensure standardization between the groups, the peppermint oil can be applied for a longer duration to observe its real effects; we believe that it can soften the composite with a longer application.

Carter[20] stated that before the debonding of ceramic brackets, patients rinse their mouths with the water (at a safe temperature) supplied from the coffee machine in the clinic so that the adhesive softens, and the brackets can be removed with less damage to the enamel surface. The results of our study do not support Carter's[20] clinical experience. In our study, it was concluded that the short duration and long duration applications of water at 60 °C did not soften the composite, but in contrast, it hardened and increased the SBS statistically significantly. We think that the use of cold water to reduce the SBS should also be evaluated in future studies.

In our study, adhesive fractures were observed in a large percentage of the samples for all groups except the peppermint oil 5-minute group; cohesive fractures were observed for the peppermint oil 5-minute group. From a clinical perspective, the advantage of adhesive fracture is that the cleaning duration can be reduced due to the small amount of residual adhesive on the enamel surface. Thus, less damage will be done to the enamel while cleaning with high-speed rotating tools. Similar to the study of Larmour et al.[18], the percentage of enamel fracture (ARI score 4) was found to be 6% in our study. In studies with ceramic brackets, it has been emphasized that the biggest disadvantage of ceramic brackets is that they cause enamel fractures during debonding.[33,34] In our study, bracket fracture (ARI score 5) was observed with a rate of 9%. Bracket fractures were mostly observed on the occlusal side of the bracket. We believe that this is because the direction of the debonding force is from occlusal to the gingival. Additionally, for monocrystalline ceramic brackets, cracks in Griffith defects, which are the areas where stress is concentrated, can spread and cause fractures in these areas.

Considering the debonding test results, the highest SBS belongs to the ethanol groups among all groups. According to SEM images, it was observed that the most damaging solution to the enamel surface was ethanol. Additionally, although microcracks were observed in all groups, the depth of the cracks was significantly higher in the ethanol group. Based on these results, we think that ethanol is the most damaging solution to the enamel surface and is not suitable for clinical use.

CONCLUSION

Following outcomes can be concluded:

• Ethanol is the most damaging chemical solution to the enamel tissue and is not appropriate for clinical use.

• Acetone application can be used as an alternative method in the clinics to facilitate the debonding of ceramic brackets.

• However, further research is required to determine the techniques and methods that will enable the clinical use of these chemical solutions.

Ethics

Ethics Committee Approval: Ethical committee approval was received from the University of Istanbul Ethics Committee in Istanbul, Turkey (Protocol number: 2019/11, date: February 14, 2019).

Informed Consent: N/A.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - H.U.; Design - S.E.Ö.; Supervision - S.E.Ö.; Materials - H.U. and S.E.Ö.; Data Collection and/or Processing - H.U.; Analysis and/or Interpretation - H.U.; Literature Review - H.U.; Writing - H.U.; Critical Review - S.E.Ö.

Declaration of Interests: The authors have no conflicts of interest to declare.

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