UNIVERSITÉ DE STRASBOURG
UNIVERSITÉ SAINT-JOSEPH DE BEYROUTH
FACULTÉ DE MÉDECINE DENTAIRE

ÉCOLE DOCTORALE 182
Laboratoire BioMatériaux et BioIngénierie UMR-S 1121
ÉCOLE DOCTORALE SCIENCES ET SANTÉ
Laboratoire de Recherche Cranio-Faciale

THÈSE présentée par :

Rim BOURGI

Soutenue le: **10 Septembre 2024**

Pour obtenir le grade de: **Docteur de l'Université de Strasbourg** (Discipline/ Spécialité: Sciences Médicales/Odontologie) et **Docteur de l'Université Saint-Joseph de Beyrouth** (Discipline/ Spécialité: Biologie et Matériaux du Milieu Buccal/Dentisterie Esthétique et Prothétique)

Effect of different application modalities and temperature of warm air evaporation on the bonding performance of four adhesive systems to dentin

THÈSE dirigée par:	
Monsieur Haïkel Youssef	PU-PH, Université de Strasbourg
Monsieur Hardan Louis	PU, Université Saint-Joseph
RAPPORTEURS:	
Madame Perez Fabienne	PU-PH, Université de Nantes
Madame Şar Sancakli Hande	PU, Université d'Istanbul
AUTRES MEMBRES DU JURY:	
Madame Farhat Mchayleh Nada	PU, Université Saint-Joseph
Monsieur Engels-Deutsch Marc	PU-PH, Université de Lorraine
Madame Abboud Mehanna Marie	PU-PH, Université Saint-Joseph
Monsieur Kharouf Naji	PU-associé, Université de Strasbourg

Table of Contents

List of Figures

List of Publications

1. **Bourgi, R.;** Hardan, L.; Cuevas-Suárez, C.E.; Scavello, F.; Mancino, D.; Kharouf, N.; Haikel, Y. The Use of Warm Air for Solvent Evaporation in Adhesive Dentistry: A Meta-Analysis of In Vitro Studies. *J. Funct. Biomater*. **2023**, *14*, 285. https://doi.org/10.3390/jfb14050285
2. **Bourgi, R.;** Hardan, L.; Cuevas-Suárez, C.E.; Devoto, W.; Kassis, C.; Kharma, K.; Harouny, R.; Ashi, T.; Mancino, D.; Kharouf, N.; Haikel, Y. Effectiveness of Different Application Modalities on the Bond Performance of Four Polymeric Adhesive Systems to Dentin. *Polymers* **2023**, *15*, 3924. https://doi.org/10.3390/polym15193924
3. **Bourgi, R.;** Kharouf, N.; Cuevas-Suárez, C.E.; Lukomska-Szymańska, M.; Devoto, W.; Kassis, C.; Hasbini, O.; Mancino, D.; Haikel, Y.; Hardan, L. Effect of Modified Triple-Layer Application on the Bond Strength of Different Dental Adhesive Systems to Dentin. *J. Funct. Biomater*. **2023**, *14*, 522. https://doi.org/10.3390/jfb14100522
4. **Bourgi, R.;** Kharouf, N.; Cuevas-Suárez, C.E.; Lukomska-Szymanska, M.; Kharma, K.; Moussa, F.H.; Metlej, M.; Haikel, Y.; Hardan, L. Warm Air Delivery in Adhesive Application: Effect on Bonding Performance and Morphological Outcomes. *Biomimetics* **2024**, *9*, 194. https://doi.org/10.3390/biomimetics9040194
5. **Bourgi, R.;** Kharouf, N.; Cuevas-Suárez, C.E.; Kassis, C.; Monjaras-Avila, A.J.; Qaddomi, M.; Abi Raad, S.; Al Hasani, M.; Haikel, Y.; Hardan, L. Assessment of Clinical Performance of Universal Adhesives Versus Other Adhesive Systems: A Systematic Review and Meta-Analysis of Clinical Trials. *Int. Arab J. Dent.* **2024**, *15*, 204-230. https://doi.org/10.70174/iajd.v15i2.1046
6. **Bourgi, R.;** Kharouf, N.; Cuevas-Suárez, C.E.; Lukomska-Szymanska, M.; Haikel, Y.; Hardan, L. A Literature Review of Adhesive Systems in Dentistry: Key Components and Their Clinical Applications. *Appl. Sci.* **2024**, *14*, 8111. https://doi.org/10.3390/app14188111

List of Tables

List of Abbreviations & Symbols

10-MDP: 10-methacryloyloxydecyl dihydrogen phosphate.
3D: three-dimensional.
4-MET: 4-methacryloxyethyl trimellitic acid.
4-MET: 4-methacryloxyethyl trimellitic acid.
4-META: 4-methacryloxyethyl trimellitate anhydride.
A: single active application.
AA: active application.
AAA: Active–Active–Active.
AAP: Active–Active–Passive.
ABT: active bonding technique.
AD concept: Adhesion-Decalcification concept.
AFR: annual failure rate.
ANOVA: analysis of variance.
AO: aluminum oxide.
APA: airborne particle abrasion.
APP: Active–Passive–Passive.
AWB: acetone wet-bonding.
BAC: benzalkonium chloride.
Bis-GMA: bisphenol A-glycidyl methacrylate.
BS: bond strength.
BSs: bond strengths.
C-factor: configuration-factor.
Ca: calcium.
CA/CAs: contact angle/contact angles.
CHX: chlorhexidine.
CQ: camphorquinone.
CSE: Clearfil SE Bond.
CV: micro-vibration with Compo-Vibes.
CVM: Compo-Vibes modified application.
DEJ: dentinoenamel junction.
ECM: extracellular organic dentinal matrix.
EDC: ethyl-3-[3-dimethylaminopropyl] Carbodiimide Hydrochloride.
EDTA: ethylenediaminetetraacetic acid.
ER II: two-step etch-and-rinse.
ER III: three-step etch-and-rinse.
ER: etch-and-rinse.
EWB: ethanol wet-bonding.
GA: glutaraldehyde.
GPDM: glycero-phosphate dimethacrylate.
h: hour/hours.
H_3PO_4: phosphoric acid.
HAp: hydroxyapatite.
HEMA: 2-hydroxy ethyl methacrylate.
HIFU: high-intensity focused ultrasound.
HL: hybrid layer.

ISO: International Organization for Standardization.
ITD: intertubular dentin.
LED: Light-Emitting Diode.
MA: methacrylic acid.
MDPB: methacryloyloxydodecylpyridinium bromide.
Micro-CT: micro-computed tomography.
min: minute/minutes.
MLA: multiple-layer application.
MLAs: multiple-layer applications.
MMP: matrix metalloproteinase.
MMPs: matrix metalloproteinases.
MTLA: modified triple-layer application.
NL: nanoleakage.
NTAP: non-thermal atmospheric plasma.
OBFL: OptiBond FL.
OBU: OptiBond Universal.
PA: passive application.
PBU: Prime&Bond Universal.
PENTA: dipentaerythritol pentaacrylate phosphate.
Phenyl-P: (methacryloyloxyethyl)phenyl hydrogenphosphate.
Phosphate: P.
PTD: peritubular dentin.
QAS: quaternary ammonium salts.
RTs: resin tags.
s: second/seconds.
SBS: shear bond strength.
SD: standard deviation.
SDE: selective dentin etching.
SE I: one-step self-etch.
SE II: two-step self-etch.
SE: self-etch.
SEE: selective etching of enamel margins.
SEM: scanning electron microscopy.
SiC: silicon carbide papers.
TEGDMA: triethylene glycol dimethacrylate.
TEM: transmission electron microscopy.
TS: Technical Specification.
UA: universal adhesive.
UAs: universal adhesives.
UDMA: urethane dimethacrylates.
ULA: ultrasonic agitation.
UVA: ultraviolet A radiation.
μTBS: micro-tensile bond strength.

Acknowledgment

In the present world of competition, there is a race of existence in which those who have a will to come forward, succeed. A project is like a bridge between theoretical and practical working. With this willing, I joined this particular project. In fact, I feel that I have learned a lot from writing this thesis, searching for the truth of science and life. This is the great treasure I will cherish not only in my future academic career but in my whole life as well. I would like to take this opportunity to express my immense gratitude to all those who have given their invaluable support and assistance.

My appreciation to the Dean of Saint-Joseph University, School of dentistry, Pr Nada FARHAT MCHAYLEH, and to the Dean of Strasbourg University, School of Dentistry, Pr Florent MEYER, for their support and for providing the necessary resources for the completion of this research. Further, thank you to the directors of the doctoral schools, Pr Aziz DINIA (Strasbourg) and Pr Nassim FARES (Beirut) for their invaluable assistance in facilitating the international convention between France and Lebanon.

I would like to explicit my deepest respect to my thesis director, Pr Youssef HAIKEL, who has the attitude and the substance of intelligence. Your exceptional qualities and profound knowledge have guided me with invaluable support and unwavering encouragement throughout this journey. He led me to an understanding of some of the more subtle challenges to our ability to thrive. His expertise, patience, and dedication have been instrumental in shaping this work. I am deeply thankful and hold great recognition for your outstanding leadership and expertise in the field of dentistry.

I want to express my sincere gratitude to my director and role model, Pr Louis HARDAN, for the invaluable mentorship and patronage he has provided me since my undergraduate studies. His dedication to my academic and professional growth has been a cornerstone of my journey, from undergrad to postgrad, and now into my Ph.D. program. I am profoundly grateful for the opportunities he has afforded me and the knowledge he has imparted, which have greatly enriched my educational and research experiences. It was a great privilege and honor to work and study under your supervision over these years. I could not have imagined having a better advisor for my study. Your mentorship as a genius in your field has been a source of inspiration and motivation, driving me to strive for excellence. Thank you for your continued belief in me and for the invaluable lessons.

I am also profoundly grateful to my co-director, Pr Naji KHAROUF, for his insightful feedback, constructive criticism, and mentorship. His expertise and understanding throughout the challenging journey have greatly contributed to the success of this thesis. He continually and convincingly conveyed a spirit of adventure in regard to research. Without his guidance and persistent help, this work would not have been possible. Your sustenance, understanding, and love have been a constant source of strength throughout this journey.

I want to convey my sincere appreciation to all the jury members for graciously agreeing to evaluate my thesis. Your willingness to dedicate your time and expertise to this endeavor is deeply appreciated. Your insights and feedback will undoubtedly contribute to the refinement and success of this work.

I extend my sincerest gratitude to the Head of the Department of Esthetic and Restorative Dentistry, Dr Cynthia KASSIS, for her exceptional guidance. It has been an honor and privilege to be a member of this esteemed department.

I wish to express my sincerest thankfulness to Pr Carlos Enrique CUEVAS SUÁREZ from Autonomous University of Hidalgo State, Mexico for his encouragement, insightful comments, and kindness in gathering and giving me precious advice throughout the entire process of completing this thesis. His knowledge, dedication, and mentorship have been instrumental in ensuring the success and rigor of this research.

Further, a thank you to Pr Davide Mancino from Strasbourg University for his valuable comments and reviews. A special thank you from my heart is presented to my dear friends, colleagues, and professors, "Pr Monika LUKOMSKA-SZYMAŃSKA, Eng. Abbas AL SHAB, Dr Khalil KHARMA, RA Fabienne El Hajj, Dr Omar HASBINI, Dr Manar METLEJ, Dr Mohammad QADDOMI, Dr Rima DAOUI, Pr Walter DEVOTO, Dr Reda CHARAFEDINE, Pr Issam KHALIL, Dr Mohamed AL HASANI, Dr Tarek ASHI, Dr Carol MOUSSA, Dr Elie DAHER, Sophie ABI RAAD, and Dr Fadi JERBAKA" for their continuous support throughout the development of this project.

I spread my heartfelt appreciation to the laboratories team in France and Lebanon for their assistance and collaboration throughout this research endeavor: "Dr Philipe LAVALLE, Dr Jihad ZGHAL, Dr Hamdi JMAL, Pr Nadia BAHLOULI, Dr Wassim MANHAL, Dr Roula HACHEM, Dr Marie-louise SLIM, Mr Charbel MANSOUR, Pr Carol CHAKAR, Pr Joseph BOU SERHAL, and Dr Georges NAJJAR". An exceptional thank you to Dr Ryan HAROUNY for his effortless help and guidance through this thesis.

I am deeply grateful to the surgery team: "Dr Nicolas EL KHOURY, Dr Anthony CHIDIAC, Dr Stephanie MRAD, Dr Elie NICOLAS, Dr Mohamed ABOU KHALIL, Dr Hassan KOMAYHA, Dr Hassan ABDALLAH, and Dr Imad ABOU SALEH" for their generous contribution to the collection of the extracted teeth, which were essential for conducting the research presented in this thesis. Their willingness has significantly enriched the scope and depth of this study.

Last, but not least, I would like to express my deepest appreciativeness to my parents (Salam and Nadia) for their unwavering love and encouragement throughout my academic journey. Their sacrifices, guidance, and belief in my abilities have been the foundation of my achievements. I am forever indebted to them for their endless encouragement and faith in me. To my two sisters (Racha and Dana) and my brother Dr Ali BOURGI, thank you for always being there for me, offering words of encouragement, and providing a source of inspiration. Without their support, I do not think that I could overcome the difficulties during these years.

Abstract

The central aim of adhesive dentistry is to improve the compatibility between current adhesives and a range of substrates by employing diverse application techniques. Therefore, the overarching objective of this thesis was (1) to evaluate the bond performance of four adhesive systems—Prime&Bond Universal (PBU), Clearfil SE Bond (CSE), OptiBond Universal (OBU), and OptiBond FL (OBFL)—to dentin using various application modes [passive application (PA), active application (AA), Compo-Vibes modified application (CVM), and Compo-Vibes application (CV)]. Furthermore, the study aimed (2) to assess the impact of modified triple-layer application (MTLA) in conjunction with the active bonding technique (ABT) on the bond strength (BS) of these adhesives to the dentinal substrate. The adhesives were applied according to the following strategies: single active application (A) and triple adhesive layer application including Active–Passive–Passive (APP); Active–Active–Passive (AAP); and Active–Active–Active (AAA). Moreover, the research sought (3) to investigate whether varying air temperatures (20 °C, 40 °C, and 60 °C) during solvent evaporation could enhance the performance of the tested adhesive systems on dentin.

Based on the different approaches employed, non-carious human molar teeth were randomly prepared and divided for micro-tensile bond strength (μTBS) test and failure mode analysis after 24 h and 6 months, as well as scanning electron microscopy (SEM) of the composite–dentin interface morphology was assessed after 24 h. For application modalities, the adhesive contact angle (CA) was measured on prepared dentinal surfaces. In addition, for air-dry temperature, solvent evaporation rate was examined as a secondary variable in small light-proof glass containers of known weight. A two-way analysis of variance (ANOVA) was conducted to assess the BS of all tested modalities. The BS was examined separately after 24 h and 6 months of aging. Tukey's post hoc test was employed for multiple comparisons. Additionally, data from the adhesive CA underwent a one-way ANOVA with multiple comparisons using the Bonferroni test. A significance level of $\alpha = 0.05$ was applied to all analyses.

For (1): After 24 h, a significant difference with a higher BS value was found for PBU in the AA modality and for CSE in the CVM modality ($p < 0.05$). However, no significant difference in BS was shown between the techniques used among the other adhesives (OBFL and OBU with $p > 0.05$). Additionally, at 24 h, only the PA demonstrated significant differences in BS between the tested materials ($p < 0.05$). After 6 months, CSE, PBU, and OBU exhibited significant differences between the techniques ($p < 0.05$), with higher BS observed for CSE in AA and CVM modalities, for PBU in AA modality, and for OBU in AA and PA modalities. No significant differences in BS were found between the techniques used among the OBFL ($p > 0.05$). Furthermore, only the CVM technique demonstrated significant differences in BS between the tested materials after 6 months ($p < 0.05$). CV and CVM indicated a significant decline in values after aging for CSE and PBU, respectively ($p < 0.05$). However, all the modalities presented a significant decrease in BS for OBU and OBFL after aging ($p < 0.05$). All the adhesives showed marked resin infiltration into dentinal tubules in AA among all the modalities tested. Both universal adhesive systems (OBU and PBU) demonstrated statistically lower CA when compared to the other systems (CSE and OBFL) ($p < 0.05$) when applied in the PA mode. Concerning the AA mode, only CSE and OBFL were tested. The AA demonstrated lower CA values compared to the same adhesives in PA ($p < 0.05$).

For (2): At 24 h of aging, all of the factors tested were not significant ($p > 0.05$) for CSE. For OBFL, OBU, and PBU, statistically higher values were observed for the A technique ($p < 0.05$). Plus, there were no significant variations in BS between the APP, AAP, and AAA techniques ($p > 0.05$) for OBFL and PBU. Though, for OBU, there were no significant differences in BS between the A and AAA techniques ($p > 0.05$).

After 6 months of aging, the A technique showed statistically higher values when compared to the other techniques ($p < 0.01$), except for OBFL, where the A and AAA techniques showed promising outcomes when compared to APP and AAP ($p < 0.001$). When evaluating the BS values of 24 h and 6 months, only for PBU, all of the techniques used resulted in BS stability over time ($p > 0.05$). Thicker adhesive layers were observed when MTLA was applied. Only the OBFL adhesive showed the formation of resin tags (RTs) in all of the modalities tested.

For (3): BS values were similar among all the adhesive systems used ($p > 0.05$). Also, the factor aging did not affect the BS ($p > 0.05$). Only the temperature factor used for solvent evaporation resulted in a statistically significant effect ($p < 0.05$), with the temperature of 60 °C yielding the highest values ($p < 0.05$). The evaluation of failure modes revealed predominantly adhesive or mixed failures, regardless of the application methods (application modes, MTLA in conjunction with the ABT, and variation in air temperatures (20 °C, 40 °C, and 60 °C)) for each adhesive system tested. The thickness of the adhesive layer and the creation of RTs varied amongst the temperatures evaluated. For all adhesive systems tested, the use of 40 °C or 60 °C air for solvent evaporation led to an increased mass loss.

To conclude, it can be inferred that both materials and application techniques influence BS. The AA technique emerges as the recommended gold-standard for adhesive system application to dentin. Moreover, the CV and CVM modalities, after 6 months of aging, exhibit stability for PBU and CSE, respectively. Thus, the performance of these adhesive systems could differ with other application modalities, warranting further investigation. The bonding performances of the different layer application techniques used were material-dependent. CSE, OBU, and PBU were benefited by the A technique; for OBFL, the use of the AAA technique could be recommended to achieve stability in the adhesive layer and adhesive-dentin interface. Besides, optimizing solvent evaporation with warmer air temperatures (40 °C and 60 °C) significantly improves μTBS, providing a practical means to enhance the quality and longevity of adhesive restorations in esthetic dentistry.

Chapter I: Literature Review

1.1. Introduction: Adhesion

Throughout the years, adhesive systems have undergone significant advancements in various aspects of modern restorative dentistry. However, challenges persist regarding the long-term durability of the resin-dentin bond interface [1]. Bonding to enamel structure has become a predictable and a well-established procedure [2], whereas bonding to dentin, due to its heterogenous structure and histology, was considered challenging [3,4]. Indeed, the attainment of optimal interdiffusion of the adhesive system within collagen fibrils and the preservation of stability at the resin-dentin interface are critically significant [5]. As a result, it is fundamental to understand the mechanism of dentin hybridization during which an interdiffusion zone, also known as a hybrid layer (HL), is formed, leading to the development of micro-mechanical retention of the dental restoration [6]. Thereby, the HL is made up of residual hydroxyapatite (HAp), solvents, collagen, and resin monomers; its level of strength is ultimately influenced by each component's resistance to degrading occurrences [7,8].

During adhesion procedure, the mineral components are partially or totally removed by acidic monomers in self-etch (SE) or etch-and-rinse (ER) adhesive systems [9]. After the dentin and the enamel substrates have been totally etched with phosphoric acid (H_3PO_4), ER adhesives are applied, and thus the smear layer is removed [10]. On the contrary, the acid etching phase is removed for dentin with SE adhesives since they include monomers with acidic functional groups that concurrently etch and prepare the dental substrate [11]. So, the smear layer is modified and incorporated in the hybridized complex [12]. ER adhesive systems have two or three application step variations, whereas SE adhesive systems have one or two [9].

With regard to the ER adhesives, OptiBond FL (OBFL, Kerr Co., Orange, CA, USA), a three-step ER (ER III) adhesive, is recognized by many as one of the gold-standards of multiple bottle systems [10]. The adhesive used (OBFL) contains a highly hydrophobic bonding ingredient called glycero-phosphate dimethacrylate (GPDM), which can chemically react with HAp in the etched and prepared enamel and dentin substrate to improve bond strength (BS) [13]. SE systems were then implemented, which eliminated on dentin the use of H_3PO_4 and the accompanying rinsing phase [9]. Clearfil SE Bond (CSE, Kuraray Noritake Dental, Tokyo, Japan) has been documented as the gold-standard in this class; the primer and the adhesive of this system consist of 10-methacryloyloxydecyl dihydrogen phosphate (10-MDP), which interacts with calcium (Ca) to establish a strong and stable bond, hence forming nano-layers of 10-MDP-Ca [14]. Most recently, manufacturers have developed broader-ranging adhesive systems that can be utilized in both bonding procedures (ER and SE), in addition to the selective etching of enamel margins (SEE). The manufacturers propose that practitioners adopt bonding procedures based on their preferences and the type of tooth structure. This innovative set of dental adhesives, known as "multi-mode" or "universal adhesives” (UAs), is the newest version of dental adhesives [15,16].

Presently, these dentin bonding agents consist of monomers containing both hydrophobic and hydrophilic groups, along with polymerization modulators and relatively high levels of organic solvents [17]. These solvents serve as diluents and improve the spreading, wetting, and penetration of monomers into the micro-porosities of the exposed, acid-demineralized collagen network [18]. It is imperative to emphasize that the higher the content of solvent inside the polymer, the lower the resin-dentinal BS and the mechanical properties of a cured resin [19].

Supremely, any excess solvent should be evaporated from the dentinal surface through air-drying the applied adhesive before photopolymerization. The existence of residual solvent could jeopardize the photopolymerization of resin monomers, leading to compromised bond integrity and the formation of unwanted voids in the adhesive interface. These voids can perform as defect-initiator sites, delivering a trail for nanoleakage (NL) and producing a reduction in the BS [20,21]. Solvent evaporation can be accomplished by incorporating an evaporation period between the application and curing of the adhesive, or by employing air-drying techniques with a tooth-syringe [22]. Overall, the evaporation of solvent from an adhesive depends on several factors, including the type of the solvent, operator skills, tooth-syringe distance, type of monomer, and air temperature, all of which appear to affect the air-drying duration of an adhesive system [23].

Moreover, there are various strategies available to facilitate the removal of solvents and enhance the longevity of adhesive systems, including amplified light-curing time, prolonged application time, active bonding application, multiple adhesive layers, extended air-drying, and using warm air stream on the primer or the adhesive [24-27].

Additionally, the active application (AA) or ultrasonic agitation (ULA) of adhesive systems improved dentin bond functioning of the etching mode by simplifying the infiltration of dental adhesives inside the dentinal tubules [28,29]. Essentially, the AA (with or without ultrasonic energy) of adhesives through a scrubbing technique leads to the penetration of a higher number of monomers within the smear layer, eases solvent evaporation, and so improves adhesive-interface feature [30]. Further, the ULA increases the chemical interaction of an adhesive system with the dental structure, yet, it necessitates a special device for ultrasonic vibration. Lately, a novel device called Compo-Vibes (CV, Smile Line, St-Imier, Switzerland) was launched for an easier, faster, and better composite's modeling. This device emits micro-vibrations for more precise composite application, and this could be possible by different tips. This device generates micro-vibrations of 0.158 kHz or 158 Hz with a tolerance of approximately +/−15%, enabling accurate composite applications with various tips. Additionally, a micro-brush, which has multiple functions, replaced the usual brush that comes with the device. Till now, to the best of researcher knowledge, there have been no studies that have simultaneously compared the bonding effectiveness of four application modalities, passive application (PA), (applying the adhesive without any agitation), AA (applying the adhesive with active agitation), micro-vibration with CV (Smile Line, St-Imier, Switzerland) (applying the adhesive with the help of a CV (Smile Line, St-Imier, Switzerland) tip used as a brush for bonding), or CV (Smile Line, St-Imier, Switzerland) modified application (CVM) using a micro-brush.

On the other hand, the use of multiple-layer application (MLA) increased immediate BS; but this result may not be observed after aging [25]. This means it is regarded as essential to understand how many adhesive coats must be placed on dentin structure for the purpose of enhancing bond effectiveness. Present-day bonding trends appear to favor a single application of adhesive treatments, albeit insufficient for creating a thicker HL or adhesive layer conductive to micro-mechanical retention with the underlying composite resin. Previous studies claimed that double or triple adhesive coats promote BS by enhancing monomer infiltration into the HL and increasing chemical interactions [31,32]. Further advancements in adhesive dentistry required the incorporation of novel molecules into adhesive compositions: 10-MDP, 2-(methacryloyloxyethyl)phenylhydrogenphosphate (Phenyl-P), and 4-methacryloxyethyl trimellitic acid (4-MET) [33,34]. They were identified as functional monomers and were thought to chemically link with Ca in HAp [34]. Among these compounds, MDP has been identified as having the strongest chemical attachment potential to HAp, resulting in stable Ca salts through nano-layering [35]. As an outcome, an extra layer of application needs to be recognized as a vital clinical step. Supplementary, MDP monomer requires a proper duration of 20 s for chemical contact to occur; nevertheless, adding a second layer of such a monomer without polymerizing the first one allows the first layer to appropriately engage with HAp, promoting additional bonding [36]. Consequently, there are no prior studies available in the scientific literature that relies on the adhesive layer application including the triple adhesive layers in conjunction with the "active bonding technique" (ABT), called modified triple-layer application (MTLA). Appropriately, a description of this novel technique could be interesting for dentists aiming for better adhesion to dentin.

The use of warm air streams has been suggested as an effective method to evaporate solvents from an adhesive solution [7,37]. Furthermore, this technique increases resin infiltration to prepared dentin, which improves dentinal BS. It is noteworthy to point out that the warm air stream within the dentinal pulp organ's thermal tolerance zone (29 °C-56 °C) has no adverse pathological effect on the dentin pulp organ, and dentin responds physiologically to these warm air blowing [38,39]. Yet, according to a previous systematic review and meta-analysis, dentin BS of ER or SE adhesive systems can be perfected by employing the warm air stream for solvent evaporation. Numerous warm air temperatures, embracing 37 °C, 38 °C, 50 °C, 60 °C, and 80 °C, were identified in the aforementioned review [7]. Complementary, it was established that none of the elaborated manuscripts determined a standard temperature when using warmer air. Approximately 40 °C and 60 °C warmer temperatures were efficient for enhancing solvent evaporation; nonetheless, the 60 °C temperature was more in favor in terms of stable BS and less bond degradation [7,40]. Properly, a better definition of the gold-standard temperature for air-drying should be given serious consideration.

Accordingly, ABT, MLA (2 layers and more), and the use of warm air for solvent evaporation should be proposed by clinicians in their daily practice in order to improve the BS of adhesive systems to dentin. The issue is that until now, there is no specific protocol for achieving stable and optimal adhesion of adhesive systems to dentin. Likewise, improvement in BS can be realized by means of several strategies, and thus, advocated by various previous studies [7,25,41].

Hence, this thesis aims: (1) to assess the bonding performance of four adhesive systems for various application methods: PA, AA, CV, and CVM; (2) to determine the effect of ABT with MLA (one layer (control), triple adhesive layers with activation of the first coat, the first two coats, and all three coats, while the remaining coats are passive) of four adhesive systems on dentin BS as well as the correlation between these parameters; and (3) to evaluate whether the development of a warm air prototype for solvent evaporation improves the performance of an adhesive system. In addition, to define a standard temperature for solvent air-drying by comparing the effect of 3 different temperatures [(20 °C), (40 °C), and (60 °C)]. According to the null hypothesis: (1) there is no effect of the application method on the immediate and long-term BS of the four adhesive systems to dentin following the four modalities; and on dentinal wettability following AA and PA; (2) there is no effect of the MTLA of four adhesive systems on the dentin BS as well as the correlation between these parameters at 24 h and 6 months of aging; and (3) the use of warm air streams for solvent evaporation does not affect the immediate and long-term BS and morphological properties of different adhesives to dentinal substrate. Further, air-drying temperatures of 20 °C, 40 °C, and 60 °C have no similar effect on the BS and morphological properties of the adhesive systems tested.

Keywords: Adhesive layer, adhesive systems, dental bonding, dentin, rubbing, solvent based, warm air.

1.2. Enamel and Dentin-An Overview

A main objective of restorative dentistry is to bond restorative materials to enamel, dentin, or both [33]. Chemically, enamel structure is a highly mineralized crystalline substance comprising 95 to 98% inorganic matter by weight. The inorganic content of enamel relies on HAp, the largest mineral component, which is present at concentrations of 90–92% by volume, and its proper arrangement as enamel prisms to maintain its structure [42]. However, in the free spaces between the HAp crystals, a network of organic materials exists. A resilient mineral, formed by the interaction between minerals, collagen I fibrils, and other proteins, is present within dentin and bone. Despite this, enamel is much tougher due to being more mineralized than bone. Also, enamel does not contain collagen; though, when it matures, a small quantity of specialized matrix proteins is produced inside the enamel [43]. The remaining enamel constituents comprise an organic phase, which reports for about 1 to 2%, and water (3 to 4%), which accounts for about 4% by weight [44].

The rods of enamel are tightly packed and interlaced in a wavy pattern that extends from the dentinoenamel junction (DEJ) to the tooth's exterior surface. Aprismatic enamel has an optic axis approximately parallel to the enamel's surface, with an acid-resistant surface that protects against enamel degradation in the oral setting [45]. The DEJ, or transition zone between dentin and enamel, together with the enamel tufts made of hypomineralized crack-like defects, plays a crucial part in tooth resilience and preventing the cracks propagation [46]. Typically, enamel rods are positioned perpendicular to both the DEJ and the tooth surface. After the enamel has been treated with an acidic conditioner, the "ends of the enamel rods" onto the surfaces are exposed for the bonding agent [44,45]. Yet, the rods can be placed parallel to the interior surface of a tooth preparation, when the "sides of the enamel rods" are revealed following acid conditioning [44].

Dentin is essential in the clinical use of adhesive restorations. Dentin is a complex tissue, and although known to be highly mineralized, it has a lower mineral level (70 wt% mineral by weight and 45% by volume) and a higher organic composition (20 wt% organic phase by weight and 33% by volume), with water making up the remaining fraction. Despite being less mineralized than enamel, dentin has a higher mineral content than bone or cementum [45].

The morphology of dentin is very complex. Its microstructure is naturally well-oriented, containing several dentinal tubules occupied by odontoblast processes or their residues, with a density ranging between (19-45) × 1000/mm^2 and an average diameter of 0.8-2.5 μm [47]. Dentinal tubules spread through the whole dentin thickness, starting from the DEJ or the cementum to the pulp [21,48,49]. These tubules are bounded by two dissimilar dentinal phases: the intertubular dentin (ITD) and the peritubular dentin (PTD) [50]. The larger part of the dentin volume is surrounded by ITD, a composite containing type I collagen fibrils irregularly fortified with nanoplatelets of carbonated HAp [45]. This configuration makes the dentin tougher and stronger. The PTD contains no collagen and is more mineralized, harder, and stiffer than the bordering ITD [51,52].

An increase in the diameter of the dentinal tubules inside the deep dentin, along with the convergence point of the tubules toward the pulp chamber, results in an exponential surge in the dentin permeability when the dentin is prepared deeper [53]. So, in the superficial dentin, bonding is primarily intertubular, while in the deep dentin, bonding is mainly intratubular [54] (Fig.1).

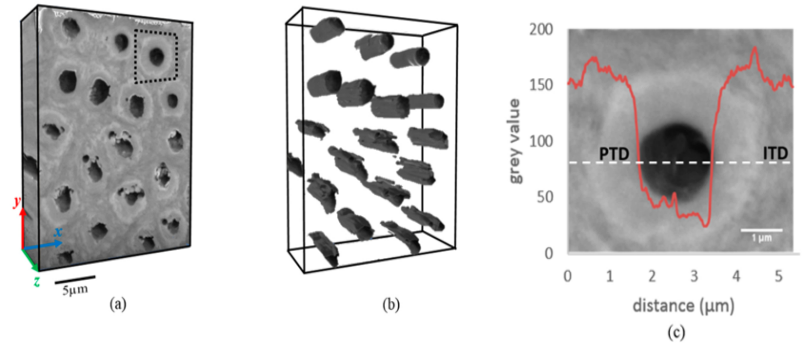


Figure 1: Three-dimensional (3D) focused ion beam-scanning electron microscopy tomography of a representative volume of dentin. (a) 3D reconstruction of the dentin structure composed of tubules. (b) 3D spatial distribution of dentinal tubules (dark grey). (c) The variation of grey scale values across the centre of a representative single dentinal tubule (marked by the dashed region in image (a)) [47].

Enamel adhesion to dentin is very puzzling due to the high fluid content (10 wt%) present in the form of unbound and bound water, along with the extracellular protein content. Dentin, being hydrophilic, makes the infiltration of resin monomers unsuitable. Yet, an adequate dentin-resin bonding is possible with hydrophilic and amphiphilic resin chemistry only. The hydrophilic resin monomers might penetrate the demineralized surface of the dentin, rich in type I collagen fibrils, encasing the exposed dentinal matrix, then forming the so-called HL [4,55]. The hybridization of the dentin surface is the main mechanism for the micro-mechanical retention of bonding systems [56].

1.3. Histology of Enamel and Dentin Structures

Enamel is a dry substrate with no vital structures, making it closely perfect for forming a tight adhesive bond [3]. Ameloblasts are particular epithelial cells that generate enamel. During development, amorph matrix rich in proteins, acellular, and avascular ameloblasts cover the whole surface of the forming tooth, which is eventually occupied with ribbon-like crystals of carbonate-HAp. Away from the dentin, these crystals are arranged in rod and interrod spaces. Ameloblasts produce tight connections and membrane infoldings from the apical ends of the cells during the second phase of enamel maturation, altering the pH from moderately acidic to near-physiologic and allowing the matrix to crystallize [57].

The Retzius lines are the bands of enamel rods that emerge in a histologic slice of mature enamel. Strong Retzius lines are created following ameloblast traumas and are distinguished by uneven enamel crystal structures. Enamel is nearly devoid of soft organic matrix in its mature condition. The thickness of the enamel is thinner in the cervical region and thicker in the masticatory surfaces (incisal ridge and cusps) [58].

Mature enamel is composed of long, thin HAp crystal rods. The histological sections cannot assess its assembly as the crystals dissolve through decalcification, a process that allows cutting the teeth when making the specimen. Amelogenin, enamelin, and perlecan are three proteins found in enamel. The latter is found in the dental papilla and follicular intercellular gaps. The enamel epithelium and dental mesenchyme form the contact between dentin and enamel in the growing tooth. Coronal dentin is covered by enamel, while radicular dentin is covered by cementum [58,59].

Dentin is the major structure of the teeth, so understanding this complicated tissue in connection to resin-dentin bonding necessitates an outline of the dentinal organic matrix that is embedded in a collagen fiber mesh [60]. The extracellular organic dentinal matrix (ECM) is constituted generally of a three-dimensional (3D) network of fibrillar collagens, specifically type I collagen (90%) with traces of type V and III collagens. [61]. The remaining ECM components are non-collagenous proteins, mostly proteoglycans. Dentin is found in the following substances: sialoproteins, phosphoproteins, bone morphogenic proteins, enzymes, and growth factors [62].

Collagen is thin (diameter=1.5nm) and lengthy (300 nm). The bordering collagens are shifted from one another by one-quarter of their length=67 nm [63]. Fibrillar collagens (types I, II, III, V, XI, XXIV, and XXVII) predominate [64]. The three α chains possess N-terminal and C-terminal ends (Fig. 2). The latter is associated with globular structure formation: the C-terminal propeptide.

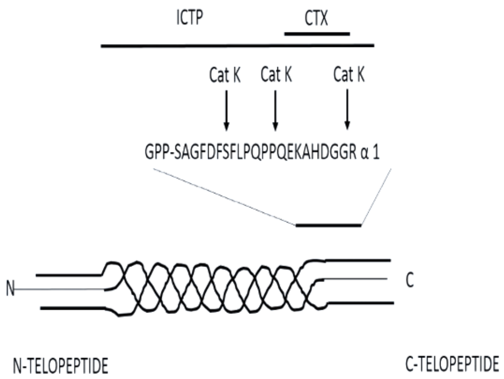


Figure 2: Orientation of type I collagen molecules in hard-tissues. N- and C-terminal ends of successive type I collagen fragments as specific biological markers of degradation. (Courtesy of Prof Umer Daood).

The Glycine-X-Y triplets of the chains then align to the N-terminus where the globular N-terminal propeptide generates a triple helix. The formed structure flanked by the N- and C-terminal propeptides created is named procollagen, which will subsequently be converted into collagen type 1 [60,64] (Fig. 3).

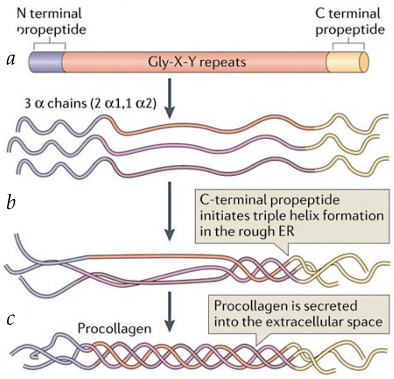


Figure 3: (a) Structure of the 3 chains α. (b) Initiation of the formation of the triple helix at the level of the C-terminal propeptide. (c) Representation of the structure of the procollagen triple helix. ER = Endoplasmic reticulum.

Bound water molecules occupied the voids inside and between the collagen fibers during the mineralization process of the dentin. Consequently, water is gradually substituted by minerals [61,64]. There was no evidence of resin infiltration in the mineralized dentin [60,64] (Fig. 4).

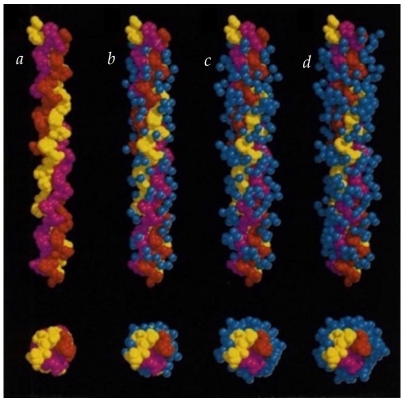


Figure 4: Representation of the progressive hydration of the collagen Glycine-Alanine peptide. Top row presents the perpendicular and the bottom row parallel view to the molecular axis at the same hydration level. (a) A view of the non-hydrated collagen, with the three peptide chains shown in different colors. (b) The first shell of water molecules (blue spheres), directly hydrogen-bonded to carbonyl, hydroxyl or amide groups on the peptide surface. (c) The second shell of water molecules, hydrogen bond to the water in the first shell, demonstrating the filling of the superhelical groove. (d) The third shell of water molecules [64].

Interest in tooth adhesion is driven by the chemical interaction between the mineral platelets in hard tissues and the acidic monomers of SE and ER adhesive systems [33]. This process builds a channel for the resin to enter and enclose the collagen fibrils, enabling hybridization [3,9]. In the HL, the interfibrillar gaps between the collagen are adequately large (30 ± 11 nm) [8] which could simplify the penetration of small hydrophilic monomers such as bisphenol A-glycidyl methacrylate (Bis-GMA) (512 Da) and 2-hydroxy ethyl methacrylate (HEMA) (100 Da) [60]. A previous study proposes that molecules greater than 40 kDa were excluded from collagen water infiltration, while molecules smaller than 6 kDa in size diffused easily. While an obstacle occurs in the intrafibrillar space (1.26–1.33 nm), which is made of up to hundreds packed collagen molecules [65], other aspects should be taken into consideration such as the concentration (the ability of adhesive monomers to dislodge water from the collagen is restricted by their relative concentrations : water has a [55 mol/L] concentration, while co-monomers have a [3-4 mol/L] concentration), and viscosity: lower viscosity of monomeric bonding is obligatory to exhibit collagen water [60,66] (Fig. 5).

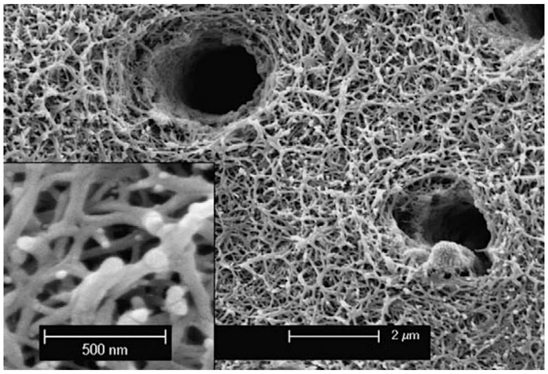


Figure 5: Scanning electron micrograph of acid-etched dentin showing two dentinal tubules containing remnants of peritubular dentin matrix. INSERT: High magnification of branching collagen fibrils (ca. 75 nm in diameter) separated by interfibrillar spaces that serve as channels for resin infiltrations during bonding [10].

Note that the hydrogen bonds between the collagen fibers are crucial for the hydration process, helping to prevent the collapse of the dentinal matrix before resin penetration [60].

1.4. Effect of Dentin Structure on Resin-Dentin Bonding

The main goal of any bonding agent is to achieve a firm and enduring adaptation of the restorative material to dental substrates [9]. The major challenge for any new dental adhesive is to be equally effective on both enamel and dentin surfaces [33]. To accomplish this goal, several obstacles must be overcome [9]. Bonding efficiently to the organic and wet dentin is a baffling task in adhesive dentistry. Nevertheless, bonding to enamel can be consistently achieved through the micro-mechanical interlocking of the resin tags (RTs) within the arrangement of micro-porosities of demineralized enamel, which successfully seals the margins of the restoration against leakage [3,7,33].

It has long been argued that the base of adhesion to dentin is imperfect [67]. On a nanoscale level, completely enveloping the collagen fibrils by monomers to fill up all the spaces is practically impossible [68]. Furthermore, methacrylic acid (MA)-based resin monomers are required for a higher possibility of penetration into the interfibrillar spaces of the collagen matrix because of this monomer's low viscosity and relative hydrophilic nature. However, this may lead to hydrolysis [69,70]. Ultimately, the presence of an exposed collagen, in addition to water empty spaces which are naturally present within the dentin collagen, can result in both hydrolytic and enzymatic degradation simultaneously [33,71]. These reasons led Bertassoni et al., [72] to determine that a suitable resin-dentin network is an important pre-requisite for a successful adhesion on a molecular level.

Acid etching is a process occurring as part of the mechanism of dentin binding. This procedure is used to demineralize between 5 and 8 μm of the ITD network in an effort to generate porosities at a nanoscale level in the collagen matrix. This results in the opening of dentin tubules, exposure of collagen fibers, and modification or elimination of the smear layer [3,10,17,73].

Thus, it is crucial to fully grasp the knowledge behind the behavior and properties of the smear layer in bonding mechanisms [74].

The production of the smear layer occurs while preparing the dental cavity. It manifests on the dentinal surface after the application of the instruments and is made up of varying debris and an altered morphology [75]. The resulting porous layer, with a thickness ranging between 0.5 and 7 μm is comprised of saliva, water, HAp, bacteria, blood, and modified collagen [76]. The quality and thickness of the smear layer depend on the instrumentation used, the mode of use, the dentin site, and whether a splash of water is applied. A rougher surface is produced through diamond burs rather than carbide burs, and stronger friction is created by dry cutting than by wet cutting [75,77].

As soon as the layer binds to the dentinal surface, the entrance of the dentin tubules is plugged to a depth between 1 and 10 μm, effectively blocking any direct contact of materials with the dentinal substrate. The final layer is referred to as "Smear Plugs", which reduce the permeability of the dentin by 86% [78,79].

Addressing the issue created by the smear layer requires a certain level of etching prior to chemical adhesion to the dentinal substrate. There are two possible effective options:

- The full elimination of the smear layer with H_3PO_4 before bonding after an ER approach (smear layer-removal approach) [74].

- The application of bonding agents that can enter beyond the smear layer (various acidic primers are used), while integrating it following a SE approach (smear layer-modified approach) [80].

The bond to dentin depends on micro-mechanical interlocking in both processes [9,17].

Role of the smear layer in dentin bonding

In early generations, adhesives were bonded directly to the surface which is covered by the smear layer [81,82]. The BS of these adhesives in an *in vitro* setting is lower than 5 MPa, which might lead to clinical debonding [83]. The specimens appearing after debonding are classified mainly as a cohesive failure inside the smear layer due to the adhesive resin being hydrophobic which prevents it from entering through the debris zone [84].

In the initial phases of adhesive research, the most frequently used abrasive paper for generating a standard smear layer across dentin surfaces in research laboratories was 600-grit silicon carbide papers (SiC) (average particle size: 29 µm) [85-87]. Also, they are regularly employed by manufacturers before introducing a new adhesive system. Consequently, clinicians extrapolate these outcomes to clinical substrates, which are markedly different. For example, the smear layer generated by regular-grit diamond burs (average particle size: 100 µm) is denser, thicker, and rougher compared to that produced by 600-grit SiC [88]. Consequently, it can weaken the dentin bond, especially when SE adhesives are used [89,90], impacting material selection and eventually, the quality of bonded resin restoration. Previous studies addressing such issues have recommended using coarser SiC, such as 180-grit (average particle size: 63 µm) [31,91-93], or 120-grit (approximately 125 µm in thickness) and 400-grit SiC (about 35 µm in thickness) for dentin preparation [94]. The aforementioned factors that contribute to the characteristics of the smear layer, and the smear layer's influence on the bond performance of adhesive systems should always be studied and highlighted.

1.5. Resin-Dentin Bonding

Following Oskar Hagger's groundbreaking work, Michael Buonocore emerged as a prominent advocate for adhesive technology in dentistry. Hagger, a chemist at DeTrey/Amalgamated Dental Company, introduced Sevriton Cavity Seal in 1949, an acidic adhesive that interacted with the tooth surface on a molecular level. This innovative product earned Hagger the title of the true "Father of Modern Dental Adhesives," as his concept laid the foundation for subsequent generations of dental adhesives. Buonocore further advanced this field with his seminal research in 1955, demonstrating that enamel could be acid-etched to create an ideal surface for resin bonding. His work established enamel etching as a fundamental step in bonding procedures, revolutionizing dental practice and paving the way for the development of various adhesive systems that are now essential in restorative dentistry [30,33,95,96].

Dental adhesives have the following characteristics: they reduce marginal discoloration, minimize microleakage, reinforce the dentin or the enamel, preserve the tooth structure, and may even decrease postoperative sensitivity [97]. Indeed, years after Buonocore's work, significant progress has been made in the area of adhesives in restorative dentistry. The development and evolution of reliable enamel and dentin bonding agents is one such example [9,33,97].

Adhesive systems have progressed from the largely ineffective systems of the 1970s and early 1980s to the relatively successful ER and SE systems of today. The latest players in the adhesive marketplace are the so-called UAs [3,9,33].

This is the "cosmetic revolution" in dentistry, blossomed in large part due to dramatic advances in adhesive technology. In fact, the longevity and predictability of many if not most current restorative procedures are wholly predicated on the dentist's ability to bond various materials to tooth tissues [33]. Recent advances in the development of new bonding systems have resulted in higher bond strengths (BSs). Each adhesive system must be handled with careful attention to the details of application for maximal success [33,98].

1.5.1. Resin Adhesive Application

The field of application of adhesive systems is very large and their contribution to the development of more conservative, more aesthetic and more biocompatible therapies is obvious.

These systems are currently in widespread use and not limited to the following applications:

- Restoration of traumatic and carious lesions of classes I, II, III, IV, V and VI.
- Repair existing restorations (amalgam, composite, crown).
- Bonding fractured fragments of anterior teeth.
- Sealing of cracks.
- Sealing pits and fissures.
- Desensitization of exposed root surfaces.
- Bonding of ceramic restorations (all-ceramic crowns, inlays, onlays, veneers).
- Improved retention of porcelain fused to metal crowns.
- Bonding of molded or prefabricated metal and fiber posts.
- Reinforcing fragile endodontically treated roots internally.
- Bonding of orthodontic brackets.
- Bonding splints in periodontology [99,100].

1.5.2. Mechanism of Adhesion

Adhesion occurs when two different molecules react upon being brought into contact as a result of a force of attraction between them [101]. The material used to cause adhesion is known as an "adhesive" and the substrate to which the adhesive is applied is named "adherent" [102,103].

Adhesion mechanisms that are normally used in dentistry are as follows:

1. Physical adhesion includes:
   a. Van der Waals interactions which is the attraction among opposite charges on dipoles and ions.
   b. Dispersion forces which is the interaction of induced dipoles.

   c. Hydrogen bond, an especially strong bond, can be involved in physical forces [101,104].

2. Chemical adhesion includes:
   a. Covalent bonding that includes sharing electrons between two molecules. It is a strong bond that liberates considerable amounts of energy. A covalent bond is existent in all organic compounds.
   b. Ionic bond that includes a transfer of electrons from an atom to another like the ion exchange adhesion mechanism observed in glass ionomer cements.
   c. Metallic bond is the characteristics of the chemical bond of metals in which mobile electrons are exchanged among atoms in a typically stable crystalline assembly [101,104,105].

3. Mechanical adhesion includes:
   a. A diffusion of a material into another at a microscopic level. For instance, in composite resins the bonding includes the diffusion of resin into the enamel and the dentin substrates and the establishment of RTs [101].

After exploring the various adhesion mechanisms, suitable adhesion results are achieved by following these steps: dissolution of the smear layer from the enamel and dentin substrates; preservation of the collagen matrix; ensuring adequate wetting; effective monomer infiltration; photopolymerization within the tooth structure; and copolymerization with the resin composite matrix [102,106,107].

1.5.3. Factors Influencing Adhesion

A- Wetting

The adhesive, often a viscous fluid, is made of a material or film that joins two substrates and solidifies them [108].

The adherent is the initial support, material or substrate on which the adhesive is applied. The types of adherents are enamel, dentin, metal alloy, and ceramic material [79]. Indeed, the contact of the adhesive with the adherent depends on the wettability of the substrate and its surface free energy [108].

Wettability is the ability of a liquid to come into intimate contact with a solid. It is the phenomenon that controls the spread of a drop of liquid on the surface of a solid, when a drop of liquid is deposited on the surface of a solid; either the liquid spreads (on the so-called "wet" surface), or it forms a drop, making an angle of contact with the surface of the solid [109]. The wettability and the spreading velocity are also reliant on the chemical composition of adhesive agents [110]. As the viscosity of an adhesive increases, it becomes more challenging to achieve proper wetting of a substrate [111]. Wettability studies are generally based on the measurement of contact angles (CAs) as main data, which designates the degree of wetting when a solid and a liquid interact [112,113]. Small CAs lower than 90 ° (< 90 °) resemble to high wettability, while large CAs (> 90 °) correspond to low wettability [109]. The contact angle (CA) is defined as the angle formed by the intersection of the liquid-solid interface. Surface energy is also called surface tension or interface energy [109,112,114]. Surface tension is a force that exists at any interface between two different media (between a solid or a liquid and a gas). The tension between identical media—whether it is two solids, two liquids, or even between a liquid and a solid—is typically referred to as interfacial tension. This force is what enables a drop of water to resist spreading on paper or allows certain insects to walk on water, often associated with the concept of capillarity [109].

When dentin and enamel are demineralized by acid-etching, different changes in the surface energy of substrates could be observed. The surface free energy of enamel is improved, simplifying wettability [115]. Nonetheless, in dentin the opposite will occur, while mineral is removed and collagen fibrils are exposed, surface free energy decreases [116]. To enhance the surface energy of dentin, it is essential to use an appropriate adhesive system that promotes good wettability [117].

Finally, for optimal adhesion, the adhesive must completely "wet" the surface to be bonded [79,108,109]. "Wetting" means that the adhesive flows and covers a surface to maximize the contact surface and the forces of attraction between the adhesive and the bonding surface. Complete wetting occurs at a CA of 0 ° and no wetting occurs at an angle of 180 °. In order, for a liquid adhesive, to effectively wet a surface, the surface tension of the adhesive must be lower than the energy of the surface of the substrate to be bonded, or the energy of the surface of the substrate must be increased [108,109].

Micro-tensile bond strength (μTBS) of composite to dentin cavity floor has been shown to be affected by several factors, including dentinal tubule density, diameter, and sclerosis degree, as well as the presence of sclerotic dentin. Other influential factors encompass cavity preparation design, such as cavity shape and size, as well as the presence of bevels or chamfers. Additionally, the adhesive type and application protocol, the presence of contaminants like saliva or blood, and the method of polymerization can significantly impact μTBS values. Furthermore, factors related to substrate characteristics, such as dentin age, composition, and moisture content, play a crucial role in determining BS outcomes. Additional considerations include the presence of secondary caries, thermal and mechanical stresses, and the use of desensitizing agents or cavity liners [33,118,119].

B- Substrate Variations

The BS of composite resin on dentin near the pulp is generally 30-40% lower than that on superficial dentin [120]. Hence, the remaining dentin thickness plays an important role on the strength of dentin bonding agents [119]. It has been previously shown that the direction of dentin tubules can influence both the intrinsic wetness of the surface and BS. Bonding to parallel-oriented tubules (= occlusal wall) had higher μTBS than bonding to perpendicularly-oriented tubules (= gingival wall) [121]. Furthermore, permanent dentin has higher concentrations of phosphate (P) and Ca compared to primary dentin. Therefore, one might speculate that etching times for deciduous dentinal surfaces are typically shorter than those for permanent teeth. However, BS tends to be lower in primary teeth regardless of the different etching times applied compared to permanent teeth [122].

C- Dentin Humidity

One of the trickiest aspects of adhesive dentistry is maintaining proper moisture control [123,124], and one should consider that the average of oral temperature and relative humidity are approximately 30 °C and 80% correspondingly, with humidity varying from 74% to 94% [125,126]. In this manner, wetness of the dentin surface is an influencing factor that may affect bonding to dentin [127]. Successful adhesion to dentin could be negatively affected by both internal and external humidity.

Internal humidity of dentin came from the outward of dentinal fluid inside dentinal tubules. Therefore, interference with monomer infiltration into dentin and the polymerization of the resin could be observed. Thus, in order to simulate physiological bonding conditions, some authors have proposed conducting *in vitro* studies of bonding agents under hydrostatic pulpal pressure [128,129]. Various factors of external dentin humidity that could affect BS are numerous: blood, saliva, crevicular fluid, air humidity in the oral cavity, ambient air humidity, and water that could be contaminated from the air syringe [130].

In an attempt to resolve the above-mentioned drawback, the use of rubber dam is required in restorative dentistry [131,132]. So, the humidity is reduced to a similar level as that of the ambient air, hence encouraging optimal and stable adhesion to the dentin [133]. It is imperative to state that the use of a rubber dam offers a dry field for improving the visibility, and it enhances visual contrast [134]. Additionally, it is a low-cost material with a high effectiveness [135].

D- Configuration-factor

The configuration-factor (C-factor, ratio between bonded and unbonded areas) is an influencing factor for dentin adhesion [136]. Numerous studies indicated that with an increase in C-factor, the BS decreases [137,138]. A rupture of dentin interface occurs when BS is lower than polymerization stress, and this process depends on the C-factor. Below 1, the interface could be preserved in a flat dentin, for example, with values above 2, failures at the adhesive interface could be more likely to occur. This is because the higher the confinement level, the lower the shrinkage stress that can be relieved by the flow of the free surfaces [139,140].

E- Age of The Patient (Sclerotic Dentin)

Sclerotic dentin is a clinically challenging binding substrate in which dentin has been physiologically and pathologically altered, relatively as the body's natural defense mechanism, or as a result of colonization by the oral microflora. It is also characterized by a partial or complete obliteration of the dentinal tubules by mineral deposits. Dentin becomes transparent and insensitive, while the surface of lesions appears smooth. The thickness of the sclerotic dentin layer is variable [141].

The sclerotic deposits which obliterate the dentinal tubules were always present after the acidic conditioning of the sclerotic dentin, resulting in minimal formation even of zero "tags". In addition, the sclerotic dentin area impregnated with resin was found to be thinner compared to normal dentin [142].

Another morphological alteration of sclerotic dentin is the formation of a hypermineralized layer on the surface. This layer resists etching agents, thereby preventing the formation of the HL, which is essential for the adhesion process [143]. To overcome the diffusion barrier, the use of a rotary instrument can be a solution to remove the hypermineralized layer and thus obtain intertubular retention [144]. However, this method could be detrimental when the lesion is near the pulp.

All in all, adhesion to sclerotic dentin was lower than the normal dentin which ultimately influenced the longevity of restorations [142,143]. A recommendation has been done by Hedge et al., [144] suggesting that the optimal approach to restore such a lesion is by removing a thin layer from the surface of the hypermineralized dentin. This method effectively removes the adherent bacteria layer on the surface as well, facilitating better adhesion of the dentinal substrate.

1.6. Resin Adhesive Systems

1.6.1. Composition of the Adhesive Systems

A dental adhesive system's fundamental parts are as follows:

Etchant, presently H_3PO_4 at a concentration ranging between 30% and 40%. The common H_3PO_4 gels are thickened using silica microparticles, while some incorporate alternative thickeners like xanthan gum. To enhance the application precision and guarantee that all gel is rinsed out, a color dye should be integrated. Glycol is frequently used to increase wettability and lessen viscosity. The etchant is constantly washed from the dental surface [3,96,145].

A hydrophilic solution including resin monomers, organic solvent (alcohol or acetone), water, and stabilizers is used as a primer [9]. The hydrophilic groups enhance the dentin wettability, which is located in a humid setting. Primers have a similar role in dentin adhesives as they do in paints [3]. The primer binds to surfaces and generates a binding layer that prepares the surface for the paint, in this case, the bonding resin [3,9]. Because of its high hydrophilicity and solvent-like properties, HEMA is the popular primer used [33]. Primers are often not washed or cured after being applied to the tooth surface; they are just air-dried [3].

The bonding resin is a low-viscosity solvent-free (hydrophobic) resin that is placed over the primer and then polymerized [9]. The hydrophobic groups engage and copolymerize with the restorative material, increasing the stability and durability of dentin bonding by sealing the bonded interface against NL [3]. The hydrophobic resin enhances both the primer's polymerization rate and the mechanical assets of both the adhesive and the HL [3,146]. Adhesive systems with this independent bonding phase produce better results. Most adhesive resins are made up of hydrophobic dimethacrylates such as Bis-GMA, triethylene glycol dimethacrylate (TEGDMA), and urethane dimethacrylates (UDMA) [3,17].

Additional components were present in the composition of the adhesive systems including initiators [for a self-cure resin system with an initiator such as benzoyl peroxide, the polymerization process can be triggered using a photo-initiator system consisting of the photosensitizer (e.g., camphorquinone) and an activator (e.g., tertiary amine)], fillers (silica particles), and other ingredients (paraben used as antimicrobials, glutaraldehyde (GA) used as desensitizer, fluoride for prevention of secondary caries, and chlorhexidine (CHX) used to inhibit collagen breakdown) [15,33].

All in all, the chemistry of an adhesive system is clarified by the following formula M-R-X, where "M" is a methacrylate group that combines with the resin matrix, "R" is a spacer, and "X" is a functional group for adherence to dental surfaces [107].

1.6.1.1. Acidic Components

In the ER strategy, the etching agent applied is 35-37% H_3PO_4, with a pH fluctuating between 0.5 and 1 (Fig. 6). This pH becomes superior than 1 for the SE strategy using acidic monomers resultant from the esterification of H_3PO_4. This acidic pH prepares both the enamel and the dentin substrates to receive the bonding agents [147].

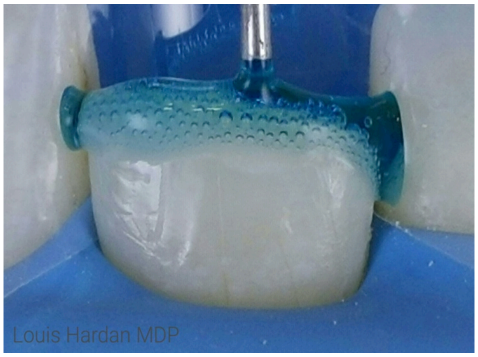


Figure 6: The formation of bubbles resulting from the chemical reaction between the acid and a mineral structure. (Positive sign of a chemical reaction). (Courtesy of Prof Louis Hardan).

On enamel, the etching phase cleans the enamel, creates a complex 3D microtopography at the surface of enamel, rises the enamel surface area accessible for bonding, creates micropores into which the resin mechanically interlocks (Fig. 7) and increases wettability by exposing more reactive surface layer [104,148].

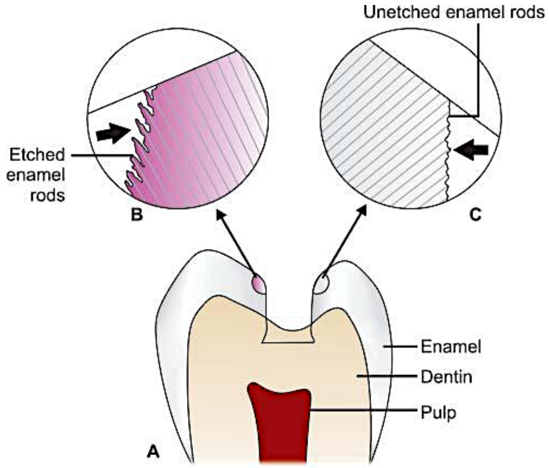
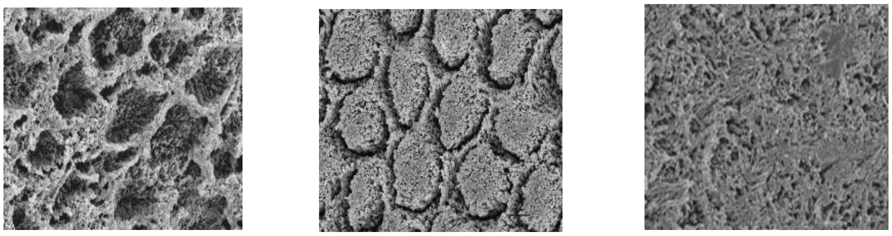


Figure 7: Difference in appearance of etched and unetched enamel rods [148].

Three types of enamel etching patterns may be detected under a microscope [148-150] (Fig. 8):



Type I Type II Type III

Figure 8: Types of etched enamel [79].

- Type I of etched enamel: privileged demineralization of the enamel prism core while keeping the prism periphery intact. The matching tags in this case are cone-shaped.
- Type II of etched enamel: the inter prismatic enamel is removed preferentially, leaving the prism cores intact. The matching enamel tags are cup-shaped.
- Type III of etched enamel: the pattern is less apparent, with portions that match type I and II patterns and others that bore no similarity to enamel prism [148-150].

Various acids have been lately developed for demineralization including nitric acid, citric acid and oxalic acids. These acids produce mild conditioning, hence for ER, the use of H_3PO_4 is recommended [148].

Acid etching with H_3PO_4 essentially creates a microporous layer, 5-50 μm deep, into which resin monomer flows [148,151]. This leads to a long-lasting enamel bond established by micro-mechanical interlocking of the resin and enamel. While H_3PO_4 cleans the enamel surface, it triggers salts precipitation on the etched surface; these salts might be eliminated more advantageously by means of rubbing the acid and rinsing it, delivering an ideal interface for the bonding [151].

Among the features that affect the acid etching on enamel substrate: the acid form (gel or liquid), the acid concentration and time of etched enamel, the acid type, the chemical type of enamel, the type of dentition (primary or permanent), and whether the enamel is demineralized or fluoridated [148,152].

On dentin, the etching stage removes or modifies the smear layer, and demineralizes 5-8 μm of the ITD matrix to create nanoscale porosities in the underlying collagen fibrillar matrix. Numerous acids or/and Ca chelators are used [153].

For acids: in operative dentistry, the most commonly used acid is 37% H_3PO_4 in both liquid and gel forms. Although H_3PO_4 liquid has a lower pH, H_3PO_4 gel has a superior etching impact on dentin than liquid acid. This is due to the fact that gel acids stay on the tooth surface longer than liquid acids, and this contact time has a higher influence on dentin depth than pH. Acids not only eliminate the smear layer, but also open the dentinal tubules, expose the collagen network into which resin monomers infiltrate, and modify the dentin's wetness and permeability [148,154] (Fig. 9).

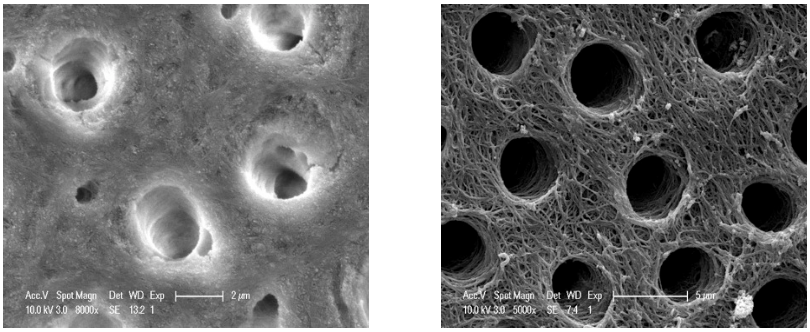


Figure 9: Mineralized dentin (left), demineralized dentin (right). (Courtesy of Prof Umer Daood).

There are many other acids used for conditioning the dentin like maleic acid, nitric acid, oxalic acid, citric acid, and hydrochloric acid [148].

For Ca chelators: these are used to remove and/or alter the smear layer while leaving the surface of dentinal layer undamaged. Ethylenediaminetetraacetic acid (EDTA) is the common chelator used [4,148].

Among the features that affect the acid etching on dentin substrate: the removal of cutting debris, the effective cavity preparation, the partial conditioning, and the formation of micropores [155].

As a result, the etching acid's form and pH are crucial. The degree and intensity of demineralization are induced by these variables. According to a previous research, the primary variables influencing the dentin–conditioner interaction have been determined to be the acid content, osmolality, pH, and viscosity created by the thickening agents [156]. The dentist should clean the tooth surface and get it ready for bonding by using H_3PO_4 (liquid or gel). Compared to liquid acid, gel acid has advantages such as improved control during application and longer retention on the tooth surface [154] (Fig. 10).

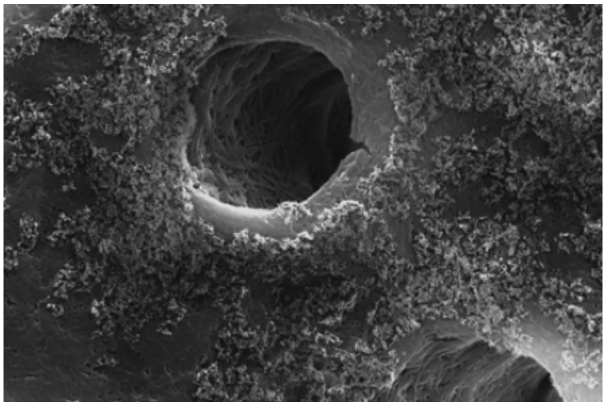


Figure 10: Higher magnification of dentin etched with phosphoric acid gel 37%. Amounts of small debris (silica) are clearly observed [154].

Since the advent of lasers in dentistry in 1960, there has been fast advancement, and the application field of lasers has grown dramatically [157]. The laser interacts with the target tissues through absorption, transmission, scattering, and reflection. Chromophores found in both soft and hard tooth tissues include hemoglobin, melanin, water, and HAp. The choice of laser is determined by tissue characterization since they have an affinity for specific wavelengths [158]. In addition to soft tissue applications, dentists frequently use lasers on dental hard tissues for cavity preparation, treating dentin hypersensitivity, caries removal, and surface conditioning [157]. Erbium lasers are often used for these hard tissue applications because their wavelengths are selectively absorbed by the HAp and water content of enamel and dentin. Another application for lasers is enamel and dentinal conditioning before the bonding process. On one hand, erbium lasers act on dentin by making a visible rough surface, opening dentinal tubules without a smear layer, and producing micro-irregularities caused by selective ablation of ITD [159]. Choosing the correct laser parameters is critical, since it may create changes in dentin collagen, which may have an unfavorable effect on adhesion. On the other hand, treating the enamel surface by means of an erbium laser produces an irregular, uneven surface that permits the adhesive to penetrate. As a result, the production of RTs enhanced the micro-mechanical retention [157]. Some studies have indicated that laser irradiation improves micro-mechanical retention by increasing surface roughness and surface area at the enamel-resin interface [160,161]. Prior investigation discovered that surfaces conditioned with erbium lasers or H_3PO_4 exhibit similar micro-irregularities [162]. Overall, there has been extensive research on the use of lasers in conjunction with or as an alternative to H_3PO_4 etching [158,163-165]. Although the ideal strategy for adhering to enamel and dentin remains unknown, clinicians prefer to employ H_3PO_4.

1.6.1.2. Cross-linking and Functional Monomers

There are two main types of monomers: the functional monomers that correspond to the dentinal primers and the cross-linking monomers that correspond to the adhesive resin [48] (Fig. 11 and Fig. 12).

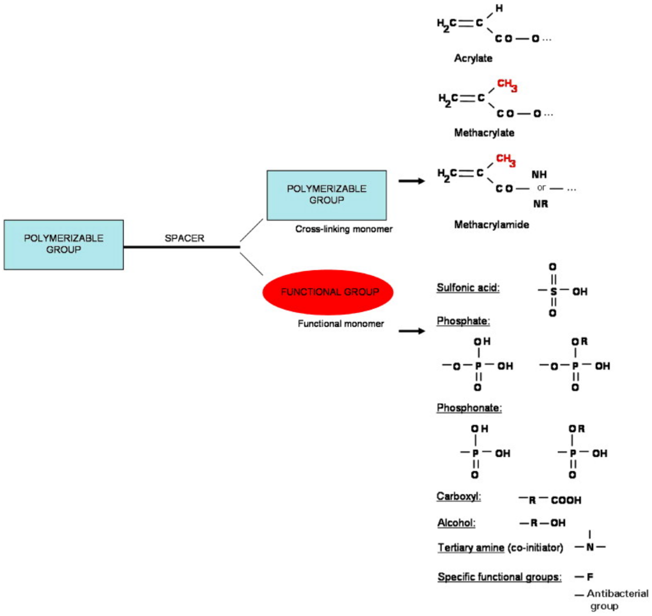


Figure 11: The typical configuration of cross-linking and functional monomers, with adhesive monomers commonly falling under the category of methacrylates [48].

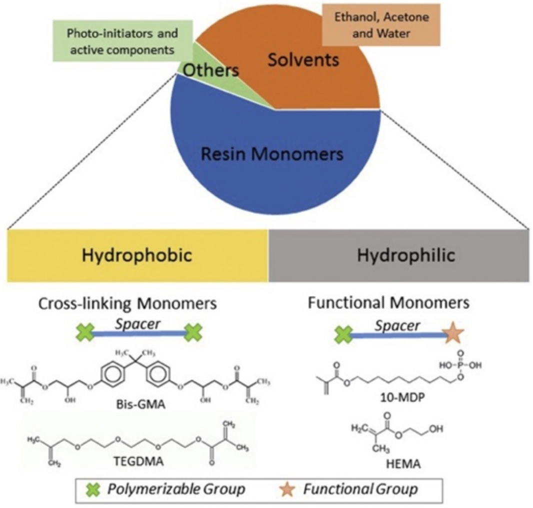


Figure 12: Composition of dental adhesives and examples of cross-linking and functional monomers used in contemporary adhesive systems [45].

A- Cross-linking monomers

All cross-linking monomers are hydrophobic, designed to stabilize the HL and interact with the overlying restoration material, as well as functional monomers. Acrylic systems are tasteless, colorless, and present an easy radical for polymerization reaction [166]. Different kinds of polymerizable groups, and hence resin systems exist:

- Acrylates (-CH_2=CHCOO-): compounds characterized by double bonds that exhibit higher reactivity than methacrylates, causing problems in shelf-life and biocompatibility, and containing an ester group [48].
- Methacrylates (-CH_2-C(CH_3)=CH_2): compounds containing acrylates (double bonds), methyl group (CH_3), and ester group (Example: UDMA, Ethylene glycol dimethylacrylate, TEGDMA, or Bis-GMA) [167].

Both acrylates and methacrylates are susceptible to water degradation because of the presence of an ester group (R_1–CO–OR_2) in their formulations [69].

- Methacrylamides: compounds composed of a methacrylate group and an amide group (R_1–CO–NH–R_2) instead of an ester group [48].

Methacrylamides are more resistant to water degradation compared to methacrylates, primarily due to the presence of the amide group [49].

B- Spacer

The spacer in dental materials plays a crucial role in determining various properties. It consists of an alkyl chain whose size corresponds to that of the monomers. Smaller monomers tend to be more volatile, while larger ones are less so. Additionally, the polarity of the spacer influences the solubility of the monomer in water. The presence of voluminous groups within the spacer can modify the reactivity of polymerizable or functional groups. Increasing the distance between methacrylate groups, for example, can enhance monomer reactivity. However, voluminous groups may also contribute to incomplete polymerization. Therefore, careful consideration of spacer characteristics is essential for optimizing the performance of dental materials including adhesive systems [48,166,167].

C- Functional monomers

Functional monomers serve several purposes in dental adhesives. Firstly, they improve wetting owing to their hydrophilic nature. Additionally, they function as adhesion-promoting agents, effectively enhancing BS to demineralized dentin [48]. In ER systems, functional monomers are tailored to match the dentinal primer, mainly aimed at enhancing the wettability of collapsed collagen. On the other hand, in SE systems, functional monomers, often termed SE primers, are acidic in nature. These acids demineralize dental surfaces and facilitate the smooth infiltration of the adhesive resin. SE systems are broadly categorized into two major families: those containing phosphorus groups (like 10-MDP, dipentaerythritol pentaacrylate phosphate (PENTA), and HEMA-P) and those containing carboxylic acids (such as 4-MET and 4-methacryloxyethyl trimellitate anhydride (4-META)) [48,86]. The acidity of these functional groups determines the etching aggressiveness, with sulfonic acid being the most aggressive, followed by phosphonic, phosphoric, carboxylic acid, and alcohol [168]. However, it is important to note that carboxyl and P groups are susceptible to water degradation [48]. This classification provides valuable insights into the diverse roles and properties of functional monomers in dental adhesive systems, aiding in the selection and optimization of adhesive formulations for clinical applications.

There are a variety of functional monomers in dental adhesive systems:

1. Pentamethacryloyloxyethylcyclohexaphosphazene monofluoride (Dentsply company): monomer with 5 methacrylate-alkyl chains and a fluoride as a functional group [48].
2. N-phenylglycine glycidyl methacrylate and N-tolylglycine glycidyl methacrylate: monomer with tertiary aromatic amine group [48].
3. Dimethylaminoethyl methacrylate: monomer with tertiary amine group [169].
4. Methacryloyloxydodecylpyridinium bromide (MDPB): monomer patented by Kuarary company with antibacterial agent and a methacrylate group. This molecule is hydrophobic when compared to other hydrophilic functional monomers [170].
5. N-methacryloyl-5-aminosalicylic acid: monomer patented by Kuraray company and presented in adhesive systems with a salicyl group (desensitizing outcome) [48].
6. MA: monomer rarely used in adhesives due to its risk of allergic reactions [48].
7. Methyl methacrylate: old monomer rarely used in adhesive formulation like MA monomer [48].
8. 4-META: monomer with hydrophobic aromatic group, functional hydrophilic carboxyl groups, and demineralization assets. The adhesion capacity of 4-META has been well defined in literature and depends on the interaction between the substrate and the carboxyl groups, that substitutes P ions with Ca ions in HAp [17,33]. The resulting 4-META-Ca presents a low chemical stability [17,33,48]. This procedure is followed by the superficial dissolution of HAp due to the attack of hydronium ions resulting from the water protonation reaction with 4-META. After extracting Ca, P, and hydroxyl ions from the apatite surface, the solution turns out to be acidic, leading to the formation of dicalcium phosphate dihydrate precipitate [48]. Previous analysis showed that 4-META-Ca solubilized quicker than 10-MDP-Ca, which leads to decreased molecular stability [34]. This discovery supports the "Adhesion-Decalcification concept" (AD concept), which stipulates that the lower the solubility of Ca salt in the acidic molecule, the stronger and more stable the adhesion with the HAp substrate [17,34].
9. 4-MET: 4-META+water = 4-MET: two carboxylic groups attached to aromatic groups with methacrylate group as polymerizable group [48].
10. 4-acryloyloxyethyl trimellitate anhydride: patented by Shofu company (Kyoto, Japan), two carboxylic groups linked to aromatic groups similar to 4-MET except the presence of acrylate group instead of methacrylate group [48].
11. 11-methacryloyloxy-1,1′-undecanedicarboxylic acid: monomer patented by Tokuyama company, information regarding this monomer in the literature is quite sparse, 10 carbon atoms comparable to 10-MDP, with a hydrophobic spacer [48].
12. Phenyl-P: monomer with monohydrogenphosphate group [48].
13. HEMA-P: monomer with methacrylated H_3PO_4–HEMA esters group [48].
14. HEMA: monomer with low molecular weight (small size) and often utilized in several adhesive systems [171,172]. This hydrophilic monomer is frequently included in the formulation of adhesives because of its solvent like nature. It consists of a mixture of hydrophilic and hydrophobic polymers. Hydrophilic monomers are usually transported in a water-soluble solvent (acetone, ethanol, water) to encourage an adequate flow and a penetration in the hydrophilic dentin (to influence the strength of the resulting bonding), while hydrophobic monomers promote the chemical bond with resin layer [17,172,173]. This increases stability and helps in preserving hydrophobic and hydrophilic monomers in the mixture by reducing phase separation in the presence of water [174]. Adhesives lacking HEMA

monomer might have issues related to phase separation [175]. Although HEMA has numerous positive attributes, it also has drawbacks. HEMA, both in the unpolymerized and polymerized state, certainly absorbs water from the underlying dentin through osmosis and from the outer oral environment [174]. Once polymerized, it can swell, discolor and contribute to the hydrolysis of the adhesive interface (water blisters become entrapped in the adhesive layer) [48]. Finally, HEMA has been correlated with biocompatibility concerns, as it has been assigned rather substantial allergic potential, and even contributes to probable genotoxicity [176]. All in all, the most notable disadvantages of HEMA are as follow: low polymerization capacity, low mechanical strength, high water sorption, and critical biocompatibility in terms of allergic reaction. When the HEMA concentration declines beneath a critical level, phase separation will happen between the adhesive monomers and water, and a strong air-stream is needed to eliminate the water-containing droplets from the adhesives [177]. High amounts of HEMA might lessen the mechanical characteristics of the resulting polymer [178]. This will result in flexible polymers with inferior qualities. PolyHEMA is basically a flexible porous polymer ('gel'). As such, high concentrations of HEMA in an adhesive may have deteriorating effects on the mechanical properties of the resulting polymer. HEMA also reduces the vapor pressure of water, and probably also of alcohol [48,178]. High amounts may therefore hinder good solvent evaporation from adhesive solutions. Like all methacrylates, HEMA is vulnerable to hydrolysis, especially at basic pH, but also at acidic pH [178]. Uncured HEMA also has the ability to lower the vapor pressure of water and can make evaporation more difficult through the air-drying stage [48]. The ideal HEMA concentration to obtain higher BSs in primer/adhesive is between 30-40% [179], and 5-25 wt% in single-bottle adhesives [17], although the use of HEMA remains controversial. Some studies have shown no significant differences between the clinical performances of HEMA vs HEMA-free based adhesive systems [180,181]. While other findings revealed clinically significant difference between HEMA and HEMA-free adhesive systems [182,183]. In current adhesives, manufacturers strive to significantly lower the HEMA contents or even substitute HEMA with other monomers such as methacrylamide monomer [33]. To conclude, it may be stated that in very favorable conditions, the presence or absence of HEMA monomer might not influence the clinical behavior of adhesive systems. However, it is critical to have a thorough understanding of the advantages and limitations of HEMA to make informed decisions and select the best adhesive system based on the clinical situation.

15. 10-MDP: this monomer was patented by Kuraray (today Kuraray Noritake, Tokyo, Japan) and introduced in 1981 (following 'CSE' Technical Information from Kuraray Noritake). 10-MDP is used in many UAs including All-Bond Universal (Bisco, Inc., Schaumburg, Illinois, USA), Adhese Universal (Ivoclar Vivadent, Schaan, Liechtenstein), G-Premio Bond (GC, Tokyo, Japan), Futurabond U (Voco, Cuxhaven, Germany), Clearfil Universal Bond (Kuraray Noritake, Tokyo, Japan) and Scotchbond Universal (3M ESPE, St. Paul, MN, USA) [184]. In addition, 10-MDP is a major constituent of SE adhesive systems, with dihydrogenphosphate group qualified to bond the tooth substrate, long carbonyl chains that render this monomer hydrophobic, and a methacrylate group on the other side capable of bonding to methacrylate-based materials [185]. 10-MDP outperformed the other functional monomers studied in terms of chemical bonding potential. This monomer was documented to self-assemble into "nano-layering", a process focused on the deposition of 10-MDP-Ca salts with low solubility in order to obtain an optimum hybridization [186,187]. Each nano-layering involves two sublayers of parallel 10-MDP monomers placed in reverse direction. This monomer's methacrylate group is pointed inwards, allowing mutual co-polymerization among two contrasting monomers. Its functional P group is oriented outwards, collecting Ca released from dentin structure [184,185,188] (Fig. 13).

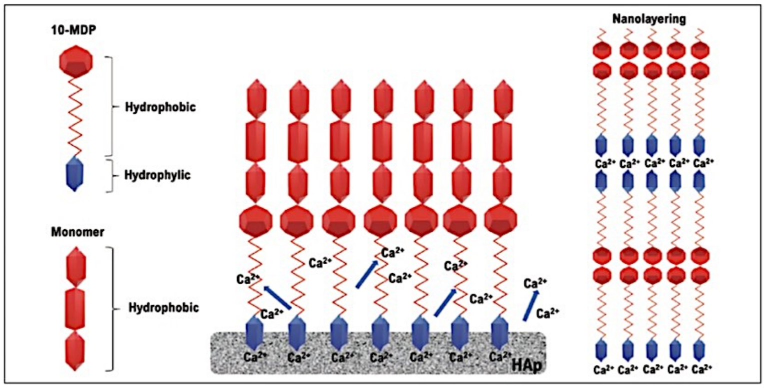


Figure 13: Nano-layering of 10-methacryloyloxydecyl dihydrogen phosphate-Calcium salt [146].

The extended carbon-spacer group successfully reduces steric hindrance between the methacrylate and H_3PO_4 ester group while simultaneously providing hydrophobicity to decrease water sorption and enables parallel self-alignment of neighboring 10-MDP molecules during nano-layering [172]. Furthermore, the noteworthy etching influence makes 10-MDP distinctive among functional monomers, causing micro-retention and therefore permitting micro-mechanical interlocking, but also considerably releasing Ca from dentin as the driving force of 10-MDP nano-layering. Additional study is needed to determine the impact of nano-layering on adhesive interface stability [184]. Ca salts formed from the acidic molecule 10-MDP have higher chemical stability than 4-META. This could be explained by the fact that superficial HAp is dissolved by means of hydronium ions in the MDP and resulting in a larger concentration of Ca ions than 4-META. The nucleation and development of 10-MDP-Ca crystals on the HAp surface result in a 4 nm layered structure made up of two MDP molecules. This nano-sized molecular alignment is not seen in 4-META when bonding to dentin occurs. This bonding is more solid and durable than the one created by 4-META and GPDM. However, the chemical interaction of the functional groups with the HAp crystals in enamel is not as effective as in dentin, most likely due to the HAp crystal structure and/or size, highlighting the need for enamel acid etching prior to adhesive procedures using SE or UAs (SEE method) [17].

Inappropriate storage of some adhesives based on 10-MDP for a long period of time leads to the degradation of the MDP monomer [189]. The degradation proceeds via the hydrolysis of the functional group, producing compounds such as MA and 10-hydroxydecyl dihydrogen phosphate, which may eventually weaken the HL quality, due to poor monomer transport, penetration, and curing [17].

Variability in the bonding efficacy of several commercial 10-MDP-based adhesives was noticed [190,191]. The most logical explanation is a difference in chemical composition. BS was displayed to be dependent on the concentration of 10-MDP [36]. But in the presence of HEMA, even in a low concentration, the mechanical integrity of the nano-layers is reduced. For that reason, an HEMA-free adhesive system (like Prime&Bond Universal (PBU), Dentsply DeTrey GmbH, Konstanz, Germany, used in this thesis) hypothetically has a stronger ionic binding potential compared to the HEMA-rich system.

MDP is durable in an oral environment due to its hydrolysis stability and more favorable for chemical bonding than 4-MET and Phenyl-P [17, 192]. In addition, a previous research demonstrated that zinc can be a competitor to MDP-Ca salts, not only HEMA or other components [193].

In 2017, Yaguchi et al., [194] suggested that UAs with less concentration of 10-MDP generate weak adhesion. Similarly, Fujita et al., [195] in 2018 suggested that the rate of 10-MDP-Ca salt formed by the demineralization of enamel and dentin relies on the components that are found in the commercial adhesive rather than on the MDP and water concentrations.

In 2018, Yoshihara et al., [196] proposed that higher bonding effectiveness of 10-MDP must not only be attributed to their more intense chemical bonding to tooth substrate, but to its higher etching potential as well (by measuring the HAp-dissolving capacity). Other functional monomers (GPDM, Phenyl-P, 4-META) lacked this combination.

In 2018, Putzeys et al., [197] suggested that the minimal toxic concentration of the functional monomer 10-MDP can stimulate an inflammatory response and suppress an odontoblastic differentiation.

In 2019, Zhou et al., [192] proved that HEMA-free adhesives are preferred since HEMA prevents the MDP-collagen protection.

In 2021, Fehrenbach et al., [198] showed that adhesives including 10-MDP presented higher bonding capacity than materials formulated with other acidic ingredients, although this outcome was dependent on the type of mechanical testing, the nature of the substrate, the acidic content of the adhesive, and the application category of the adhesive.

In 2022, Jin et al., [199] demonstrated that adhesives based on 10-MDP preserve the collagen inside the HL by concurrently enhancing collagen's resistance to exogenous enzymes and hindering matrix metalloproteinases (MMPs) activity, both of which provide the durability of resin-dentin bonding.

In 2023, de Oliveira et al., [200] demonstrated that the combination of HEMA and 10-MDP monomers in self-etching adhesives had no effect on the clinical performance of restorations in terms of retention, postoperative sensitivity, and secondary caries incidence. However, this combination favorably affected the marginal adaption and marginal staining during the two-year follow-up.

16. GPDM: in 1949, Oskar Hagger invented the first adhesive technique by combining GPDM in a liquid cavity sealer with a chemically cured resin-based restorative substance (Sevriton®) [201]. GPDM is a monomer with two methacrylate groups linked by a short carbon spacer to one P acidic functional group. Due to the presence of two polymerizable methacrylate groups, GPDM can promote better polymer formation than 4-META, 10-MDP, and HEMA [17]. The hydrophilicity of GPDM aids in adhesive infiltration into the demineralized dentin due to having similar characteristics to HEMA monomer [13]. GPDM also enhances the interaction between the bonding agents and HAp, comparable in function to 4-META which forms an unstable GPDM-Ca salt. GPDM behaves in a decalcification route, but unlike 10-MDP, it does not expose collagen, but promotes the creation of a thick HL with exposed collagen. Though, the variances in chemical bonding do not eliminate the actual bonding effectiveness of adhesive systems comprising GPDM [13,17]. The interaction between GPDM and the co-monomers should be further assessed to gain a better understanding of the positive outcomes with regards to bonding durability of adhesive systems containing this monomer [17,33].
17. PENTA-P: this monomer is characterized by P ester monomers containing carbon=carbon double bonds and a P group [$-OP(=O)(OH)_2$]. When compared to 10-MDP functional monomer, the chain of PENTA is shorter. PENTA has five vinyl groups compared to one in 10-MDP monomer, and these four additional vinyl groups make PENTA more resilient to hydrolytic degradation [51,202,203]. Thus,

when hydrolysis occurs and eliminates one vinyl group from the main structure of the monomer, four vinyl groups will still be present for the conservation of the P group. Accordingly, copolymerization to other monomers and adhesion to tooth structure happen at the same time [189,202]. This finding could be explained by a previous study which demonstrated that PENTA incorporated into the formulation of the adhesive Prime&Bond Elect (Dentsply Caulk, Milford, DE, USA) had more stability than 10-MDP because the BS is maintained even at the end of their shelf-life. This is explained by the sustained connection between these four vinyl groups and the P group [202,204] (Fig. 14).

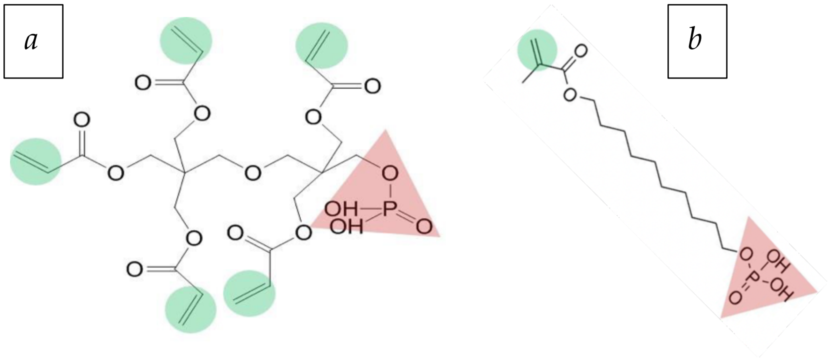


Figure 14: (a) Dipentaerythritol pentaacrylate phosphate has a more reliable bond than (b) 10-methacryloyloxydecyl dihydrogen phosphate-based adhesives. Reactive double bonds (circles) and acidic moieties (triangles) are marked [204].

Both MDP and PENTA monomers are acidic, so, they react with the dental surface by adhering to Ca ions. Thus, these ions were integrated into HL by forming Ca-P complexes. PENTA monomer, unlike 10-MDP, is unable to show a nano-layer (like MDP-Ca salts) due to its massive structure, however, with five double bonds, and a hydrophilic core (unlike MDP: hydrophobic), this molecule is capable of improving the wetting process [205,206].

A difference in the interfacial interaction of each functional monomer has been designated in the AD concept that displayed the way molecules interact with HAp-based tissues [33]. This model displays that, primarily, all acids chemically bond to Ca of HAp (Phase 1). This primary bonding phase drives together with a release of hydroxide and P ions from HAp into the solution to achieve an electron neutrality. The stability of the correspondingly generated monomer-Ca salt determines whether the monomer will stay bonded (Phase 2, “adhesion route”) or de-bond coupled with an abundant decalcification (Phase 2, “decalcification route”) [33,207]. As an example, since 10-MDP_Ca follows the adhesion route while GPDM_Ca essentially follows the decalcification route, the 10-MDP_Ca salt is more stable than the GPDM_Ca salt [207].

Knowing that there is a large number of bonding agents in the dental market, it is challenging to choose the best version. Additionally, a number of these adhesives are introduced as modifications of previous iterations. Therefore, it is crucial to emphasize the features of each component inside the adhesive of choice for better performance. Moreover, the incorporation of various co-monomers (cross-linkers or adhesion promoters), catalysts, and solvents strongly altered the adhesive film properties, which affected the BS of the adhesive system [208].

1.6.1.3. Solvents

The wetting ability of adhesives is amplified by the addition of different solvents and hydrophilic monomers [26,171]. The former eliminates the water, which is present between the collagen fibers, and dissolves the amphiphilic resin which increases the surface tension. The main solvents used in adhesive systems are acetone, ethanol, and water, each with a different evaporation time [17].

It is important to recall that the air-drying method is more intricate and reliant on pressure, position, angle, distance, and time [209]. Collagen fibrils collapse as a result of this technique, which also reduces monomer penetration and produces weaker BSs. It is advisable to investigate a different, more regulated approach. One of these methods is the blot-drying method, which quickly eliminates extra water by using a foam pellet (tissue or a sponge) to ensure that adhesives penetrate well [22]. The adhesive should ideally be allowed to air-dry on the dental surface in order to remove any leftover solvent, as this could disrupt the polymerization of the resin monomers and leave unwanted voids in the adhesive interface that could serve as defect initiator sites and weaken the BS [210].

A fundamental component of the bonding ability of modern adhesives is solvent evaporation [211]. Various factors need to be considered in order to effectively carry out this clinical step. In this regard, the clinician must take into account that the evaporation capacity varies throughout solvents, which is caused by the vapor pressure (mmHg) [17,212]. The pressure value at which a liquid transforms into a gas is defined by this pressure [213]. The higher the vapor pressure, the more volatile the solvent is, that is to say, it evaporates more easily [49]. The capacity of solvents to attach to hydrogen is another crucial feature; this property permits collagen to expand again upon dehydration, hence enhancing resin dispersion and self-bonding [17] (Table 1).

Solvent	**Dipole moment**	**Dielectric constant**	**Boiling point**	**Vapor pressure (mmHg 25 °C)**	**Ability to form hydrogen bonds**
Water	1.85	80	100	23.8	High
Ethanol	1.69	24.3	78.5	54.1	Medium
Acetone	2.88	20.7	56.2	200	Low
Tert-Butanol	1.7	12.5	82.4	46	Medium

Table 1: Properties of solvents most used in dental adhesives [17].

Polar solvents play a crucial role in dental adhesive systems. They have the ability to form hydrogen bonds with their solutes, facilitating effective bonding.

Dipole moment is a measure of the separation of positive and negative electrical charges within a molecule. It is an indication of the degree of polarity of a molecule, with higher dipole moments demonstrating greater polarity. In summary, it measures how much a molecule's electrons are shared unequally between atoms, resulting in a partial positive charge on one end and a partial negative charge on the other. In the context of solvents, those with high dipole moments have strong polar properties, which make them effective at dissolving polar substances and enhancing interactions with other polar molecules, such as water [64]. Additionally, solvents with high dipole moments and excellent evaporation capacities exhibit good water-removing capabilities, which are essential for optimal adhesive performance. The hydrogen-bonding capacity of a solvent is particularly significant in re-expanding the shrunken demineralized collagen network after dehydration. Solvents with a higher affinity for forming hydrogen bonds can disrupt stabilizing hydrogen bonds and other forces that maintain collagen in a shrunken state, thereby facilitating adhesive interactions. [17,48].

The dielectric constant is the measure of a material's capacity to store electrical energy in an electric field. It is signified by the symbol ε (epsilon) and is a quantification of the degree to which a material can polarize in reaction to an external electric field. For solvents, the dielectric constant specifies the solvent's ability to reduce the strength of electrostatic forces between charged particles. Solvents with higher dielectric constants have a greater ability to stabilize charges and dissolve ionic or polar substances. In regard to the adhesive performance, solvents with higher dielectric constants can be beneficial because they are capable of effectively dissolving and removing water from the substrate, expediting the interaction between the adhesive and the substrate surface. Additionally, they aid in stabilizing the charged species within the adhesive, promoting better bonding and wetting [17].

The boiling point of a solvent is defined as the temperature at which the vapor pressure of the liquid is equal to the atmospheric pressure, leading to the transformation of a liquid into a gas. It is a crucial characteristic that determines the volatility and evaporation speed of the solvent [17,48].

Acetone is an organic solvent, has a high vapor pressure of 200 mmHg, but lacks an H-Bonding capacity, evaporates quickly (Evaporation Temperature 56.2 °C), and requires the shortest drying time in the mouth [17,26,209,214]. Acetone-based systems require and tolerate higher humidity levels without any loss of adhesion. Other systems, especially those based on ethanol, require a drier surface [26]. In acetone-based systems, the evaporation point of the water is lowered, while that of acetone is raised when acetone and water come into contact in the dentin. This is known as the azeotropic phenomenon, which is defined as a mixture of two liquids that are distilled at a constant temperature and produce a set composition vapor at a certain pressure [215]. As a result, acetone and water are evaporated, and the resin is able to pass through.

For this reason, acetone-based adhesives should not be brushed during their application in order to avoid their rapid evaporation before the infiltration of the resin monomers into the demineralized dentin [48,216]. It is important to note that achieving a moist surface does not imply tolerance to contaminating agents such as blood, gingival fluid, or saliva [17,48].

Acetone allows a mixture of polar and nonpolar chemicals due to its dipole moment and dielectric constant, which aids single-bottle adhesives that contain hydrophobic and hydrophilic monomers

[17,48,217,218]. Yet, due to its higher vapor pressure compared to ethanol, it is more volatile, necessitating higher solvent concentrations that lower monomer concentration and typically require the application of two or more bonding layers to achieve the optimum BS [216]. In fact, reports have shown that acetone-containing adhesives have an inferior BS than ethanol-based solutions [215,219,220]. Additionally, acetone's higher volatilization compared to other solvents is likely to shorten its shelf-life and prevent certain manufacturers from using it [17].

Ethanol is a polar solvent, has a vapor pressure of 54.1 mmHg, average H-Bonding capacity, evaporates more slowly (Evaporation Temperature 78.3 °C) than acetone, and requires a moderate drying time [17,48,221,222]. With suitable materials like water, ethanol produces hydrogen bonds [222]. Even though this solvent has a higher vapor pressure than water, it cannot be completely eliminated from the dental adhesive in a clinically feasible amount of time [221]. A prior investigation revealed that ethanol was still present in the adhesive for 60 s after volatilization [223].

Dental adhesives' sorption, solubility, and curing rates can all be hampered by excessive ethanol [17,223]. According to Ye et al., [224] ethanol concentrations of 20% or below are optimal for adhesive systems since they have a lower resin viscosity and enhance molecular mobility and polymer conversion. Higher concentrations may impair the adhesive's mechanical qualities and encourage the phase separation of hydrophobic and hydrophilic constituents [225].

The dentinal collagen matrix could expand and become more rigid when ethanol is added, which makes it easier for monomers to penetrate the demineralized dentin's collagen network. Nonetheless, as ethanol's hydroxyl group esterifies carboxylic groups, it may interfere with the capacity of the acidified chains to etch the tooth surface when paired with monomers that have carboxyl groups such as 10-MDP. Therefore, ethanol is inappropriate for monomers with carboxylic acid moieties [17,48]. Furthermore, residual excess ethanol from air-drying may enhance the adhesive's water sorption and solubility, promoting hydrolytic breakdown and raising the risk of cytotoxicity for human dental pulp cells [225,226].

The single-bottle adhesives' hydrophobic and hydrophilic monomers may not separate as a result of the presence of ethanol. Also, the aqueous ethanol solution creates an azeotrope, which facilitates vaporization of the remaining water within the demineralized dentin substrate [29,227]. However, it is impossible to completely remove both bound and unbound water from the demineralized dentin [228], since ethanol vaporizes slower than acetone [29,229].

Water is strongly polar, has a vapor pressure of 23.8 mmHg, high H-Bonding capacity [10], but because of the low vapor pressure and high boiling temperature (100 °C) [230], water evaporates very slowly and requires the longest drying time [48]. Agreeing to Pashley et al., [10] water has a strong capacity to break hydrogen bonds between collagen fibrils, allowing for further resin infiltration and re-expansion. This is essential for the creation of a HL in ER adhesive systems. As was previously mentioned, this solvent's capacity to ionize the acidic monomers found in SE adhesives—which are in charge of the chemical adhesion of these systems—is another crucial feature [231]. However, due to water's low vapor pressure, it is difficult to completely remove this solvent from the adhesive layer. As a result, to facilitate the evaporation of such a solvent, it is advised to combine it with additional solvents (ethanol and acetone), resulting in an azeotropic mixture [232]. This leads to superior vaporization, which will increase the adhesive's degree of conversion and create a higher-quality of HL that will strengthen the bond [17].

Achieving the optimal moist state is not always simple, particularly when dealing with massive tooth cavities and the intraradicular space. As a result, new adhesive compositions were created to decrease the sensitivity of modern adhesives to moisture. Certain materials even permit dentin hybridization to occur properly, independent of the substrate's moisture content. All things considered, these adhesives have solvents other than water, ethanol, and acetone (such as tertiary butanol) [233].

Tert-butanol, also known as 2-methyl-2-propanol, has a vapor pressure of nearly 26 mmHg that is close to the vapor pressure of water (46 mmHg) [17]. Compared to other alcohols, tert-butanol has a molecular chain with fewer hydrogen atoms and a superior molecular weight [234]. Contrary to ethanol-based systems, the molecular structure, which consists of four carbons and one alcohol group surrounded by three methyl groups, offers better stability and compatibility with both water and polymerizable resins [17,235]. Furthermore, due to tert-butanol's higher boiling point compared to acetone and ethanol, the dentin collagen matrix is prone to less shrinkage, the evaporation is slower, and the HL in dry or wet dentin is more resistant [17]. Although butanol-based adhesives are indicated for both "dry" and "wet-bonding" approaches, prior research indicates that BS is higher in wet dentin than in dry dentin [236]. Dentsply company added tert-butanol (Tertiary butanol) to a two-step ER (ER II) adhesive (Prime&Bond Xp (Dentsply Sirona, York, PA, USA)) because of this solvent's similar vapor pressure to ethanol, which leads to better stability to the chemical reaction with the monomers [2,17].

Later on, Prime&Bond Universal (Dentsply DeTrey GmbH, Konstanz, Germany) was introduced and launched at IDS 2017. In this thesis, this adhesive, which contains a water solvent of 5-24.5% with a new co-solvent "isopropanol" (10-24.5%), was used [237]. Isopropanol has a pleasant odor, a boiling point of 82.3 °C (close to that of ethanol (78.5 °C)) [173], soluble in water at 25 °C [238], and a vapor pressure of 45.4 mm Hg. The polarity of isopropanol (0.546) is lower than that of alcohol and ethanol (0.654) [239]. The viscosity of isopropanol (2.4 mPa*s at 20 °C) is more than 400-fold lower than that of water (1000 Pa*s at 20 °C) and twice as high as that of ethanol. This may lead to diverse solubility, wetting, and evaporation properties when combined with water in more complex adhesive mixtures [240].

The following figure presents a solvent overview of common systems used in dental adhesives including the respective pros and cons [204] (Fig. 15).

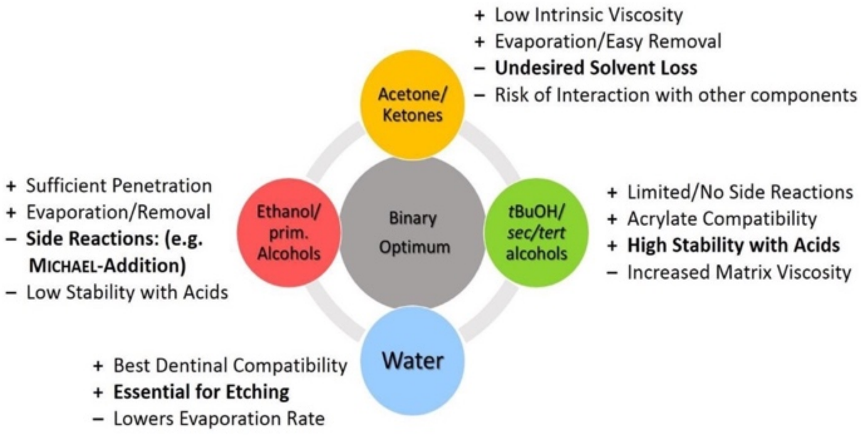


Figure 15: Solvent overview of common systems used in dental adhesives including the respective pros and cons [204].

In essence, solvents are chemicals that have the capacity to disperse one or more substances. They play a crucial part in removing moisture from the dental substrate during the evaporation procedure and are in charge of enhancing its infiltration throughout the demineralized matrix [241]. Accordingly, considering all the findings discussed, the solvent composition of adhesives and the substrate's moisture content are critical factors that affect the durability of adhesive interfaces over time, as well as the BS and bonding stability of resin-based restorations [2,7,9,241]. Adhesives based on water or ethanol are an excellent choice for bonding agents, yet their BS may quickly deteriorate. Adhesives based on acetone might work better in overly dry environments, but not on excessively moist substrates [17,33,233]. Tert-butanol-containing adhesives might be vulnerable to dry conditions when dentin hybridization is taking place [233].

1.6.1.4. Other components

Some manufacturers include filler particles in their adhesive formulations to enhance the mechanical features of an adhesive layer (for example, Tetric N Bond Total Etch (Ivoclar Vivadent, Schaan, Liechtenstein), and Gluma 2Bond, (Kulzer GmbH, Hanau, Germany)). Others incorporate CHX into their adhesive solutions to improve bond stability by reducing adhesive bond deterioration (for example, Peak Universal Bond (Ultradent Products, Inc., South Jordan, Utah, USA) and Futurabond U (VOCO GmbH, Cuxhaven, Germany)). Another chemical added by manufacturers to dental adhesives is GA, which helps in minimizing post-operative sensitivity and maintain the collagen fibers in the HL, improving durability (for example, iBond Total Etch (Heraeus Kulzer GmbH, Hanau, Germany)). To avoid secondary caries beneath restorations, companies use antibacterial agents in the adhesive formulation [33]. An example of an antimicrobial component incorporated in some adhesive agents is the Clearfil Protect Bond (Kuraray, Tokyo, Japan), which is MDPB-based. Cetylpyridinium chloride is also an extremely efficient broad-spectrum anti-bacterial agent. A further example is the use of fluoride inside FL-Bond II (Shofu, Kyoto, Japan) and Futurabond NR (VOCO GmbH, Cuxhaven, Germany). In addition, the use of polymerizing agents (for example, Camphorquinone (CQ)) is necessary to initiate the polymerization of dental adhesives. Certain producers incorporate dyes into their adhesives to facilitate uniform mixing of the ingredients and serve as an indicator throughout the process, with the resulting bond becoming colorless after curing (Universal Bond by Tokuyama company (Tokuyama Dental, Tokyo, Japan)). In general, the influence of these compounds on the performance of adhesive agents is still uncertain and should be considered in future studies [15,33].

Referencing a critical element, such as the use of fillers, is essential for comprehending their impact on the properties of the adhesive agent [242]. One causal aspect for debonding of the dental restoration might rise from the low mechanical properties of the adhesive layer that bonds the dental substrate with the resin composite. Actually, among the substrates of this bonded area, the adhesive layer has the lowest modulus of elasticity [243]. When subjected to masticatory forces, the adhesive layer experiences higher level of stress among the constituents. In general, stress that surpasses the intrinsic strength of an adhesive layer causes cracks, defects, or failure in the resin-dentinal bond [242,244].

Usually, adhesive agents do not include filler particles in their formulations [245]. Though, from a theoretical viewpoint and in line with composite resin, adding fillers increases the mechanical assets of an adhesive layer [48]. This idea was known as the elastic cavity wall concept [242]. Previously, manufacturers incorporated variable quantities of glass filler particles (1-5 μm in diameter) in the hydrophobic bonding bottle of ER III adhesive systems [48,242,246]. These filled adhesives were loaded up to 40-50 wt%, such as OBFL (Kerr Co, Orange, CA, USA) and PermaQuick (Ultradent, South Jordan, UT, USA) adhesives [247].

Due to the fact that these densely filled adhesives performed exceptionally well in previous studies [248,249], the same method was applied to ER II adhesive systems and SE adhesive systems [250].

Hydrophobic resins are paired with priming and/or acidic monomers in simplified adhesive systems, preventing the inclusion of significantly large amounts of filler. For example, ER II adhesive systems comprise approximately 8.5-15 wt% of fillers (OptiBond Solo (Kerr Co, Orange, CA, USA); One-Step Plus (Bisco, Inc., Schaumburg, Illinois, USA)) [251,252], which is less than half of the quantity applied in ER III adhesive systems [49].

Instead of microfillers, nanofillers have been used in the adhesive agents [253]. Nanofillers have the ability to penetrate dentin tubules and the collagen network, thereby enhancing the strength of the adhesive layer [251]. Nanometer-sized silica (pure silicon dioxide) less than 20 nm is typically added as nanofiller [230]. Some ER II adhesive systems (Prime & Bond NT and XP Bond (Dentsply Sirona, York, PA, USA), and Adper Scotchbond 2 XT (3M ESPE, St. Paul, MN, USA)) and one-step SE adhesive systems (SE I) (Clearfil S3 Bond (Kuraray, Tokyo, Japan) and G-Bond (GC Corp, Tokyo, Japan)) include nanofillers in an amount typically ranging between 5 wt% and 10 wt% [48].

Investigations have denoted that simpler adhesives containing nanofillers might have superior mechanical features than unfilled bonding agents; nevertheless, such variations are considered material-dependent [254,255]. Moreover, studies have shown that adding nanofillers does not strengthen bonding to dentin substrate [256,257]. A detailed examination returned inconclusive outcomes when filled and unfilled adhesives were compared [258,259].

All in all, the purpose of fillers is to improve the mechanical and physical properties of adhesives. The nanoparticles are intended to increase the viscosity of the adhesive, so that it can be used in a single layer. They make it possible to obtain a sufficiently thick resin layer above the HL, since even if they do not penetrate the collagen network, the film they generate stabilizes the HL. This charged film creates an elastic buffer zone which decreases the stress generated by polymerization shrinkage. In addition, the presence of fillers would increase the wettability of the adhesive and facilitate the infiltration of monomers into the dentin [260,261]. Yet, adhesives become more viscous as filler levels increase (high filler amounts), compromising the wettability of dental substrates [242]. However, a potential drawback of fillers not penetrating the collagen network is that the adhesive bond might rely more heavily on the mechanical interlocking and less on chemical interactions with the collagen, which could affect the overall durability and integrity of the bond over time. Furthermore, if the fillers are not sufficiently integrated with the collagen matrix, there is a risk of microleakage or weaker BS in the long-term [262].

Dental adhesive systems involve complex composites with features that are affected by the presence and quantity of each component. The type and ratio of monomers, solvents, and initiators employed have a direct impact on the enhancement of their physical-chemical characteristics as well as their bonding effectiveness with dental substrates. In this context, being aware of the components and their interaction is crucial not only for inventing novel materials, but also to correctly identify their therapeutic application in each clinical circumstance [17].

1.6.2. Etch-and-Rinse Adhesive Strategy

When it comes to adhesive agents, the dental practitioner has various options, each with its clinical considerations. Choosing an adhesive agent is a critical decision that will affect the procedure’s long-term success. Therefore, knowing the classification of the contemporary adhesive agents will assist the general dental practitioner in making decisions [15]. In 2003, Van Meerbeek et al., [263] suggested two different strategies of adhesive systems according to the way they interact with the dental substrate, these being the ER technique and the SE technique. The ER technique necessitates etching followed by rinsing prior to their use, whereas the SE products are applied directly to the dental substrate without any prior treatment. This class includes all SE adhesive systems.

Each of these classes can either be applied in three or two steps for conventional adhesives requiring pre-etching, or two or one-step for SE adhesives [3,9].

Irrespective of the adhesive system used, the bonding process starts with acid treatment to remove or stabilize the smear layer [9]. Behind this layer, this acidic treatment affects the enamel and dentinal surfaces. This process makes micro-roughness favorable to the penetration and diffusion of resin monomers. An adherent interphase and an ideal seal between dental substrate and biomaterial restoration will be formed after photopolymerization [9,15,33]. Essentially, the primary consideration in dental adhesion lies in determining whether to replace demineralized HAp or entirely remove the resin [10,14].

According to a previous research, the key component of adhesion to dental tissue is mostly micro-mechanical [4] (Fig. 16).

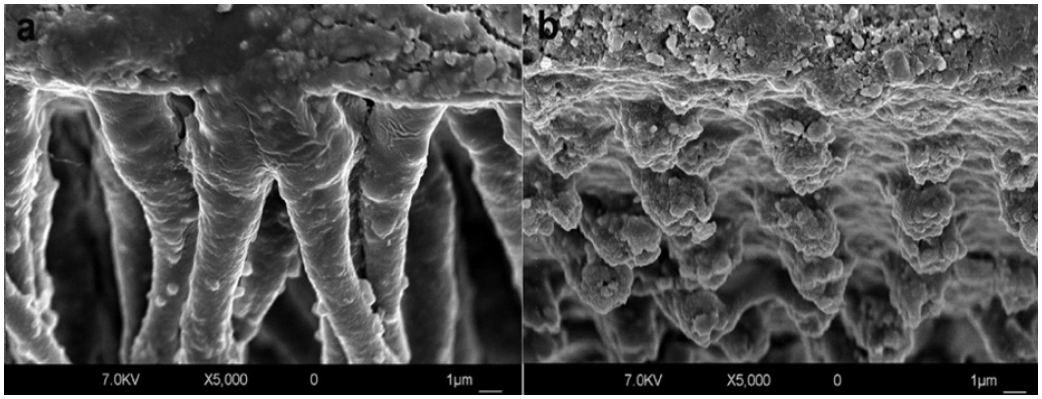


Figure 16: Micrographs of (a) an etch-and-rinse (ER) and (b) a self-etch (SE) adhesive system. Resin tags are clearly detectable in the ER adhesive systems (a), since they infiltrated dentin tubules funneled by the etching agent. SE adhesives often infiltrate no further than the smear layer and smear plugs, revealing a more homogenous morphology that is empty of long resin tags [4].

However, additional chemical interactions may also contribute to binding when the adhesive comprises functional monomers capable of connecting to the HAp [43,264]. This chemical component, whose short-term effect is masked by the tenacity of the micro-mechanical anchorage, could play a significant role in the adhesion potential of certain low-acid self-etching adhesives and in the durability of bonded joints [4]. This simple ranking makes it possible to classify all the varieties of products currently marketed into four categories: ER III, ER II, two-step SE (SE II), and SE I [9,15,265] (Fig. 17).

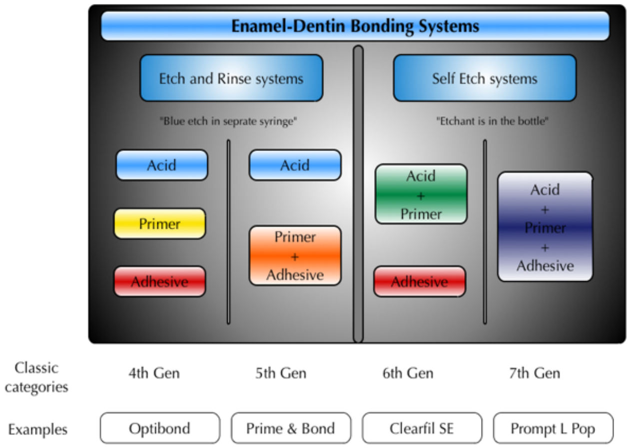


Figure 17: Classification of bonding systems [9].

ER III was introduced in the early 1990s as a family of adhesive systems [266]. ER III materials were the first to allow the complete removal of the smear layer and are still considered the gold-standard for dentin bonding [33]. In this system, the three main components (etching agent, primer, and adhesive resin) are generally packaged in separate containers and applied sequentially [10].

This concept of total-etching of the ER III systems involves:

- Application of a solution or gel, usually H_3PO_4 (with a pH of 0.1 to 0,4), for a period of 15-30 s on the enamel and a maximum of 15 s on the dentin (a duration longer than 15 s will cause “over-etching”) [33,267]. Etching agents are mostly colored gels (thickened by means of silica microparticles) that regulate the application and ensure that all the gel is rinsed off the tooth substrate [15].
- Copious rinsing (15 s and more) using an air/water spray to remove the residues that result from the chemical reaction between the acid and the minerals. However, the surface must remain moist in order to prevent collagen collapse. This is done using a dry applicator, absorbent paper points, or air that removes any excess humidity [9,10,266].
- Once the dentin is moist, the application of a hydrophilic primer solution on enamel and dentin in several layers will be necessary to infiltrate the exposed collagen network, followed by a slight air pump for 5 s to eliminate the solvent (depending on the solvent). Thus, the dentin will exhibit a glossy appearance [9,10].
- Application of adhesive resin on enamel and dentin, followed by the elimination of excess adhesive by a dry micro-brush. Afterwards, polymerization is done according to the manufacturer’s recommendation. Thus, the HL is formed by the resin infiltrated surface layer on dentin and enamel. The purpose of the ideal hybridization for these adhesives is to gain high BSs [9], typically in the range of 20 MPa for both enamel and dentin substrates [262].

This system was very sensitive and required a controlled etching technique, followed by an application of two or more components on both enamel and dentin [33]. However, they are very effective when used correctly, and are the most versatile of all adhesive generations, as they can be used for any bonding protocol (direct, indirect) or photopolymerization (self-cure, dual-cure). These systems are still the standards by which new systems are judged. Nevertheless, they can be very confusing and time-consuming with so many bottles and application steps [9,10,33].

Due to the complexity of ER III (All-Bond 2 and All-Bond 3 (Bisco, Inc., Schaumburg, Illinois, USA), Clearfil Liner Bond (Kuraray, Tokyo, Japan), Scotchbond Multi-Purpose and Adper Scotchbond Multi-Purpose Plus (3M ESPE, St. Paul, MN, USA), OBFL (Kerr Co, Orange, CA, USA), Syntac ClassicBond-it (Ivoclar Vivadent, Schaan, Liechtenstein), Permaquick (Ultradent, South Jordan, UT, USA), Amalgabond (Parkell, Edgewood, NY, USA), Gluma CPS (Heraeus Kulzer, Hanau, Germany), FL Bond (Shofu, Kyoto, Japan)), dentists sought a simpler adhesive solution. It is not just about the timing and number of bottles, but also the etching process, rinsing, and drying durations [9,33]. This marked a significant turning point in adhesive dentistry [266].

ER II systems were created in the late 1990s with a commercial focus on simplicity and speed of action, hence their general name of "single-component systems" or "one-bottle systems". Notable products include Admira Bond, Solobond M, Polibond by VOCO (Cuxhaven, Germany); Excite, Excite DSC, Excite F, Single Layer Bond by Ivoclar Vivadent (Schaan, Liechtenstein); Optibond Solo Plus by Kerr (Orange, CA, USA); Prime&Bond 2.0, Prime&Bond 2.1 by Dentsply DeTrey GmbH (Konstanz, Germany); Prime&Bond NT, Prime&Bond XP by Dentsply Sirona (York, PA, USA); One Step, One-Step Plus by Bisco (Schaumburg, Illinois, USA); Single Bond Adper 2, Scotchbond1 by 3M ESPE (St. Paul, MN, USA); and Clearfil Liner Bond 2 by Kuraray (Tokyo, Japan) [9].

In addition, there was a need to improve the prevention of collagen collapse of demineralized dentin and minimize, if not completely eliminate, postoperative sensitivity. The most common simplification method is therefore the "one-bottle system" which combines the hydrophilic primer and the hydrophobic adhesive resin in a single bottle with a solvent, to be applied simultaneously to enamel and dentin after etching with 35 to 37% of H_3PO_4 (etching on enamel for 15 to 30 s and on dentin for a maximum of 15 s) [268].

Their usage is unlikely to be simple due to their low tolerance to handling. Furthermore, their performance is closely related to the moisture of the treated dentinal substrate. All ER II adhesives are incompatible with dual- and self-cured materials. This could be explained by the lower pH of the oxygen-inhibited layer, or the monomers in some simplified products, deactivating the tertiary amine in chemically cured composites [9,33,266].

Several long-term studies of ER II dental adhesives showed high clinical bonding strengths (~25 MPa) [262]. Despite this, the resin-dentin bond is prone to water degradation. ER III adhesives are less prone to water degradation than ER II dental adhesives [9,266]. This is due to the high concentration of HEMA monomer inside the ER II. HEMA monomer should be added in higher concentrations to stabilize the mixture of ER II and to facilitate the infiltration of the self-priming adhesive inside the demineralized collagen fibrils [15].

The phenomenon of over-wetting in which water prevents the formation of a continuous adhesive seal, intensifies the importance of the issue of removing excess water from the surface of the etched-and-rinsed dentin before applying the adhesive [269]. Conversely, a collapse of collagen can occur as a result of intense drying. The difficulty which the clinician now faces is finding the correct degree of dentinal moisture to provide optimal adhesive penetration [266]. Unfortunately, it is very difficult to control this state. Several techniques have been proposed for this purpose: progressive air-drying, elimination of excess water by simple aspiration with the saliva ejector, absorption of excess water by using wet cotton pellet or "micro-brushes” or drying the cavity with compressed air followed by rehydration by wet cotton [270]. ER II adhesives containing acetone are considered more sensitive to the moisture control of dentin than those containing alcohol [9,271].

ER adhesives, such as ER III and ER II, have several advantages [9,10,33]. They rely on an efficient diffusion-based bonding mechanism, enabling profound micro-mechanical interlocking at both the enamel and the dentin surfaces. The aggressive nature of the etchant, normally H_3PO_4, guarantees complete removal of the smear layer, thereby improving the bonding performance. ER techniques are mainly effective for enamel bonding, with a recognized long-term adhesion durability. Specific ER adhesives, like ER III OBFL (Kerr Co., Orange, CA, USA), boast a longstanding presence in the dental market, signifying reliability over more than two decades. Furthermore, independent clinical trials accomplished over 10 years acknowledge the persistent bond efficiency of ER adhesives, yet the outcomes may vary based on the product. But, ER adhesives also present disadvantages. The aggressive nature of H_3PO_4 can result in excessive demineralization of the dentin, affecting its structural integrity. Complete dissolution of dentinal HAp and exposure of the collagen matrix can occur, necessitating the formation of a thicker HL within a limited clinical timeframe. This thick HL might be prone to microleakage, enzymatic degradation, and weak secondary chemical interactions, potentially destabilizing the long-term bond durability [10,33,15].

1.6.3. Self-Etch Adhesive Strategy

All SE systems contain water component [33]. Water is needed to activate the ionization potential of their acidic functional monomers [9]. Thus, water is usually used as a co-solvent in SE adhesives, either alone or in combination with ethanol [14]. As they participate in the polymerization, the rinsing step is not required after their application, so they differ technically from ER adhesive systems [272].

Their acidic monomers may be derivatives of carboxylic acid groups (4-META) or P acid groups (Phenyl-P, 10-MDP, PENTA) [9,48]. They demineralize and simultaneously infiltrate both the enamel and the dentin substrates [33,273]. At the dentin level, the mineral phase of the smear layer is dissolved before superficially attacking the 5 µm of underlying mineralized dentin [8]. The Ca and P ions pass into the solution in the liquid adhesive. The carboxyl groups or phosphates of certain functional monomers can form chemical bonds with the dissolved HAp phases, contributing to an enhanced cohesion of the infiltrated resin after polymerization and probably to better resistance to hydrolysis of this zone [266]. The smear layer is not completely eliminated but infiltrated. After the polymerization process, the organic constituents of this layer are impregnated with the resin of the adhesive, as well as the collagen fibers of the treated dentinal surface [9]. The hybrid zone therefore contains both the proteins of the smear layer and dentin [33]. Since the pH of the monomers is in the range of 0.8-2.5, the HL is thinner (0.5–1.5 µm for mild or moderate SE adhesives) than the one formed after H_3PO_4 etching ($pH < 1$), which is more acidic (5 µm for ER adhesives) [75]. Nevertheless, it is clear that adhesion to dentin does not depend on the thickness of the HL [274], nor the length of RTs [275].

The acidity of SE primers can be significant in terms of enamel efficiency and the durability of the bond they form [15,33]. In 2003, Van Meerbeek et al., [263] classified SE adhesives according to their acidity: primer and / or strong acid adhesives ($pH < 1$), intermediate ($pH = 1.5$), and those with weaker acids ($pH > 2$). Thus, there are self-etching systems that require the successive application of 2 different products (SE II) and others that require only one application (SE I) [9].

Usually, SE adhesive systems do not provide a selective demineralization of the enamel, similar to that with 35% H_3PO_4 [9]. Thus, SEE in a separate step with 35% H_3PO_4 has been recommended [190,276] (Fig. 18).

Figure 18: Selective enamel etching. (Courtesy of Prof Louis Hardan).

SE II systems utilize a two-bottle approach, with the first bottle containing a self-etching primer and the second containing the adhesive resin [15]. The self-etching primer modifies the smear layer on the surface of the dentin and incorporates the products into the coating layer [266]. These systems were introduced in the latter part of the 1990s and early 2000s. They dissolve the smear layer when applied and do not require rinsing, thus, they sought to eliminate the etching step, or chemically include it in one of the other steps: acidic primer applied to the tooth first, followed by an adhesive (self-etching primer + adhesive) [9], or (self-etching adhesive): two bottles or one dose containing an acidic primer and adhesive; a drop of each liquid is mixed and applied to the dental substrate [277]. Obviously, the biggest advantage of this system is that their effectiveness seems less dependent on the hydration state of dentinal surface [9,278].

Unfortunately, early evaluation of these systems showed sufficient bonding to the etched dentin (41 MPa at 24 h), whereas bonding to enamel was less effective (25%) [9]. This could be related to the fact that they are constituted of an acidic solution with insufficient pH to etch the enamel properly, which is difficult to keep in place and must be continually refreshed [279]. In order to overcome this problem, etching the enamel first with traditional H_3PO_4 at a pH of less than 1.5 is preferred [45,280]. However, some of these products are slightly acidic, with a pH as high as 3.3 [9].

In addition, practitioners using this technique should be careful to confine H_3PO_4 only to enamel. Further etching of the dentin with H_3PO_4 could create a conflict; "over-etching", where the demineralization zone is too deep for the subsequently placed primers to penetrate completely into the demineralized dentin [9,278]. These systems are popular because they are easy to use, with a lower postoperative sensitivity. The reason that self-etching systems tend to minimize postoperative sensitivity is that the smear plugs in the dentinal tubule are left intact [33]. The benefit of SE II adhesives is that their effectiveness is less reliant on the level of dentin's moisture comparing to ER adhesives. Normally, SE II adhesives were described to have better bond stability when compared to SE I adhesives [15,33]. Further, SE II systems are classified into 2 types:

- Type I adhesives, which are self-etching primer and adhesive systems such as CSE (Kuraray Noritake Dental, Tokyo, Japan), Prelude SE (Danville Materials, San Ramon, CA, USA), and

Ultradent Peak SE (Ultradent Products Inc, South Jordan, UT, USA). These adhesives have liquid components including a self-etching and an adhesive resin liquid primer which are applied separately to the tooth and are generally compatible with self-cured composites.

- Type II adhesive systems such as All-Bond SE (Bisco, Inc., Schaumburg, Illinois, USA), Brush&Bond (Parkell, Edgewood, NY, USA), Futurabond NR (VOCO America, Inc., Cuspis, CA, USA), Touch&Bond (Parkell, Edgewood, NY, USA), Adper Prompt L Pop (3M ESPE, St. Paul, MN, USA), and Xeno III (DENTSPLY Caulk, Milford, DE, USA). They use a self-etching primer and adhesive that are mixed together prior to placement and are not compatible with self-cured composites [9,15,33].

Note that the enamel and dentin BS of SE II is lower compared to the ER III and ER II [9]. However, this might be controversial for other researchers [33,266].

SE I (all-in-one) adhesives were introduced in the late 1999 and early 2005 [9,266]. They contain a formulation that mixes a self-etching primer and an adhesive resin in a single bottle [49,278]. SE I systems are theoretically capable of etching and infiltrating both enamel and dentin. The self-etching primer creates a resin layer that bonds with the composite material through photopolymerization [15].

Clinically, this system is the easiest to use, and BS values are generally acceptable [9,262]. Despite the simplicity of the bonding operation, it was possible to eliminate the errors that could occur while mixing several separate components [33]. However, placing and incorporating all the chemistry required for an adhesive system into a single bottle, and keeping it stable for a reasonable period of time, is a significant challenge [9]. These acidic systems contain a significant amount of hydrophilic monomer in their formulations contributing to the increased permeability of the HL and may be subjected to hydrolysis and chemical decomposition [281].

In addition, once the SE I systems are placed and polymerized, they are mostly more hydrophilic than SE II systems; this condition forms water-filled channels that limit the depth of infiltration of the resin into the dental surface and leads to water infiltration from the dentin through the HL. This phenomenon creates voids with a poor sealing ability (Fig. 19). The hydrophobic monomers contribute to more stable polymers [23].

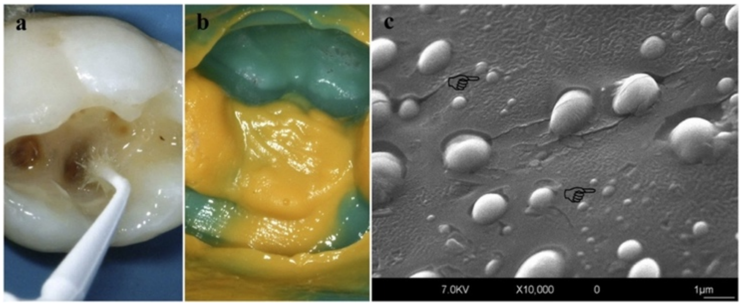


Figure 19: Illustrative steps of the *in vivo* analysis of the permeability of adhesives [283,284]. A cavity was prepared and bonded (a), and an impression of the cavity floor was obtained (b). After pouring a cast with epoxy resin, specimens analyzed under a scanning electron microscope revealed water droplets emanating from the adhesive surface (c). These droplets are the morphological evidence of water that seeped from the adhesive layer during the setting time of the hydrophobic impression material, forming major droplets as well as minor droplets (pointing finger) over the adhesive [267].

SE I adhesives have proven to have the lowest initial and long-term BS of all adhesives on the market. However, this can be considered a disadvantage [282]. In addition, they presented an incompatibility with self-curing resins and a reduction in shelf-life [15].

For instance, some of these products are: One Coat 7.0 (Coltene, Altstätten, Switzerland), Xeno IV (Dentsply Sirona, York, PA, USA), G-BOND (GC Corporation, Tokyo, Japan), OptiBond All-In-One (Kerr Corporation, Orange, CA, USA), Clearfil S3 Bond Plus (Kuraray Co., Ltd., Tokyo, Japan), Adper Easy One (3M ESPE Dental Products, St. Paul, MN, USA), Clearfill DC Bond (Kuraray Co., Ltd., Tokyo, Japan), Xeno DC IV (Dentsply Sirona, York, PA, USA), and Futurabond DC (VOCO GmbH, Cuxhaven, Germany) [9].

The SE I and ER II adhesives are simpler versions of the ER III and SE II adhesives [9,33]. It should be emphasized that simplified adhesives are user-friendly and have gained popularity as clinicians prefer easier-to-use dental materials [9,33]. Despite its simplicity of use and decreased technique sensitivity, the simplified adhesive approach has led to a decrease in effectiveness and durability [15]. Because of their hydrophilicity and the absence of hydrophobic bonding resin coating, cured adhesive films can act as permeable membranes, enabling water to move across the adhesive layer [9]. Based on existing literature, dental adhesives with a hydrophobic bonding resin as the last stage of the clinical procedure, such as ER III adhesives and SE II adhesives, are more stable and provide longer-lasting restorations compared to their simplified equivalents [15,33]. Certain suppliers provide hydrophobic liners paired with the SE I adhesive (All-Bond SE/All-Bond SE liner (Bisco, Schaumburg, IL, USA)) [15].

Furthermore, simplified adhesives are not compatible with dual or chemically activated resin composites. Once chemical-cure and dual-cure resin composites are combined with simplified adhesives, leftover uncured acidic monomers from the cured adhesives' oxygen-inhibited layer (not covered by a hydrophobic bonding resin) come into direct contact with the composite material [285]. The acid deactivates the aromatic tertiary amines in the dual-cure or self-cure compound, preventing their polymerization [286-288]. This could become more troublesome if clinicians employ composites and adhesives from various suppliers. Some simplified adhesives are specifically designed to be used in conjunction with their patented dual-cure or self-cure composites, with the adhesive requiring independent photopolymerization (for example, Clearfil S3 Bond Plus/Clearfil DC Core Plus (Kuraray Co., Ltd., Tokyo, Japan)). Other SE bonding systems claim incompatibility with self-cured or dual-cured composites is addressed by mixing the adhesive with a dual-cure or self-cure activator (for example, AdheSE/AdheSE DC (Ivoclar Vivadent, Schaan, Liechtenstein)) [15].

SE adhesives, including SE II and SE I, offer several advantages [9,15,33]. Mild SE adhesives achieve shallow hybridization around 1 µm, allowing easy resin diffusion in a short clinical period. This results in a high-quality HL rather than focusing on its thickness. The dentinal substrate is only moderately demineralized, permitting micro-mechanical interlocking. Limited collagen exposure makes it more resistant to enzymatic destruction. SE adhesives, especially SE II, have a proven track record, with products like CSE (Kuraray Noritake Dental, Tokyo, Japan) being reliable for over 20 years. Functional monomers like 10-MDP enhance chemical interactions and long-term bonding. Clinical evidence supports SE adhesives' long-term efficacy, with SE II adhesives showing a lower average annual failure rate (AFR) compared to SE I and ER adhesives. However, SE adhesives may have inadequate self-etching on enamel, requiring supplementary etching with H_3PO_4 for optimal retention. Additionally, smear layer interference can affect bonding, and the hydrolytic stability of 10-MDP, while efficient, is not perfect [33].

1.6.4. Universal Adhesives

Multi-mode universal bonding agents were released a few years ago, continuing the trend of simplifying adhesive methods [25]. This eighth-generation system can be employed with either ER, SE, or SEE procedures, relying on the clinical circumstances and the operator's personal preferences [9,41,172] (Fig. 20). SEE is frequently indicated, and UAs can be used on either dry or wet dentin [15,267].

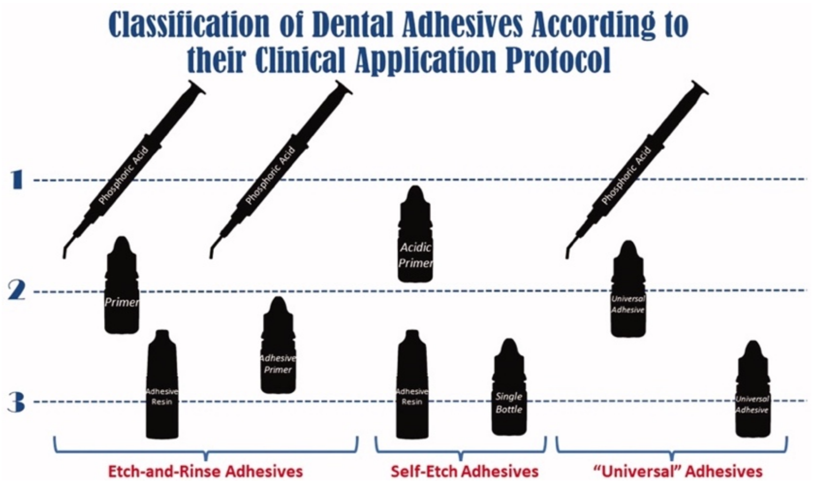


Figure 20: Classification of dental adhesive systems according to their protocol of clinical application (etch-and-rinse, self-etch, or "universal"; and one, two, or three steps).

UAs have quickly gained popularity in clinical practice due to their ability to simplify and speed up the clinical bonding process by mixing the primer and adhesive resin in a single bottle [289]. Nonetheless, UAs are still viewed as adhesives that compromise efficiency for simplicity of use since:

- UAs integrate the primer and the adhesive resin, each with a distinct purpose, in a single application step [15].
- UAs generally contain less resin and more solvent compared to systems with separate primer and adhesive components. This formulation can impact the adhesive layer's thickness and its properties. The increased solvent content aids in better wetting and penetration of the adhesive into the tooth structure, but it may also lead to thinner adhesive layers after evaporation and curing, which could be prone to suboptimal polymerization [9,290].
- UA's film thickness is usually less than 10 µm, influenced by air blowing pressure and time. This thin layer can result in suboptimal polymerization due to polymerization-inhibition by oxygen, suboptimal adhesive interface stabilization, and reduced ability to absorb stress from the restorative composite [33]. Both excessively thin and overly thick adhesive resin films can negatively impact BS, emphasizing the need for an optimal film thickness to ensure effective adhesion and durability [291].
- UAs are more hydrophilic and do not fully convert the adhesive surface to a hydrophobic situation [292,293].
- UAs absorb much more water and have lower hydrolytic resistance [294].

UAs have a pH range of 1.5-3.2 and are classified as ultra-mild (pH > 2.5), mild (pH < 2), or intermediately strong (pH between 1 and 2) [41]. To create suitable UAs, extremely precise functional and crosslinking monomers with multifunctional properties are necessary [276,295]. They must be able to react with a variety of substrates, co-polymerize with resin-based restorations and cements, and have a hydrophobic property to prevent water sorption after polymerization. Furthermore, they must be hydrophilic in order to "wet" the dentinal substrate, which contains a high-water content [172]. Also, they must be acidic enough to be effective in a SE technique while not being highly acidic for successful polymerization [287]. (The initiators of dual- and self-cure resin cement are interrupted in the case of UAs with high acidity).

Some manufacturers also claim that UAs can be used as adhesive primers for zirconia, alloys, ceramics, and composites in indirect restoration applications [15,295]. Additionally, a direct relationship occurred between the pH and the compatibility of UAs with cements and composites made from self- or dual-cure resin. The company says that some UAs are compatible with dual-cure and self-cure composite materials. As a simplification, the more acidic the adhesive, the less compatible it is with the self-cure mode of the dual-cure resin-based materials [287,296]. This is mainly due to the acid deactivation of aromatic tertiary amines which play a fundamental role in the chemical curing mechanisms of these materials [297]. To alleviate this difficulty, numerous UAs, when used in conjunction with this mode, require the inclusion of a separate "activator" (typically arylsulfinate salts) that should be mixed with the UAs if using an amine-containing cement [172]. The thickness of the polymerized adhesive film must be thin in order for it not to occupy the seating of the indirect restorations. Scotchbond Universal Dual Cure Activator (Scotchbond Universal, 3M ESPE, St. Paul, MN, USA), One Coat 7 Activator (One Coat 7 Universal, Coltene, Switzerland, Altstätten), and Clearfil DC Activator (Clearfil Universal Bond Quick, Kuraray Noritake Dental Inc., Japan, Okayama) are examples of the aforementioned activator. However, some UAs like All-Bond Universal (Bisco, Inc., Schaumburg, IL, USA) does not use a separately applied activator due to its compatibility with self-curing materials. Indeed, this adhesive (All-Bond Universal with a pH= 3.2) is less acidic (not usable as SE on dentin) than other UAs (2.0 <pH <3.0) [298].

UAs are not to be confused with SE I single-bottle or "all-in-one" systems. These adhesives have distinct chemical compositions characterized by the presence of carboxylate or P monomers. The most often used monomer is 10-MDP. Nevertheless, UAs contain a variety of additional functional monomers, including GPDM, PENTA, 4-MET, and 4-META [15].

The acidic monomer 10-MDP, which had been utilized by one SE adhesive system (CSE (Kuraray Noritake Dental, Tokyo, Japan)) for years, was incorporated to UAs once the patent expired [34]. The pioneering product of this category, Scotchbond Universal by 3M ESPE in St. Paul, MN, USA, featured 10-MDP [299]. This was followed by numerous adhesive systems made by different manufacturers. This 10-MDP monomer proved to generate a stronger and more stable bond with the tooth structure than the acidic monomers previously employed [34]. These UAs enable both micro-mechanical retention and chemical bonding with the dental substrates [15,172]. 10-MDP has a high affinity for HAp and forms chemical bonds with apatite crystallites via ionic bonding. The concentration of 10-MDP differs across UAs. It has been demonstrated that the higher the monomer concentration, the higher the adhesive's BS [15].

UAs strengthen adhesion to ceramic restorations. Indeed, UAs with 10-MDP improve adhesion to zirconia [300-303] and indirect resin-based composites [304]. On the other hand, UAs have proven incapable of replacing silane-based primers for glass ceramics such as lithium disilicate ceramics [305-307].

This class of adhesive systems should also include water in their formulation to dissociate acidic monomers and to make the SE procedure possible [287]. One of the many dilemmas confronted by chemists in evolving UAs is that water can degrade the chemistry of these systems, contribute to monomer separation, reduce shelf-life, and thus pose a challenge during evaporation [287,308]. In a previous study, Tsujimoto et al., [308] stated that UAs with 10%-15% of water (Scotchbond Universal (3M ESPE, St. Paul, MN, USA) and Prime&Bond active (Dentsply DeTrey GmbH, Konstanz, Germany)) are optimal for lowering the impact of surface wetness, while adhesives with more than 25% (G-Premio Bond (GC Corporation, Tokyo, Japan) approximately 25%) of water content and adhesives with water content < 3 vol% (All Bond Universal (Bisco, Inc., Schaumburg, Illinois, USA)) experienced phase separation. In the air-drying step, residual water may cause inadequate polymerization of the adhesive, increase hydrolysis after polymerization, and generally degrade the adhesive surface [23]. The addition of ethanol or acetone to UAs formulations increases resin wetting, infiltration of dental tissues, water elimination, and evaporation during the drying process [309].

Some UAs also state that they can be used instead of silane coupling as agents for bonding to silica-based ceramics (feldspath, lithium disilicate, etc.) [309]. Nonetheless, indirect restorations showed stronger bonding efficacy when silane and bonding resin were applied independently, resulting in a superior BS to an etched glass-based ceramic substrate after one year of water storage [304].

Several silanes are extensively utilized in the industry. Those silanes contain one or more atoms of silicone. Though, silane used for the adhesion of silica-based ceramic in dentistry, known as 3-methacryloxypropyltrimethoxysilane, is primary applied after etching of substrate with hydrofluoric acid. Before incorporating silane directly into the universal bonding agent, the treatment mentioned was the optimal choice. This advancement in UAs allowed for its use without the need for a separate application of a silane solution [172]. In application, UAs including silane simplified the adhesion procedure, but this has presented an unforeseen issue. The chemicals found in the adhesive might compromise the stability of the silane and hinder its performance. This problem, along with the manufacturers' belief that the chemical interaction of silane when used with silica-based ceramics is drastically inhibited when merged with all other monomers present in UAs, has prevented some manufacturers from adding silane to their formulations [172,310]. Preceding investigations [298,311] suggested that the incorporation of resin monomers such as MDP or Bis-GMA (used in UAs) in silane solutions considerably reduces the effectiveness of adhesion and chemical interaction of silane to silica-based lithium disilicate when compared to pure silane groups. Thus, it was previously suggested that a bond to the silicate-based ceramic can be achieved by etching the porcelain with hydrofluoric acid, then applying the pre-hydrolyzed silane (eg, RelyX™ Ceramic Primer (3M ESPE, St. Paul, Minnesota, USA), Porcelain Primer (Bisco, Inc., Schaumburg, Illinois, USA), Ultradent Silane (Ultradent Products, Inc., South Jordan, Utah, USA)), which is free of added monomers or resins (pure silane) [172]. Another study revealed the instability of silane mixed with the acidic species in UAs. Thus, the application of silane coat to acid etched glass ceramics was proposed [312].

Most UAs are commercialized in a single bottle [9]. Nonetheless, there are two-bottle UAs designed to improve performance by separating specific components. For example, the G2-Bond Universal (GC Corporation, Tokyo, Japan) is a two-bottle universal bonding agent in which the primer and bonding ingredient are in different bottles and applied independently from standard SE II adhesives [299,313-315]. The G2-Bond Universal (GC Corporation, Tokyo, Japan) features Dual-H technology, allowing the adhesive to transition smoothly from hydrophilic to hydrophobic properties, optimizing adhesion to both tooth and composite. Unlike traditional adhesives, G2-Bond Universal (GC Corporation, Tokyo, Japan) is HEMA-free, enhancing the bonding layer's durability by making it extremely hydrophobic and less prone to water sorption and deterioration. This composition reduces the risk of gap formation and microleakage, leading to superior long-term performance [299]. Similarly, Tokuyama Universal Bond (Tokuyama Dental Corporation, Tokyo, Japan) and LuxaBond Universal (DMG America LLC, Englewood, NJ, USA) are two-bottle systems, but the contents are meant to be blended before use. The separation of acidic monomers and ceramic primers in these two-bottle systems prevents the deterioration of silane coupling agents, thereby preserving their adhesive properties and extending their shelf-life [15,70,202].

HEMA is the main hydrophilic monomer in most UAs. HEMA can disrupt the interaction between 10-MDP and Ca, thereby impeding the establishment of a sufficient bond in 10-MDP-containing adhesives [15]. The presence of HEMA in the same bottle with both hydrophilic and hydrophobic components may result in water sorption and hydrolysis of the adhesive layer, reducing universal bonding adhesion durability [276]. According to previous studies, UAs are material-dependent, and long-term research is still needed to assess the stability of resin-dentin interfaces generated by modern UAs [3,16,316].

UAs' clinical performance is heavily influenced by the adhesive strategy, calling into doubt their claimed adaptability in terms of application method in a clinical situation [15]. Several systematic reviews examined which application mode (SE vs ER) was most effective for adhering to dentin and enamel. When utilizing mild adhesives, resin-dentin bonds were similar, but when using ultra-mild adhesives, they were significantly different (favoring the ER strategy) [276,317,318]. Furthermore, data suggests that SEE with H_3PO_4 prior to the application of UAs is an appropriate method for the amelioration of adhesion [15].

To enhance the performance of UAs, several factors must be considered. Firstly, ensuring complete solvent evaporation is crucial, as all adhesive systems use solvents like acetone, ethanol, water, or a combination of them. Inadequate evaporation can lead to incomplete polymerization of the resin, NL, and reduced BS. Extending air-drying times beyond the manufacturer's recommendation or using a warm air stream can help mitigate these issues [27,319]. Secondly, proper clinical technique is essential. UAs typically suggest scrubbing the adhesive for at least 20 s, followed by adequate drying and curing with a high-quality light. Adherence to these guidelines is vital for optimal results [172,33].

Additionally, checking the expiry date is important as bonding agents can degrade over time, particularly when exposed to high temperatures. Refrigeration can help maintain their efficacy, but adhesives should be stored at room temperature for at least 30 min before use [320]. Frequent bottle openings can also lead to solvent evaporation, so storing UAs in a refrigerator and securely recapping them after each use is recommended [70]. Studies have shown that the bonding performance of some adhesives decreases towards the end of their shelf-life, while others remain stable, emphasizing the need for careful shelf-life management. Furthermore, HEMA-free formulations using methacrylamides can contribute to an extended shelf-life [70,202].

Reading and following the specific instructions for each adhesive system is also critical, as different systems have unique placement and handling requirements [278]. Pre-etching with mildly acidic UAs can improve enamel BS but not dentin BS [321]. Lastly, the viscosity of the adhesive matters; applying two coats of very thin UAs can achieve the highest BS, while a single coat of more viscous adhesive is sufficient [322].

The advantages and disadvantages of UAs are summarized as follows:

Advantages:

- Suitable for ER and SE adhesives, as well as SEE, making them highly versatile [9].
- In SE mode, there is a potential for chemical interaction with HAp, thus, dentin margins are properly sealed [323,324].
- Application of this class of adhesives in SE mode with a scrubbing technique enhances the BS to enamel substrate [325].
- Keeping the dentin moist when employed in ER mode is not essential [9,324,326].
- Suitable for a wider range of restorative procedures [172].
- Used as zirconia primers [172].
- The Product Research and Evaluation by Practitioners Panel, a research group, reviewed the handling characteristics of UAs and determined that potentially all UAs scored highly for simplicity of use [327,328].
- Patient and operator factors may have a greater impact on restoration longevity than the adhesive used. When using UAs in clinical settings, isolation with a rubber dam is recommended, and moisture control is crucial. However, the reduced number of steps and associated time saving may also be considered as an important advantage [124,324,329].

Disadvantages:

- UAs do not propose etching dentin, necessitating a separate enamel acid-etching process. This increases clinical application time [172]. Clinical investigations have shown that the SE method has a lower retention rate than ER and SEE on enamel [330].
- UAs must be mixed with a dual-cure activator when used with self- or dual-cure composite materials, including build-up materials and resin cements with aromatic tertiary amines in the initiator system [331,332].
- When H_3PO_4 is used to etch dentin, they do not effectively seal the margins [333].
- UAs, like traditional SE I adhesives, can act as permeable membranes following polymerization. This allows fluids to pass through the adhesive layer and degrade the resin-dentin contact via hydrolysis [9].
- Solvent evaporation time must be extended to prevent water entrapment and NL [334].
- The addition of silane to the adhesive solution does not increase BS to glass-matrix ceramics. Thus, a separate silane solution must be employed for better adhesion to glass-matrix ceramics [312].

1.7. An Overview of the Adhesive Systems used in the Current Project

Four adhesive systems were used in this study for comparison (mild universal (HEMA-free), universal (HEMA-based), ER III, and SE II): PBU, OptiBond Universal (OBU, Kerr Co., Orange, CA, USA), OBFL and CSE. The manufacturers and compositions of the adhesives tested in the current thesis were presented in Table 2.

Adhesive and Manufacturer	Classification of the Material	Main Composition *
PBU (Dentsply DeTrey GmbH, Konstanz, Germany)	**Mild Universal** pH = 2.5	10-MDP, PENTA, isopropanol, water, photo-initiator, bi- and multifunctional acrylate

OBU (Kerr Co, Orange, CA, USA)	**Universal** pH = 2.5–3.0	Acetone, HEMA, GDMA, ethanol, GPDM
OBFL (Kerr Co, Orange, CA, USA)	**Three-step etch-and-rinse** pH primer: 1.9; pH bonding: 6.9	Etchant: 37.5% H_3PO_4 Primer: HEMA, GPDM, MMEP, water, ethanol, CQ, and BHT Adhesive: Bis-GMA, HEMA, GDMA, CQ, and filler (fumed SiO_2, barium aluminoborosilicat, Na_2SiF_6), coupling factor A174
CSE (Kuraray Noritake Dental Inc., Tokyo, Japan)	**Two-step self-etch** pH primer = 1.76 pH bond = 2	Primer: 10-MDP, HEMA, hydrophilic dimethacrylate, CQ, DEPT, water Bond: MDP, HEMA, Bis-GMA, hydrophobic dimethacrylate, CQ, DEPT, silanized colloidal silica

* Based on companies' MSDS. 10-MDP = 10-methacryloyloxydecyl dihydrogen phosphate; PENTA = dipentaerythritol pentaacrylate phosphate; HEMA = 2-hydroxy ethyl methacrylate; GDMA = glycerol-dimethacrylate; GPDM = glycerophosphate dimethacrylate; MMEP = methacryloyloxy-ethyl-dihydrogen phosphate; CQ = camphorquinone; BHT = butyl hydroxy toluene; Bis-GMA = bisphenol A-glycidyl methacrylate; DEPT = N,N-diethyl-p-toluidine; Clearfil SE Bond (CSE); OptiBond FL (OBFL); OptiBond Universal (OBU); Prime&Bond Universal (PBU).

Table 2: Manufacturers and compositions of the adhesives tested in the current research.

Among the ER III and SE II adhesives, the brands OBFL and CSE have been considered the gold-standard materials by many investigators and scientific studies [10,13,14,33]. Although this concept has been present in the literature for over 20 years, it gained popularity following the release of a meta-analytical evaluation of BS value [335]. De Munck et al., [335] determined that the two best performing adhesives in terms of BS were OBFL and CSE. A systematic literature review of clinical trials assessing the retention rates of restorations placed with the supposed gold-standards and other competitive materials displayed that OBFL did not perfom better than the other materials tested at short- and long-term follow-ups, and the same trend was observed for CSE [336]. Although these two materials have good clinical performance, the existing evidence does not support their claim to be gold-standards [337,338]. In some places, these two materials may be at least double the cost of other high-performance materials. Considering they are gold-standards; they raise the cost of restorative procedures in both private and public dental care settings [339].

While the researcher should adhere to the null hypothesis concept until there is sufficient evidence to declare OBFL and CSE as gold-standard materials, the clinician must be open to new literature discoveries [339]. In this fashion, these two adhesive systems were incorporated into all of the chapters of this thesis.

For OBFL: an ER III method that adheres effectively to both enamel and dentin in the laboratory, even after extended storage. OBFL was introduced in 1995 and was named the top adhesive solution in a benchmark article for adhesive dentistry [10,313]. Despite substantial advances in the area and the availability of innovative adhesive systems in the 25 years since OBFL was developed, no new adhesive has delivered a significantly improved bond performance, therefore it is still the adhesive of choice driven by user preference [313]. The manufacturer's guidelines for applying the priming component of OBFL include the statement "apply with a light brushing motion for 15 seconds (s)." [340]. This gold-standard ER adhesive incorporates a highly hydrophobic monomer called GPDM. This monomer also contains SE and UAs [341], and it can chemically interact with HAp in the etched and primed dental surfaces to boost bond longevity [13]. OBFL uses an adhesive material with 48 wt% fumed silicon dioxide and barium aluminoborosilicate [10,40,342,343]. Concurring to the company's directions, OBFL generates fluoride. Prior research revealed that OBFL had no antibacterial action against *S. mutans*, which could be related to the absence of a certain monomer and the high pH value [344]. OBFL does not contain MDP but incorporates HEMA and glycerol into the primer bottle [345]. Other tests showed that the primer of OBFL had a larger antibacterial impact against *S. mutans* than the adhesive, with the mixture showing no antibacterial effect. The discrepancies in antibacterial capabilities could be attributed to the pH levels of the primer and adhesive, which are 1.9 and 6.9 respectivelly. The authors proposed that while OBFL exhibited no antibacterial activity after photopolymerization, the antibacterial action of the unpolymerized bonding system could be ascribed to HEMA elution and its cytotoxic potential [346].

This bonding agent has demonstrated outstanding clinical performance in the treatment of non-carious cervical lesions. Clinical trials have found retention rates of approximately 90% at 12-13 years, with generally acceptable marginal quality [347,348,349]. The ER III adhesive (OBFL), which has been on the market for over 25 years, demonstrated the highest immediate and expected 1-year BS to dentin in a meta-analysis of over 2,000 BS tests reported in nearly 300 studies [335]. Plus, OBFL achieved a high retention rate of 94% in an independent 13-year clinical study for non-retentive class-V restorations. Notably, the 13-year clinical data were obtained when OBFL was applied using a gentle dry-bonding technique. This pivotal study emphasizes that OBFL, by providing an ethanol/water-based primer, utilizes self-rewetting mechanisms to prevent collagen collapse, thereby ensuring adequate resin infiltration, as previously suggested [347].

A previous research revealed that OBFL is the only system that has been shown to not just surpass the BS of the DEJ, but also to be the most stable over time [350,351]. This study brings a trophy to that list by establishing that this product is also the most appropriate for immediate dentin sealing, as previously mentioned while proposing this nomenclature [352]. The most significant discovery was that OBFL provided the optimum performance without the need for an extra flowable resin covering. This is due to its elastic modulus being similar to that of a flowable resin composite containing 48 wt% radiopaque filler (silica particles and barium glasses). Even after time in storage, provisional restorations, and surface cleaning, OBFL displayed a stable and a resistant adhesive surface [353].

As is clearly required for ER adhesives that supply acetone-based primers (ER III) or a combination primer/adhesive resins (ER II), the extremely technique-sensitive water wet-bonding approach seemed redundant for OBFL. Most likely, other ER adhesives that offer water-based primers (ER III) or mixed primer/adhesive resins (ER II) do not require wet-bonding [33]. In other words, not all ER adhesives must be applied using the technique-sensitive wet-bonding approach, leading ER adhesives to being incorrectly referred to as "wet-bonding" adhesives. In a meta-analysis of the clinical effectiveness of adhesives in non-retentive class-V restorations, OBFL had a low AFR of 1.8 (±0.8) % based on 6 clinical studies [148]. This clinical model is considered the most acceptable and objective way to measure adhesive efficiency [1]. Based on two meta-analytic confirmations of laboratory [335] and clinical effectiveness [250] and one independent clinical trial [347], OBFL earns the gold-standard status.

For CSE: SE II, released in 1991, and similar to OBFL [14], showed exceptional outcomes, with a near 100% retention rate in non-carious cervical lesions after 8 years [354]. This material comprises a functional monomer, 10-MDP, which forms a water-stable ionic connection with residual HAp on the dentin surface, adding to its long-term BS and clinical performance [355,356]. Also, fillers present in the composition of CSE bond increase BS and mechanical assets of the adhesive system. The presence of fillers in the material allows for the application of a rather thick adhesive layer [356-358]. According to one concept, this somewhat thick adhesive coat serves as a stress breaker and may withstand shrinkage stresses [359]. The high BSs seen with CSE in a prior investigation may have been impacted by its MDP concentration, as well as being an adhesive resin that contains fillers (particle-filled) [360]. Besides, the high degree of conversion of SE II adhesives defies water aging and enhances the initial BS and the durability of resin-dentin interface [361].

CSE is a water-based adhesive, with a pH around 2, usually used to ensure a partial demineralization of dentin, leaving a significant number of HAp crystals around the collagen fibrils [362]. Bearing in mind that 20-40% of HEMA was presented in the composition of the SE II “CSE” as described in their safety data sheet. Hence, the presence of extra percantages of HEMA would lead to a formation of an aqueous and unstable gel that needs extra modalities to be applied on the adhesive in order to achieve the optimal dentinal BS and stability over time [40].

Additionally, CSE demonstrated extremely significant antibacterial activity (5.37%) against *S. mutans* [363,364]. The integration of MDP monomer in both primer and bond composition may account for these findings. The bond's weaker antibacterial activity could be attributed to its lower MDP monomer concentration compared to the primer [345]. HEMA may also have an effect on the adhesive's antibacterial properties and overall cytotoxicity. A prior investigation found that HEMA was readily released from the primer [365]. The findings of a previous literature on SEAs' antibacterial activity against *S. mutans* demonstrated the absence of or extremely poor antibacterial potential [345]. Yet, due to its mild pH, it does not forcefully etch the enamel, hence its enamel BS, particularly uninstrumented enamel, is only moderately high. As a result, selectively etching a preparation's enamel margins first is proposed, which improves marginal quality [349].

Unexpectedly, CSE Bond had a weaker effect on tooth discoloration prevention than the other bond systems (OBFL and OBU). The yellowish color of this adhesive, which could trigger coloration, is one probable explanation. Another reason for this outcome might involve the application of the primer on the unetched surface, which may produce discoloration, according to the company (Fig. 21) [366].

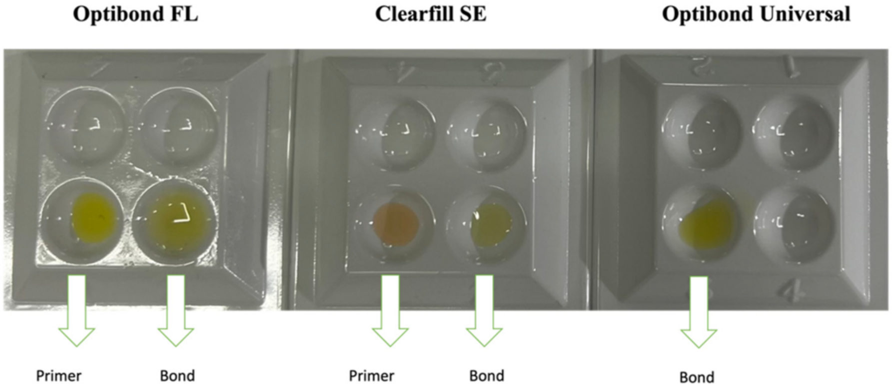


Figure 21: Tooth discoloration and dentin bonding agents [366].

Having been on the market for more than 20 years, CSE ((Kuraray Noritake Dental, Tokyo, Japan); currently succeeded by CSE bond 2 with claimed higher polymerization efficiency) was found to have the second highest mean immediate and predicted 1-year BS to dentin in a meta-analysis of over 2000 BS tests in nearly 300 papers [335]. CSE has a 13-year retention rate of 96%, the highest documented percentage in any independent long-term clinical trial of non-retentive class-V restorations [338].

A meta-analysis of the clinical effectiveness of adhesives in non-retentive class-V restorations found CSE to have a low AFR of 2.2 (±1.7) % based on 12 randomized control trials [250]. Based on two meta-analytic evidence of laboratory [335] and clinical effectiveness [250], as well as one independent clinical trial [347], CSE deserves to be regarded as the gold-standard SE adhesive.

After consistently producing promising laboratory bonding effectiveness data that have been confirmed by long-term clinical bonding-effectiveness data, it is expected that both the gold-standard ER adhesive OBFL and the gold-standard SE adhesive CSE are frequently employed as control/references in laboratory studies [33,335]. On top of that, part of the beneficial bonding efficiency of these gold-standard adhesives is probably attributed to the independent application of the primer and adhesive, but perhaps also to the generally thick film thickness of the adhesive-resin coat. The polymerization shrinkage of the covering resin composite produces tensile stress on the interface of the adhesive. An elastic intermediate layer of adequate thickness between the stiff dentin and the restorative composite may absorb the given stress without interfacial de-bonding [294].

All in all, when laboratory and clinical research provide significant and consistent proof of positive long-term bonding performance, commercial adhesives can be considered gold-standard [33]. In this respect, OBFL and CSE were used in the current thesis.

Bond durability is affected by two major bond-degradation pathways: hydrolytic bond degradation caused by water sorption and the resulting hydrolysis effects, and enzymatic bio-degradation caused by MMPs and cathepsins [4,8]. Due to its small size and high hydrophilicity, the mono-functional monomer HEMA, which is also frequently added to adhesives as a solvent for other monomers, might promote monomer diffusion into dentin [33]. The hydrophilic character of HEMA holds water at the adhesive interface and encourages water uptake from dentin and the external oral environment, hence accelerating hydrolytic bond breakdown and preventing long-lasting bonding [3]. Added to that, HEMA has been shown to be liberated from adhesives used in dentistry and also capable of passing via the dentinal tubules to the dental pulp, potentially causing cytotoxic and genotoxic (co-) effects [367]. Because HEMA's strengths do not appear to substantially compensate for its drawbacks, HEMA-poor/free UAs have been introduced lately [294]. For that reason, two UAs: OBU (HEMA-based) and PBU (HEMA-free) were implemented in the thesis.

In addition, UAs use acidic functional P ester monomers like 10-MDP and GPDM, which have a good affinity to HAp [13]. The adhesion/decalcification idea was proposed to better understand the chemistry of acidic functional P monomers with HAp [368]. This approach is dependent on the stability of the monomer-Ca salt produced. 10-MDP-Ca salt is slightly more stable than GPDM-Ca salt, since GPDM decalcifies whereas 10-MDP adheres to the adhesion channel [369]. It is believed that the higher etching effectiveness of the GPDM-based SE adhesives might result in equally efficient bonding compared to H_3PO_4 etching [370]. That being the case, UAs by means of GPDM-based adhesive (OBU) and 10-MDP-based adhesive (PBU) were used in this thesis in SE mode.

Another key evolutionary path for adhesive systems has been the streamlining of clinical procedures. Adhesive systems with fewer clinical processes are more sophisticated than those with more steps [371]. In light of this, two different UAs (OBU and PBU) were tested.

Based on the above background, this study examined two UAs on the dentin bonding performance of a GPDM-based adhesive, compared to an MDP-based adhesive in SE mode [370].

For OBU: a universal bonding agent with a pH of 2.5-3.0. OBU, which employs Kerr's renowned GPDM adhesive monomer and filler technology [362], achieves notable penetration into the dentinal tubules, thus providing exceptional BS and protection against microleakage and post-operative discomfort, according to the manufacturer's safety data sheet. Its particular nano-etching (micro-retentions or irregularities on the enamel surface at the nanometer level) ability enables more successful enamel etching than the other single-component adhesives, resulting in a deeper etched surface and higher mechanical retention [40,372,373].

According to the manufacturer, this material is compatible with SE, ER, and SEE processes [373]. They have a thin film thickness of approximately 5 microns. This adaptability permits the dentist to employ the adhesive in a widespread range of clinical settings. Both OBFL and OBU showed comparable BS values. Also, the fact that OBU requires fewer steps makes it a potentially appealing option in the clinical setting. Yet, further research is needed to corroborate these findings and verify the long-term effectiveness and reliability of employing OBU over OBFL [374].

At its core, the hydrophilic technology of OBU with a GPDM monomer ensures excellent adhesion to both enamel and dentin. Its equal distribution throughout the surface of the cavity is facilitated by the presence of solvents such as acetone and alcohol. The combination of solvents inside OBU guarantees the stability inside the adhesive design [40,362,375]. The use of this adhesive technique reduces the polymerization stress at the "filling-tooth" interface and improves the tightness of the adhesion between the composite and the dental surfaces. OBU also contains silane and metal primer, therefore it can be employed with indirect restoration [40,375]. In terms of marginal fit quality, OBU ranks highest, followed by Tetric N-Bond Universal (Ivoclar Vivadent, Schaan, Liechtenstein) and PBU [375].

OBU, like the OBFL Primer, had a strong antibacterial impact (96.95–91.13%) on *S. mutans*, which might be attributable to the HEMA and glycerol content. Monoalcylglycerols have been observed to suppress *S. mutans* biofilm development [345].

As stated by the manufacturer, the Optibond family were the only bonding agents in this thesis to include GPDM (OBFL and OBU) as an acidified monomer [376]. All other bonding agents (CSE and PBU) used 10-MDP. Yoshihara et al., [13] demonstrated that GPDM adsorbs well to HAp, resulting in good bonding qualities to the tooth structure. However, the water-soluble GPDM was easily removed by a water spray, unlike MDP, which remained adherent to HAp.

It is possible that composite surfaces subjected to GPDM become more water-friendly than those treated with 10-MDP. GPDM may absorb more water from the adjacent water-rich composite, potentially compromising the bond performance at the composite surface due to ester bond hydrolysis. The hydrophilic nature of GPDM relative to 10-MDP can be linked to their design. The former is somewhat short, with two hydrophobic methacrylic groups and a hydrophilic P group in the center, whereas 10-MDP contains a lengthy hydrophobic spacer chain that separates the functional groups and increases the molecule's hydrophobicity [13]. So, when the clinician needs to bond the old resin composite, 10-MDP-based adhesives should be the choice [376].

A prior study showed that OBU contains a high acetone content as a solvent, and this feature lowers the BS. Van Landuyt et al., [174] discovered that in order to avoid phase separation, the acetone solvent should be evaporated using a vigorous air-stream. As a result, it is possible that the acetone evaporation was insufficient, leading to a lower BS value. To ensure proper polymerization of the bonding agents, all solvents must be completely evaporated [40]. Polymerization is needed to avoid water uptake from the surface, which can lead to the breakdown of ester linkages by hydrolysis [376]. Plus, the OBU fitted model displayed strong aromatic peaks compatible with Bis-GMA in a prior research. This information was not included in the manufacturer's safety data sheets. However, the component ratios discovered using OBU's modeling, including Bis-GMA, showed a strong correlation with the manufacturer's patent [345]. Additionally, UDMA/acetone-based adhesives require a longer drying time than Bis-GMA/acetone-based adhesives [372].

For PBU: a universal bonding agent with a pH of 2.5 (mild etch). It spreads uniformly across the surface and simply combines with any remaining water. PBU is based on patented Active-Guard technology, which actively controls moisture [124,240,377]. Because the solvent is water, PBU is homogeneously distributed in the cavity and maintains its properties on both over-dried and water-logged dentin [326,377]. It is compatible with methacrylate light-curable restorative composites and cementing materials [375]. In dentin, the etching mode does not significantly affect the shear bond strength (SBS). Nonetheless, in enamel, SEE is mandatory in the SE mode to enhance BS [204,240]. Furthermore, a well-formed HL can be achieved using this adhesive [40,204,240,362,378]. It is also suitable for both direct and indirect restorations [89,117], has a low film thickness [379], and a high degree of conversion [380].

A prior study assessed the impact of dentin moisture levels on both BS and the ultramorphology of HL in four different UAs, including PBU. The study concluded that BS analysis revealed that PBU did not present reduced BSs after application on over-dried dentin. Interfacial ultramorphology of PBU was not affected by the degree of moisture. Yet, ultramorphological analysis disclosed some gaps, defects and reduced HL thickness for the other adhesives when applied to over-dried dentin [250]. Clinicians are not aware of which UAs should be strictly applied on a moist dentin for bonding in the ER strategy. Accordingly, another reason for choosing PBU in this study is that the clinicians can use it in either SE or ER mode (PBU with less technique sensitivity can be applied even in dry or moist dentin state) [381]. In fact, it is worth noting that PBU demonstrated remarkable clinical success with both adhesive techniques, with retention rates of 96.6% (100% for ER and 93.2% SE) following 6 months and 93.2% (95.5% for ER and 90.9% for SE) following 18 months of clinical service [382]. This could be attributable to the fact that PBU contains 10-MDP and is a non-HEMA adhesive [377]. Furthermore, methacrylamide monomers were designed to substitute HEMA in PBU, preventing phase separation and lowering water sorption within the adhesive [124,383]. Methacrylamide monomers have also been shown to be more hydrolytically stable, allowing them to be stored for longer periods of time. This could explain how stable this adhesive is under various humidity levels. Furthermore, it is probable that the solvent (isopropanol) in this bonding agent facilitates adhesive distribution between collagen fibers, even at high relative humidity levels (between 78% and 94%) [124,384]. The isopropanol solvent re-expands the collapsed collagen network, and the low-viscosity resin mixture may sufficiently permeate the inter-fibrillar spaces, thereby making an acceptable HL when adhering to demineralized dentinal surfaces [124].

In accordance to the producer, PENTA is an efficient crosslinker agent that increases PBU wettability due to its hydrophilic core and the presence of five double bonds per molecule [206]. PENTA was used in various "Prime&Bond" adhesive generations of Dentsply Sirona company, and despite the inconsistent results observed when prior generations of PENTA-containing adhesives were examined [385-387], *in vitro* investigations have demonstrated that PBU has an increased resin-dentin BS compared to other UAs [388,389]. This was one of the main justifications for adopting this material in the present thesis. Additional feature that the application time may also contribute to PBU's ideal clinical success. The company that makes the product "PBU" advises a 20 s application duration rather than 10 s. It is commonly recognized that a longer application period offers a stronger bonding values with dentin [382,390]. In addition, PBU consists of two P monomers (10-MDP and PENTA), several cross-linking agents for polymeric synthesis, and isopropyl alcohol as an organic solvent with a pH of 2.5 [124,240]. A study found that the dentin BS of PBU remained consistent and predictable for up to one year [382]. This stability was explained by the PENTA monomer, which contains five vinyl groups compared to one in the 10-MDP monomer [51,202]. These four additional vinyl groups increase PENTA's resistance to hydrolytic breakdown. Thus, when hydrolysis occurs and removes one vinyl group from the monomer's primary structure, four vinyl groups remain available to maintain the P group [16,189]. As a result, copolymerization with other monomers and attachment to tooth structure occur simultaneously [124,240]. This can provide a rationale for selecting this bonding agent in the thesis.

In the present thesis, the μTBS of both UAs applied to dentin was assessed only in the SE mode for two main reasons:

1. This mode is not inferior to the ER one in regard to BS values according to Rosa et al., [318].
2. SE mode offers more durable bonding after extended water aging due to the degradation of the resin-infiltrated collagen in the ER mode, according to Zhang et al.,[391].

1.8. Influence of Pre-Treatments and Outlook for a New Alternative in Resin-Dentin Bonding

To maximize performance and long-term outcomes of adhesive systems several strategies are reported:

1. ***Use of an additional layer of hydrophobic coating***

The hydrophilic characteristic of the monomers inside adhesives makes them permeable to water and compromises bonding durability. This is due to the affinity of the monomer for generating hydrogen bonds with the hydrophilic portion of acidic monomers present in the mixture, which modifies the formation of the polymer chains [392]. In an attempt to maintain the quality of the adhesive layer, many authors proved that placing an extra bonding layer result in: (1) higher BS, (2) higher hydrophobicity, (3) thicker film thickness, and (4) better polymerization efficiency. Although this strategy is clinically practical, it helps stabilize the adhesive interface against water sorption from the outer oral cavity and water ingress by osmosis from the dentin substrate [388,393].

Alternatively, a comparable beneficial outcome can be achieved by applying a flowable composite on top of a low film-thickness adhesive. Thicker flowable composite may serve as an internal stress absorber, maintaining the integrity of the adhesive interface over time. This may be specifically beneficial in deep proximal boxes of posterior restorations, leading to better marginal adaptation at the axial box and critical cervical margins [394-396].

SE adhesives, characterized by their composition, exhibit greater hydrophilicity compared to ER adhesives [277]. The inherently hydrophilic nature of SE adhesives leads to inferior mechanical properties in the adhesive layer, rendering it less resistant to fatigue stress [397,398]. Consequently, additional protective measures become necessary when using SE adhesives. Furthermore, even ER adhesives, particularly those containing HEMA, display hydrophilic tendencies, suggesting the potential benefits of incorporating an extra hydrophobic layer. For example, Adper Scotchbond Multi-Purpose (3M ESPE, St. Paul, MN, USA) adhesive served as the non-solvated hydrophobic resin to maintain consistency with prior clinical research that employed an additional hydrophobic bonding resin. However, it is important to note that this bonding agent contains HEMA monomer, which can lead to a decline in physical properties after 24 h due to water absorption from unreacted monomers after polymerization. In light of this, HEMA-free hydrophobic bonding agents have been utilized in certain studies, such as Heliobond (Ivoclar Vivadent, Schaan, Liechtenstein) [399-401]. Additionally, Ermis et al., [402] suggested that the bond durability of two UAs (Clearfil Universal Bond (Kuraray Noritake, Tokyo, Japan) and Single Bond Universal (3M ESPE Dental Products, St. Paul, MN, USA)), applied in a SE strategy, benefited from the application of an extra hydrophobic adhesive layer when the adhesive was first light-cured. Furthermore, Daood et al., [237] reported that applying an extra hydrophobic layer on top of simplified adhesive systems may improve BS and reduce NL. An intriguing finding of this study was shown by Ahmed et al., [388] revealing that G-premio Bond (GC, Tokyo, Japan), compared to the other two UAs Clearfil Universal Bond Quick (Kuraray Noritake Dental Inc., Japan, Okayama) and Prime&Bond active (Dentsply DeTrey GmbH, Konstanz, Germany) can solely benefit from an extra bonding layer when applied in SE mode. Ahmed et al., [388] concluded that the effect of an extra bonding layer on immediate and aged bonding efficiency is dependent on the adhesive itself first, and on the mode of adhesion used.

Emphasizing the need for comprehensive approaches that address both the inherent properties of the adhesive materials and the specific requirements of the clinical situation ensures durable and reliable outcomes in dental restorations. This clinically useful technique (additional layer of hydrophobic coating) has been promoted to enhance the functionality of simplified ER II and SE I, which mix the primer and adhesive resin in a solvent-richer and resin-poorer single-solution adhesive, in addition to UAs with a thin film thickness [33].

2. *Extending the application time*

A prior review found that decreased application periods reduced the dentin BS of SE adhesive solutions [403]. Nowadays, clinicians are beginning to escalate step reduction settlements in both ER [10] and SE adhesives [14]. A recently launched adhesive system by manufacturers, named G-Premio Bond universal (GC, Tokyo, Japan), provides dental clinicians with a substitute to the SE strategy for adhesion to dentin without requiring to wait for the adhesive to interact with the bonding substrate (no-waiting SE; Japanese version of manufacturer's instructions), or the interaction takes place after leaving the adhesive untouched for 10 s (10 s SE; international version of manufacturer’s instructions) [88]. This innovative idea of a no-waiting adhesive, while pleasing to many clinicians, should not hinder the durability and performance of adhesives when bonding to dentinal substrate. It was concluded that the no-waiting SE strategy preceding adhesive photopolymerization may give adequate BS. Nonetheless, extended application times when using the 10 s SE mode instead of the no-waiting mode enhance its short-term dentin bond performance [404]. As a result, applying a SE adhesive for a shorter duration than advised by the supplier may not be the optimum usage of the adhesive. Dentists typically work without using a watch to precisely record individual application procedures, and they expect a reduction in their patients' discomfort treatment times. Therefore, dentists may not always adhere strictly to manufacturers' suggested application times [405], theoretically affecting dentinal BS and compromising the long-term durability of dental restorations [406]. As revealed by Hardan et al., [25] a shorter application time reduces the immediate and aged BS of UAs applied to dentin using ER or SE modes. Consequently, clinicians should not implement this adjustment. Extending application duration of adhesives improved the chemical reaction between functional monomers and HAp, a key step for enhancing monomer infiltration.

3. *Non-thermal atmospheric plasma*

Dentin bonding could strengthen after treatment with non-thermal atmospheric plasma (NTAP). The use of NTAP improves the aged BS but presents no influence on the immediate BS. Plasma has been reported to improve bonding to dentin [407]. It is described as partially ionized gases that comprise electronically excited atoms and molecules, as well as ions and free radical species [408]. These particles are considered highly reactive crosslinkers, able to form chemical functional groups on the surface of dentin [407]. The use of NTAP has been shown to promote dentin wettability [409,410], resin polymerization [411], and resin infiltration [412,413]. An additional potential explanation for the increased bond influence is that the NTAP stimulates the dentin substrate by leaving free radicals or peroxides, hence intensifying the interaction between collagen fibrils and resin monomers [414]. Furthermore, matrix metalloproteinase-2 (MMP-2) and MMP-9 are naturally occurring MMPs in dentin. These enzymes may break down the collagen matrix within dentin over time, thus affecting the durability of resin-dentin connections. Accordingly, lowering the expression and activity of MMP-2 and MMP-9 may be favourable for improving the durability of resin-dentin bonds [4,8]. The previously indicated reduction in MMP-2 and MMP-9 expression and activity might perhaps be achieved by using NTAP on thyroid papillary carcinoma cells, suggesting a possible therapeutic impact of NTAP in lowering MMP activity and thereby increasing resin-dentin bonding [412,413,415]. Nonetheless, it has been demonstrated that μTBS and fracture-toughness testing have not consistently shown that dentin plasma therapy improves ER and SE bonding. Therefore, this method should not be considered effective enough [33].

4. *Ethanol wet-bonding and acetone wet-bonding*

The technique of ethanol-wet bonding (EWB) relies on the ER bonding strategy, with the goal of totally replacing water with ethanol within the exposed collagen-fibril network. Employing the EWB approach helped in improving the immediate BS. Ethanol is a favoured solvent over water because it can reduce the width of collagen fibrils while increasing interfibrillar space, allowing monomers to easily permeate the collagen fibrils [416]. This technique, known as EWB, has been recognized for effectively sealing the dentin matrix, reducing the permeability of the dentin-resin interface. This reduction in permeability can reduce the activity of collagenolytic enzymes, thereby increasing the durability of the dentinal bond [417]. In this simplified procedure, 100% ethanol is applied, which is safe for clinical use. When collagens are effectively preserved with ethanol, the adhesive interface exhibits prolonged durability, leading to a stable bond over time [418]. Other studies, however, reported that although this method is probably the most successful for improving ER bonding, it is not clinically practicable due to the time required for subsequent ethanol administrations (at least several min) [419,420]. Due to ethanol's higher viscosity compared to acetone, dental adhesives with acetone are less viscous, allowing acetone to penetrate the demineralized dental collagen matrix more effectively.

The acetone wet-bonding (AWB) procedure demonstrates the capacity to sustain BS over an extended duration. Additionally, the AWB technique introduces a new strategy that effectively improves dentin wettability to dental adhesives, facilitates adhesive monomer penetration, reduces collagen exposure, decreases NL, and mitigates collagen degradation [421]. Correspondingly, AWB emerges as a promising strategy for prolonging the lifespan of adhesive restorations [421,422]. However, further studies are needed to prove the efficiency of this technique (AWB).

5. *Multiple-layer applications*

Producing double or triple adhesive layers with simplified adhesive systems can be recommended to increase their performance [423]. Note that adhesives containing filler in their composition resulted in a thicker adhesive layer compared to non-filled adhesives [424].

Adhesives with increased thickness (by several coats) were applied on dentin in a study by Zecin-Deren et al., [423] in 2019 where one layer, two layers, and three layers were applied using four adhesives: two UAs and two SE ones. The authors found that for Xeno V and Prime&Bond One Select (Dentsply DeTrey GmbH, Konstanz, Germany), a noticeable increase in adhesive layer thickness was observed between the control (one layer) and the three layers group, along with significantly higher BS. Such findings were not observed for Adper Easy One and Single Bond Universal (3M ESPE Dental Products, St. Paul, MN, USA). In case of these adhesives, the increase in BS between the control and the three layers group was not statistically relevant, even though the thickness of the adhesive layer was significantly higher. That said, the fillers inside these two adhesives (based on their specific compositions as detailed in the manuscript [423]) produced a thicker adhesive layer. One should bear in mind that the exact application protocol is dependent on the product [423].

Filler load or percent mass load differs between adhesives according to the manufacturer's technology and it is not well described in the composition of adhesives. Also, there is a matter of concern about shrinkage of these filled adhesives after polymerization [246]. It was proven that the inclusion of nanofillers in the formulation of adhesive does not ensure a higher BS in comparison to unfilled adhesive systems [359]. Fillers may increase the viscosity of adhesives and prevent its overthinning which can provide a thicker adhesive layer and function as an elastic buffer. If that adhesive layer is too thin, the polymerization process might not completely progress due to the oxygen inhibition phenomenon, and this may lead to lower mechanical properties for the adhesive layer [425].

Nevertheless, it has been suggested that increasing the percentage of fillers or nanofillers could decrease the penetration of adhesive into demineralized dentin and hence generate a defective HL [426].

Similarly, Fujiwara et al., [427] observed that the application of two layers of UAs (Prime&Bond Elect (Dentsply Caulk, Milford, DE, USA) and Scotchbond Universal (3M ESPE Dental Products St. Paul, MN, USA)) instead of one layer improved the adhesive quality, enhanced BS, produced a more uniform adhesive layer, and compensated for possible defects of single application. Zecin-Deren et al., [423] recommended using triple adhesive layers with simplified adhesive systems in order to improve their performance while focusing on the point that achieving a more reliable bonding to dentin and hence maximum efficiency necessitates a specific protocol for each adhesive. Fujiwara et al., [427] recommended using double adhesive layers with single step adhesive systems including universal ones. The double layer method is a realistic clinical approach and may be useful for enhancing the bond quality of UAs.

Further, a preceding study found that employing this application increased immediate dentin BS but did not improve BS following aging [25]. Current bonding trends appear to prefer a single application of adhesive solutions, although this cannot result in a thicker HL or adhesive layer with micro-mechanical retention to the underlying composite resin. Though, prior research suggested that double or triple adhesive coats improve dentin BS by increasing monomer penetration into the HL and chemical interactions [31,32]. As a result, an extra layer of application should be regarded as a crucial clinical step. Moreover, it should be highlighted that the increased dentin BS with double application is the effect of many mechanisms operating simultaneously. As the solvent inside adhesives evaporates between each adhesive layer, the concentration of co-monomers that remain after each layer application increases [93], hence improving the quality of the HL [428].

According to a previous investigation [428], using numerous adhesive layers but not curing them improved dentin bond performance. This cannot be attributed to an increase in adhesive layer thickness, but rather to the superior quality of the adhesive layer. The adhesive layer thickens only after light-curing of each application. This ensures that the demineralized dentinal substrate is adequately protected, mitigating the negative consequences of oxygen inhibition via incorrect bond formation for both SE and ER adhesives. So, based on what was established about MLA, clinicians might apply a double coat while examining the material and substrate contents of each adhesive [403].

6. *Enhanced solvent evaporation by using warm air stream*

Solvent evaporation is accomplished by allowing an adequate evaporation time between the adhesive application and the polymerization, or by air-drying with a dental syringe. However, solvents and water should be thoroughly removed from the dental surface prior to photopolymerization. To achieve this evaporation, researchers propose air-drying for dental adhesion. Yet, this process is challenging because the density of the monomer rapidly increases when solvents and water evaporate [7,403]. This lowers the evaporation capacity, resulting in less water and solvent removal [211]. However, the exact amount of unevaporated solvents is unknown. What is known though is that an excess solvent might deteriorate the HL and have a negative impact on the long-term bonding performance [429,430]. Other difficulties include NL, as well as a reduced polymerization of resin monomers [18]. In this sense, it is recommended to use a warm air stream to evaporate solvents from adhesive systems [40].

In both ER and SE adhesive systems, employing a warm air stream for solvent evaporation enhanced BS, with the effectiveness of this method being influenced by the solvent composition of the adhesive. Warm air stream application resulted in improved BS for water-/alcohol-based adhesive systems, whereas no significant effect was observed for acetone-based adhesive systems. Nonetheless, a prior comprehensive analysis indicated an overall enhancement in BS for both adhesives when utilizing a warm air stream for solvent evaporation [221].

In water-/alcohol-containing adhesive systems, employing a warm air stream for solvent evaporation improved the BS [221]. This increase can be credited to the stronger attraction between ethanol and water molecules, resulting in a higher boiling temperature and making their evaporation more difficult. Findings have revealed that even after 60 s of evaporation, approximately 13% of the solvent remains in ethanol-/water-based adhesives, which can act as a plasticizer, jeopardizing both the degree of conversion and BS of an adhesive system [7,18]. Elevating the temperature of air-drying accelerates the kinetic energy of molecules in the adhesive system, promoting increased molecular vibration and facilitating the breakdown of intermolecular bonds between the solvent and polar groups of resin co-monomers, thereby favoring solvent evaporation [40,431,432]. Conversely, the application of a warm air stream increases the temperature of monomers, potentially reducing their viscosity and facilitating their diffusion into the dentin [40]. The combined effects of these factors may contribute to achieving a higher resin-dentin BS, as demonstrated by a previous meta-analysis [221].

The application of a warm air stream did not enhance the BS for acetone-based dental adhesives [7,221]. Acetone, being a highly volatile solvent with a high vapor pressure, exhibits a limited capacity for hydrogen bonding with water and monomers in the adhesive resin [433]. Consequently, acetone evaporates easily from dental adhesives during use and storage, adversely affecting their shelf-life [70,202]. Moreover, a former study indicated that the solvent evaporation rate of experimental adhesives based on acetone remained similar whether subjected to room-temperature air-stream or 40 °C air-stream [431]. These factors likely contribute to the lack of a significant improvement in BS observed with the use of a warm air stream for solvent evaporation in acetone-based adhesives [7,221].

In 2020, Klein-Junior et al., [24] assessed the influence of *in vitro* heat-air treatment on cytotoxicity and the degree of conversion of three universal SE adhesives: Ambar Universal APS (FGM, Joinville, Santa Catarina, Brazil), Scotchbond Universal Adhesive (3M ESPE, St. Paul, MN, USA), and Tetric N-Bond Universal (Ivoclar Vivadent, Schaan, Liechtenstein). The authors suggested that the jet of 10 cm/10 s hot-air (60 °C) from the substrate reduced the cytotoxicity of universal SE adhesives; but it did not enhance the degree of conversion. (It is important to mention that the hot-air was provided by a heater device coupled to an air-blow, presenting an output similar to the air jet of a dental chair).

The authors investigated various external sources of heating before the photopolymerization process, ranging within biologically safe levels [434,435]. This heat led to immediate monomer conversion gains while decreasing the concentration of the final solvent in the adhesive system [436]. Additionally, this method improves resin infiltration into the decalcified dentin, hence the increase in dentinal BS. Warm air within the dentin pulp organ's thermal tolerance zone (29-56 °C) has no negative effects and dentin responds to it physiologically [38,39]. Previously, a meta-analysis advocated that employing warm air streams for solvent evaporation could increase dentin BS in adhesive systems. The review identified numerous air temperatures for solvent evaporation, including 37 °C, 38 °C, 50 °C, 60 °C, and 80 °C. Warm air evaporation at temperatures between 40 °C and 60 °C was found to improve solvent evaporation. Nonetheless, the 60 °C temperature resulted in higher BS and less degradation [7]. A more detailed discussion of the gold-standard temperature for air-drying would be particularly useful. According to a previous study, the use of a warm air stream for solvent evaporation enhanced the bonding performance of alcohol-/water-based adhesive systems when applied to dentin [7]. In summary, the authors concluded that the gold-standard temperature of a warm air stream should be around 50 and 60 °C [221].

7. *Prolonged curing time*

Increasing the photo-activation time enhanced the strength of both immediate and aged bonds. Ideally, a restorative material must apply sufficient energy to transform monomers into stable polymers [25]. To improve polymerization (degree of conversion) and reduce permeability, increasing the time of light exposure of adhesives beyond manufacturer recommendation was preferred (ie, from 20 s to 40 s, to 60 s) [45]. In 2014, Wambier et al., [437] showed that reducing the sorption of water and the solubility of the adhesives is controlled by extending the time of light exposure of adhesives. While in 2011, Ferreira et al., [438] proved that an exposure time longer than what is recommended (20 and 40 s instead of 10 s) increases the degree of conversion of simplified adhesives (Adper Single Bond 2 (3M ESPE, St. Paul, MN, USA) and One Step Plus (Bisco, Inc., Schaumburg, Illinois, USA)) and the resin-dentin BS, but does not decrease NL. In addition, it was previously demonstrated that an extension of the exposure time during light-curing improves the quality of the resin-dentin interface [439]. Likewise, in 2019, Breschi et al., [23] suggested that the degree of conversion of adhesives in deep class II cavities might increase when extending the exposure curing time to approximately 40 s-60 s. On the other hand, they pointed out that damage to the pulp may occur because of heat generation from light-curing. The same findings were observed by Cadenero et al., [440] in 2005 and Breschi et al., [441] in 2007, where they suggested that, even below ideal laboratory conditions and longer exposure times, the exposure time proposed for adhesive systems is not sufficient to obtain an optimal polymerization.

Therefore, prolonging photopolymerization of the adhesive guarantees an adequate degree of conversion; despite this fact, one should bear in mind that even Light-Emitting Diode (LED), which were initially cold lights, produce heat up to 93% of their total energy. To solve this issue, the tooth should be air-cooled on an interval of 1 to 2 s after every 10 s of light exposure [23,442]. According to a prior meta-analysis [25], prolonged curing time for UAs reduces the adhesive's susceptibility to water sorption and may keep the CQ in a state that permits it to react with a co-initiator, resulting in an elevated energy density and amplified free radical production [443]. In this case, the exposure time specified by the manufacturer for adhesive systems is insufficient to achieve adequate polymerization [440]. As a result, a longer exposure time of up to 40 s is recommended [25].

8. *Prolonged air-blowing*

In the bonding procedure, air-drying is considered a crucial step after the application of the adhesive. During this step, some of the factors that might influence the BS are: air-blowing time, air pressure, and air temperature. Some novel formulations claimed that with reduced application time (5 s), an adequate BS will be achieved. However, there is slight evidence supporting the efficiency of a short application time, particularly on the long-term [18,22,430].

Since ethanol and water can form hydrogen bonds with each other and also with the monomer, it is challenging to remove water from ethanol-based adhesives compared to those of acetone-based adhesives [18]. Based on that rationale, it was expected that the effects of air-blowing time would be more evident for the ethanol-based adhesives. In a previous study, longer air-blowing time caused significant increases in the BS of ethanol-based adhesives (Clearfil Universal (Kuraray Noritake, Tokyo, Japan) and Scotchbond Universal (3M ESPE, St. Paul, MN, USA)) after 24 h and 1 year, whereas the BS of acetone-based adhesives (G-premio Bond (GC, Tokyo, Japan)) was not affected by the different air-blowing time. This study suggested that an extended air-blowing time increased the BS and bond durability of Clearfil Universal (Kuraray Noritake, Tokyo, Japan). Extension of air-blowing time to 15 s and 30 s improved the long-term BS of both adhesives tested respectively. In general, the recommended air-blowing duration for newer UAs ranges from 5 s to 15 s, or until the mobility of the liquid film on the surface is no longer visible. However, the specific air-blowing time is not standard [444]. Prolonged air-blowing time for 5-10 s versus 15-30 s was suggested in order to enhance the immediate adhesive properties of some UAs [19]. Prolonged or strong air-blowing of HEMA-free adhesive resulted in higher BS, and less frequent droplets entrapped in the adhesive as compared to the mild air-blowing technique [430,445]. So, the clinician must increase the air blowing time, but should note the components of the adhesive in use.

9. *Use of matrix metalloproteinase inhibitors*

Incomplete penetration of the resin into the demineralized dentinal matrix leads to the formation of exposed and water-filled collagen fibrils that are not protected against denaturation problems. These collagen fibrils can be cleaved by endogenous and exogenous collagenolytic enzymes that can be identified immunohistochemically with an Enzyme-Linked Immunosorbent Assay [446]. Host collagenolytic enzymes (MMPs and cysteine cathepsins), also called 'dentin degradomics' play a functional role in resin-dentin bond loss, during and after dentin demineralization. A research in this field is being developed to suggest new directions on the way of preventing their activity [377,447]. Adhesive layers fail because of the formation of micro gaps infiltrated by pathogens [448]. Some of the different strategies proposed to minimize this degradation are: deactivation of endogenous enzymes by using MMP inhibitors [449], reinforcement of collagen fibrils within resin-dentin HL by using crosslinking agents [447], and/or by a combination of both strategies [60].

When a portion of collagen remained unprotected within the HL, a cleavage by endogenous and exogenous collagenolytic enzymes of the family endopeptidases could occur [446]. The MMPs that were described in 1962 are an example of this process. These enzymes are localized in the extracellular matrix and depend on zinc and Ca for their activity [450]. MMPs are characterized by having four domains in their composition: the peptide-signal domain, the propeptide domain (composed of cysteine with its sulfhydryl groups), the catalytic domain (with zinc at the site of catalytic activity together with histidine and Ca residues), and the hemopexin-type domain which is the site where specific tissue inhibitors bind, and serves to bind to the substrate [446,451] (Fig. 22).

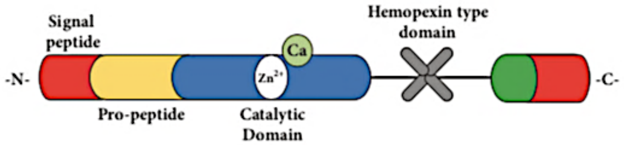


Figure 22: Basic structure of the matrix metalloproteinases [446].

Apart from MMPs, the HL may be affected by a group of enzymes, namely cysteine cathepsins, which are endopeptidases produced by various cell types, including odontoblasts and pulp tissue cells [9]. Cysteine cathepsins hydrolyze the extracellular matrix, particularly in the collagen, and, like MMPs, they appear to be involved in the degradation of the exposed collagen at the bottom of the HL [8].

The knowledge that MMPs and cysteine cathepsins are involved in the degradation process of the HL has led to the search for substances that inhibit the action of these enzymes [8,60].

Several studies have recommended the use of protease inhibitors to extend the durability of resin-dentin bonds [10,389].

CHX, a widely used antimicrobial agent, binds electrostatically to anionic sites of mineralized dentin, preserving resin-dentin bonds for up to 12 weeks [452]. It effectively inhibits MMPs, and some CHX ions are retained within the HL even after 10 years of accelerated aging, although its mild transdentinal toxicity limits its application [453,454]. Epigallocatechin-3-gallate, including a green tea polyphenol, inhibits MMP-2 and MMP-9, improving resin-dentin durability [455]. Other agents like galardin [60], tetracyclines [450], quaternary ammonium salts [456], and EDTA [273] have shown potential in inhibiting MMPs and enhancing bond stability. Commercial products, such as etching gels with benzalkonium chloride [458] and adhesives with incorporated CHX [459], also demonstrate anti-MMP effects, though their long-term efficacy varies.

10. *Use of crosslinking agents*

For years, there have been many attempts to achieve an adequate and predictable adhesion of the composite resin to the tooth structure, since a reliable bond provides high retention strength, less microleakage, and stability of the restoration [460]. Long-term adhesion is a direct result of stability and integrity of collagen fibrils within the resin-dentin HL [447]. That said, in restorative dentistry, the high mechanical properties of collagen are desirable [377]. The resin-tooth interface should also have a lower rate of biodegradation to ensure the longevity of the restoration [2]. The improvement of the mechanical stability and physico-mechanical properties of collagen can be obtained by protecting them through several biomodifications using different collagen crosslinking agents. Pre-treatment of the dentin surface with these agents prior to bonding procedures may help increase BS values and improve stiffness of the resin-dentin bond [377,447]. The covalent crosslinks produced with external crosslinking agents can be very stable over time, thereby inactivating the active sites of the dentin proteases by reducing molecular mobility and inducing conformational changes in their structure or changing the negatively charged ionized carboxyl groups to positively charged amides. This approach aims to strengthen collagen fibrils in HL by intermolecular crosslinking [461]. Correspondingly, many natural and synthetic crosslinking agents offer significant advantages in developing mechanically stable collagen scaffolds and comparing these agents can help in selecting the most effective one for clinical practice [462]. For instance, GA enhances dentin collagen properties but is hindered by its toxicity [463], while carbodiimides like Ethyl-3-[3-dimethylaminopropyl] Carbodiimide Hydrochloride (EDC) provide biocompatibility and improve mechanical properties without residual chemicals [464]. Naturally derived crosslinkers, such as proanthocyanidins [463], tannic acid [465], hesperidin [466], genipin [447], riboflavin [461], and ribose [377], also show promising results by enhancing BS and stability, inhibiting enzymatic degradation, and maintaining mechanical properties, albeit with varying mechanisms and potential drawbacks [462].

11. *Use of electric current to improve monomer impregnation*

An adhesive application protocol based on the use of an electric signal has been introduced by some investigators [467-469]. ULA is proved to be one of the modifications of standard clinical protocols which showed bonding improvements. Many studies demonstrated that ULA improves the dentin BS of both ER and SE adhesives when using an ultrasonic vibrational energy [470,471].

Additionally, it was previously proven that an application assisted by an electric current and the AA of bonding agents improved the dentinal bond performance of the etching mode by facilitating the diffusion of adhesive monomers into the dentinal tubules [403]. Additionally, the application of an adhesive by means of electric current improves the chemical interaction between resin monomers and dental substrate and, therefore, increases monomer infiltration of the demineralized dentin by altering the surface charges and hydrogen bonding potential of the dentin. On that account, dentinal wettability increases, allowing the solvent to evaporate [472]. Furthermore, electrically assisted approaches strengthen dentin bonds and minimize NL in the HL. Despite that, it requires a particular device for the adhesive application that releases the adhesive through an electrical potential difference between the adhesive system and the tooth surfaces [473]. The use of an electric current could promote resin monomer diffusion into the etched dentin as polar constituents like HEMA, polyalkanoic acid, biphenyl dimethacrylates copolymers, and PENTA, found in the adhesive formulation, may interact with the electric field [474]. It has previously been stated that electrical currents promote the mobility of an ionized substrate. Fortunately, it is still unclear if appropriate dentin hybridization may be generated by facilitating the impregnation of ionized substrates in various situations and improving water removal for SE adhesives [174,475]. Next, the application of an electric current may boost the water substitution rate by modifying water dipoles, hence favoring water-solvent exchange throughout resin infiltration [402]. It has been stated that the use of electric currents between a 30 and a 35 μA significantly increased the binding capacity and quality of the bond [80]. Bonding at 35 μA has been shown to be safe for cell viability [473]. Jang et al., [29] studied the effect of various agitation methods on adhesive layer formation of HEMA-free UA (G-Premio Bond (GC, Tokyo, Japan)). AA, PA and ULA were compared as follow:

For the PA mode, G-Premio Bond (GC, Tokyo, Japan) was applied and left undisturbed for 10 s according to the manufacturer's instructions. For the AA mode, G-Premio Bond (GC, Tokyo, Japan) was applied with AA for 10 s. For the ULA mode, G-Premio Bond (GC, Tokyo, Japan) was applied for 10 s with a micro-brush applicator (Kerr, Orange, CA, USA), in which the shank of the micro-brush was continuously touched during its application with a tip of an ultrasonic instrument (Piezon Master 400, EMS, Le Sentier, Switzerland) set at a frequency of 27-30 kHz. The authors concluded that AA or ULA applications provided better bonding performance than the PA application as G-Premio Bond Universal (GC, Tokyo, Japan) is used in the SE mode. Such findings are explained by an increase in the penetration of monomers into the demineralized dentin, which improved both the chemical and the interlocking interaction.

Ideally, the use of an electric current between 30 and 35 μA during the application of ER and SE adhesive systems has been claimed to increase the bonding of an adhesive to dentin by enhancing substrate impregnation [468]. Considering the difficult clinical application and the need of an ultrasonic device for the ULA mode, the AA mode may be a more user-friendly substitute application method for the improved bonding performance of dentin adhesives [29,60].

12. *Field control*

An optimal use of rubber dam isolation prevented contamination of the prepared tooth from saliva, hemostatic agents and/or blood, and enhanced bond durability [133].

Saliva constitutes more than 99% of water and hence causes an excess of moisture, which ultimately lowers the BS [476,477]. It was found that dental substrates contaminated with an organic film of saliva generate a very low surface tension and hinder the wetting of the adhesive, resulting in a lack of good bonding [478]. In addition, saliva contains hydrolytic enzymes such as amylase, collagenase, esterase, and ptyaline, all of which are capable of degrading collagen fibers and proteins, potentially jeopardizing the fundamental stability of the HL due to the formation of a thick smear layer or collagen fiber depletion [476,477,479].

A prior study found that contamination following etching had a negative influence on adhesion; however, blotting and applying a chemical primer may restore the BS [480]. Besides, it has been suggested that dentin contamination with saliva following etching reduces dentin bonding by 40%, and that re-etching is required to improve the BS [481]. Drying without rinsing after saliva contamination may not be effective in eliminating some organic components and salivary glycoproteins because it hinders the resin composite from interacting with the oxygen inhibition layer [482]. In consequence, rinsing is mandatory when the dentin is contaminated with saliva. This is consistent with previous results that found no difference between the non-contaminated (control) and saliva-contaminated groups that were rinsed afterwards [483,484].

Moreover, if contamination occurs after primer application, the primer's hydrophilic properties repel water from saliva, leading to a reduced degree of conversion [485]. Additionally, it has been noted that saliva contamination between etching and bonding, without rubbing the adhesive, could impact the bonding effectiveness to dentin. Therefore, rubbing the adhesive may enhance dentin BS in the presence of saliva [482]. Furthermore, in cases of salivary contamination occurring after adhesive polymerization, water decontamination should be performed, followed by reapplication of the adhesive [486].

Kim et al., [484] studied the effect of saliva decontamination procedures on dentin BS after curing of a universal bonding agent. All-Bond Universal (Bisco, Inc., Schaumburg, Illinois, USA) was used in this study and then subjected to salivary contamination after curing. The authors proposed simply rinsing and drying to restore the SBS to dentin, while re-etching and additional adhesive application proved to be effective in improving the BS.

In summary, (1) rinsing, drying, rebonding; (2) rinsing, air-drying, rebonding; (3) etching, rinsing, blot-drying, rebonding; or (4) etching, rinsing, drying might be adequate for reducing the unfavorable influence of saliva [483].

Blood is made up of macromolecules, proteins, and platelets, which form a layer on the dentin surface due to dentin's affinity for proteins, hindering resin penetration and resulting in shallower RTs development [470]. This was demonstrated by Hoorizad et al. [487], who found that blood or salivary contamination decreases resin-dentin BS in both SE and ER strategies.

Incomplete removal of blood proteins, residual water, or decreased surface tension post-washing can lead to reduced wetting ability of the resin composite surface for subsequent layers [479]. However, rinsing the contaminant substance, particularly blood, in an attempt to boost dentinal bonding strength, failed to restore non-contaminated values [488,489]. Finally, when blood contamination occurs, it is supposed that rinsing and applying an adhesive system improves adhesion to the subsequent composite layer. Moreover, using 5.25% sodium hypochlorite for less than 60 s effectively counteracted the contamination impact, owing to its nonspecific proteolytic ability to remove organic remnants without negatively affecting adhesion [485,490]. Moreover, re-etching facilitates adhesion by altering organic residues, reducing their affinity to the substrate underneath, thus making it an appropriate step for rinsing [491].

An alternative option recommended to counteract the adverse impact of blood contamination on dentin BS involves the use of hemostatic agents as preventive measures. Hemostatic agents such as aluminum chloride, ferric sulfate, and tannic acid are commonly employed to stop bleeding. However, some of these chemicals can reduce the BS of dental adhesives [492]. Typically, these agents are applied around the gingiva, where bleeding is prevalent. Prior studies have demonstrated that aluminum chloride and ferric sulfate dentin contamination can significantly reduce the BS of SE adhesive when compared to normal dentin (uncontaminated) [493,494]. This was related to the agents' proprietary fumed silica, which may have inhibited their acidic activity. Moreover, clinicians should use caution when employing these compounds in esthetic restorations due to the potential for discoloration combined with a reduction in BS [479].

Concerning the use of hemostatic agents in a clinical setting, it is noteworthy that bleeding may appear during various stages of both direct and indirect restoration procedures, such as preparation, gingival retraction, luting, and particularly in cases where a subgingival margin is involved [495,496]. In such scenarios, dental practitioners often apply the hemostatic agent to all surfaces of the teeth, leading to significant surface exposure to the agent rather than blood contamination [497]. However, due to the detrimental effect of hemostatic agents on the BS of resin-based materials, their application is not recommended in cases of blood contamination. Some experts recommend applying EDTA or CHX in order to reestablish the BS between dentin and a resin composite in cases of accidental surface contamination with a hemostatic substance [493,498].

All in all, to restore the quality of the bond after contamination, decontamination methods can include rinsing and drying followed by re-application of adhesive, drying the contaminants before re-applying adhesive, or performing re-etching and re-bonding [499].

13. Selective dentin etching

UAs systems have attracted considerable research interest in recent years, as they can be used in SE, ER, and selective-etching modes. Outstandingly, the capacity to use this new class of adhesives, regardless of dentin condition, brings up unexplored opportunities concerning resin-dentin bonding to a selectively etched substrate [500]. Van Meerbeek et al., [263] suggested that protecting collagen from hydrolysis and early degradation of bond could be achieved by keeping the HAp around collagen fibrils.

Recently, a new approach known as "Selective dentin etching" (SDE) orchestrated to improve bonding to dentin by preserving HAp crystals inside the hard-to-reach intrafibrillar collagen spaces [383] (Fig. 23).

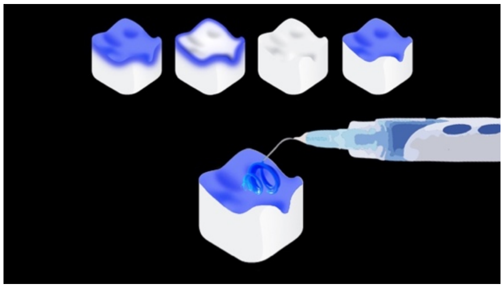


Figure 23: Selective dentin etching [383].

This technique is based on the application of H_3PO_4 during 3 s in dentin, which after rinsing and drying, leaves a partially demineralized substrate. This method has been recognized as an alternative for increasing the BS of UAs to dentin over time. Aside from improving resin-dentin BS, this modality had no negative impact on the HL integrity after challenging the bonded interface by thermocycling or long-term aging [500].

So far, etching time remains debatable, with durations ranging from 3 to 15 s (3, 5, 10 or 15 s). However, only a few studies in the literature have addressed this approach.

In 2016, Takamizawa et al., [501] determined the influence on dentin bonding of H_3PO_4 pre-etching times before the application of SE adhesives. They concluded that reducing H_3PO_4 pre-etching time can minimize the adverse effect on dentin bonding durability for the conventional SE adhesives. Also, a short H_3PO_4 pre-etching time enhances the dentin bonding performance of UAs.

In 2018, Stape et al., [500] evaluated whether SDE protocols using reduced H_3PO_4 etching-times would affect the resin-dentin interaction of a universal bonding agent to improve long-term bonding effectiveness. They advised that UAs used in SE mode produce superior long-term dentin bonding compared to the ER mode, and SDE for 3 s with conventionally used H_3PO_4 improves dentin bonding effectiveness.

In 2019, Kharouf et al., [502] evaluated the influence of etching with the rubbing technique on the BS of a universal bonding agent to dentin. They demonstrated that dentin etched with H_3PO_4 for 3 s in the ER mode with the rubbing technique for a universal adhesive (UA) system decreases the μTBS of the composite to dentin. Additionally, they confirmed that SDE with 37% H_3PO_4 for 3 s without rubbing motion before applying a UA is recommended to enhance bonding effectiveness.

In 2021, Stape et al., [503] characterized whether the bonding performance and fatigue strength of resin-dentin interfaces created by a UA would be affected by different H_3PO_4 application times to assess long-term durability more accurately. They established that smear layer removal with H_3PO_4 substantially improved the endurance limits for such bonded interfaces, especially for shorter dentin-etching times. Conventional H_3PO_4 dentin-etching improved the fatigue strength; though, such advantages could be surpassed by the overexposure of collagen fibrils and subsequent endogenous proteolytic hydrolysis on the long-term. Hence, the answer to the clinical dilemma of whether to etch or not to etch dentin, considering solely the adhesive interface quality of UAs, may reside on a less-aggressive separate etching approach.

In 2021, Hardan et al., [383] assessed the influence of AA for different time intervals after SDE for 3 s on the μTBS to dentin of two UAs. They discovered that SDE and AA improved the μTBS only for a HEMA-containing UA.

In 2022, Stape et al., [504] determined whether smear layer management, via conservative etching protocols, and the hydrophobic-rich content of HL would affect the fatigue strength of resin-dentin interfaces. They stated that current simplification trends in resin-dentin bonding constitute a trade-off between hybridization quality and easier adhesive handling. Controlled dentin etching and increasing the hydrophobic-rich content of HL could be essential to extend the longevity of mild UAs.

In 2024, Stape et al., [505] investigated the effects of extending dentin etching and the hydrophobic-rich content of hybrid layers on the fatigue strength of a mild UA after long-term aging. They observed that long-term hydrolysis has a detrimental effect on the fatigue strength of resin-dentin interfaces. The study emphasized the importance of employing less aggressive ER protocols and developing hybrid layers with higher hydrophobic content to improve the durability of mild UAs. Consequently, current trends toward oversimplification in adhesive dentistry may compromise resin-dentin bonding performance.

In spite of this, the authors of a former review believe that the allocated term SDE may confuse researchers. They propose *short dentin etching* as a more appropriate name for etching times of less than 15 s [146]. This approach may reduce the danger of unintentional dentin etching while retaining most minerals required for successful adhesion. Nevertheless, manipulating etchant for such a short length of time might be clinically demanding, and more studies are needed to find an etching technique that combines clinical needs with HAp preservation.

The viscosity of the etchant should also be considered when employing the aforementioned SDE modality, as a more viscous product enables for selective application of the etchant, lowering the chance of mishandling. Due to the heterogeneity of the dental substrate, which makes H_3PO_4 etching highly unpredictable, it would be beneficial to have a "universal etchant" qualified of effectively etching enamel and dentin concurrently. Such a material might be advantageous in difficult clinical situations such as deep posterior proximal cavities, where assessing leftover enamel and ensuring optimal bonding conditions can be problematic [3,146,383].

So, after showing the literature assessing the use of SDE for 3 s on dentin substrate, clinician could choose this approach in their daily clinical practice by taking into consideration the viscosity of the etchant. A new protocol: SDE for 3 s with ER technique is recommended before applying the UAs on the dentin surface in order to improve BS [500,501].

14. *Enhanced dentin impregnation using a scrubbing technique*

Increasing the application time of adhesive systems with a vigorous brushing method has the potential to boost dentin impregnation of resin monomers into dentinal tubules [33,60]. Hardan et al., [403] advocated the use of scrubbing motion when bonding to dentin to improve the immediate and aged BS. Moritake et al., [28] studied the effect of AA on bond durability of three UAs (All-Bond Universal (Bisco, Inc., Schaumburg, Illinois, USA), Adhese Universal (Ivoclar Vivadent, Schaan, Liechtenstein), and Scotchbond Universal (3M ESPE, St. Paul, MN, USA)). All adhesives tested are subjected to the following bonding procedure:

1) ER mode with AA; 2) ER mode with inactive application; 3) SE mode with AA; and 4) SE mode with inactive application.

Moritake et al., [28] concluded that the AA of UAs enhanced dentin bond durability of the etching mode by facilitating the penetration of adhesives into the branches of dentin tubules. Additionally, Carrilho et al., [205] proposed an adhesive application technique involving scrubbing, which enhances the impregnation of monomers into the smear layer, facilitates solvent evaporation, and thereby enhances the quality of the adhesive interface. The same finding was observed by Velasques et al., [506] who showed that AA of SE adhesive could enhance bonding as a mechanism similar to that of ER bonding agents by increasing the interaction of acidic monomers into the tooth structure and dispersing etching byproducts through the HL. Velasques et al., [506] brought attention to the fact that modifying the application time of the adhesive could influence BS. Insufficient etching and penetration of the substrate by acidic monomers may occur if a short application time is used. As a consequence, poor BS may have been generated. Furthermore, Irmak et al., [507] proposed that the rubbing action elucidates the process, revealing that it decreases the degradation rate of the HL by facilitating the penetration of resin monomers into the collagen fibrils. This highlights why manufacturers of certain adhesives advocate for an AA method. Consequently, the performance of these adhesives may vary when applied without rubbing [508]. Aside from that, after manually applying force through a rubbing motion with adhesive onto the dentinal tissue, dentin exhibits characteristics similar to a sponge, with the dentin collagen network being compressed. Compressed collagen expands when pressure is relieved, and the penetration of resin monomers into the collagen network is promoted. This method does not require any additional steps. Overall, agitation of the adhesive increases the kinetics of the moieties and allows for better distribution of monomers inward; however, the solvents spread outward [403,508].

15. *Biomimetic remineralization*

In 2008, Tay and Pashley., [509] introduced a guided tissue-remineralization technique to repair HL and prevent degradation within adhesive-dentin interfaces. However, its *in vivo* applicability remains unclear [33,510]. In response, Daoud U and Fawzy A., [511] proposed high-intensity focused ultrasound (HIFU) for dentin-substrate biomodification, showing potential for improving remineralization. They suggest HIFU as a minimally invasive technique capable of delivering HAp nanorods into etched dentin substrates, enhancing remineralization potential. This research emphasizes HIFU's impact on HAp formation and synthesis, distinguishing it from studies involving complete demineralization of dentin with less aggressive acids. Exploring dental remineralization techniques offers promise for minimally invasive restorative procedures, potentially reducing the need for extensive tissue removal in deep caries lesions [33].

16. Dentin pre-treatment with airborne particle abrasion

In modern adhesive dentistry, airborne particle abrasion (APA) is commonly recommended to finish cavity preparation for adhesive restorations. APA has become more convenient with devices that combine abrasive particles and water to control their dispersion [512]. Aluminum oxide (AO) powder, available in 30 and 50 µm sizes, is frequently used for this purpose. It enhances surface roughness and wetting ability, aiding in micro-mechanical retention [513]. While a prior study generally shows no adverse effect on enamel BS, evidence regarding its impact on dentin BS is conflicting [512]. Positive effects on dentin bonding have been reported [514], while others suggest a decrease in BS [515], especially with SE adhesives. However, indications from research suggest that AO air-abrasion is safe for dentin bonding, with no impairment noted [513].

In addition to AO powders, there are fewer abrasive powders used to clean cavity preparations and remove biofilm, plaque, or stains before restoring teeth with adhesive materials. These include sodium bicarbonate, calcium carbonate, aluminum trihydroxide, bioactive glass, glycine, and erythritol [513,516,517]. It was demonstrated that sodium bicarbonate air polishing can lead to decreased dentin BS, particularly with SE adhesives. Similar effects were observed with calcium bicarbonate and erythritol in combination with different adhesives. However, air polishing with bioactive glass and glycine did not have a negative impact on dentin BS. The significant variation in dentin bonding effectiveness across different *in vitro* studies can be attributed to the wide variety in study designs [513]. Numerous parameters impact the cutting efficiency of airborne abrasion devices, including pressure, duration of air-abrasion or polishing, distance, angle towards the dentin surface, type of dentin, nozzle diameter, powder flow rate, water shrouding flow rate, type of powder, and particle size. These parameters vary significantly between studies, and some studies do not even specify certain parameters. Moreover, the type of BS test conducted influences the final result [513,517]. Currently, there is limited literature available evaluating the effect of air-abrasion or polishing on dentin BS over time.

A previous study investigated how APA affects the strength of bonds between adhesive materials (UA) and dentin, using different air-abrasion and polishing powders. The results showed that when using a UA, applying it with the ER mode is better than the SE mode for bonding to air-abraded or polished dentin. This preference is supported by the fact that none of the air-abrasion or polishing powders had a negative effect on BS when using the ER mode. Additionally, the UA maintains good bonding effectiveness with dentin even after aging. Furthermore, air polishing with bioactive glass presnted a positive impact on dentin BS when using the UA in both application modes [513]. In summary, the effectiveness of air-abrasion in bonding to dentin can vary depending on various factors such as the type of adhesive used, the specific parameters of the air-abrasion procedure, and the type of dentin being treated. While some studies suggest that air-abrasion can enhance micro-mechanical retention and improve BS to dentin, others report conflicting results. Overall, air-abrasion may be effective in certain situations and when used with appropriate techniques, but further research is needed to fully understand its impact on dentin bonding [513,516,517].

All things considered; the clinician should use some application modalities that differ from the manufacturer's recommendations to strengthen the BS of resin-based materials to dentin. The application modalities that favored the overall BS to dentin were: hydrophobic resin layer, double adhesive application time, NTAP, EWB, AWB, multiple coat of adhesive application (2 layers and more), warm air stream on the primer or the adhesive system, curing time extended to up to 40 s, prolonged air-drying, previous application of MMP inhibitors, application of different crosslinking agents, application assisted by an electric current appropriate isolation approach, SDE for 3 s, scrubbing technique, biomimetic remineralization, and APA in specific adhesion strategies [25,383,403,512].

1.9. Research Methodology-The Essentials

The current thesis evaluated the effect of different modalities of adhesive systems on dentin. For these purposes various methodologies were used and will be explained as follows.

- µTBSs of the samples were analyzed in a universal testing machine at a crosshead speed of 1mm/min. The load required to dislodge each slab was recorded in MPa by dividing the force of debonding by the cross-sectional surface area of the specimen. N.B: The specimens were sectioned perpendicular to the bonded surface to expose the adhesive interface and to obtain 1 mm thick resin-dentin slabs. From each tooth, 12 to 14 slabs were obtained from the mid-coronal dentin. (A precise cutting procedure in order to cut each section and to expose dentin was realized by the machine « EXAKT Vertriebs GmbH, Norderstedt, Germany »).

  For each tooth, the results obtained from the beams examined were averaged, and the mean attained was then used for statistical determinations.

  - It is essential to test the strength of an adhesive under conditions similar to those in the oral cavity. For this reason, tensile BS is typically considered the most appropriate for adhesive systems [518].
  - Sano et al., [243] were the first to develop the µTBS test due to its crucial advantage of providing better stress distribution at the true interface. Because of that, this test was used in this study while respecting the guidelines for *in vitro* testing: use of flat dentin surface as a standard sample preparation method, yet, cavities are recommended for specific study purposes, aqueous storage of microspecimens (sticks) with direct water exposure or by preference in artificial saliva irrespective of the storage period, a minimum number of five teeth per experimental/control group, and a minimum number of 15 specimens per experimental/control group [519,520].
  - µTBS tends to be much higher (often 2× to 4×) than that of macro TBS values because of the defect concentration in the small cross-sectional interfacial areas is lower. “Micro” TBS requires additional research designs that “macro” tests do not, such as the elimination of tooth dependency through balanced designs and has shown reduced test variance. Accordingly, macro TBS is noticeably less commonly used test, therefore µTBS was chosen in this study [519,521].

- While μTBS was more sensitive than tensile and shear testing, it was also less expensive to perform. Given that a large number of specimens can be produced with a small amount of material, it allows for a more precise observation of the bonding between restorative materials and clinically applicable substrates by selecting specimens without bubbles and other defects, making it more reliable than shear and tensile tests. The specimens must be cut into slabs and then sectioned into a stick with a thickness of approximately 1 mm. Each stick contained substrates of tooth structure and resin composite that were bonded together and evaluated at the interface. Specimens might be prepared with either a non-trimming bar shape or trimmed with a bur at the bonding site to create an hourglass profile, which reduces the bonding area and concentrates stress at the bonding site [518,522].
- Studies showed contradictory results regarding the effects of the crosshead speed on the SBS and TBS. For example, Sood et al., [523] indicated that crosshead speed variation between 0.5 and 10 mm/min did not have an influence on diametral tensile strength of a resin composite. However, another study reported statistically higher BSs for specimens loaded at 1.0 and 5.0 mm/min compared to 0.5 and 0.75 mm/min [524]. Regarding the effect of crosshead speed on μTBS, many studies showed that it seems to be minimal [525,526]. Accordingly, this thesis employed a crosshead speed of 1 mm/min.
- Adhesion to tooth structure should ideally give retentive strength, a marginal seal, be simple to create, and be clinically durable. The authors recommended the μTBS test, particularly following a durability challenge, as a suitable surrogate assessment for dental composite restorative retention [519,527] (Fig. 24).

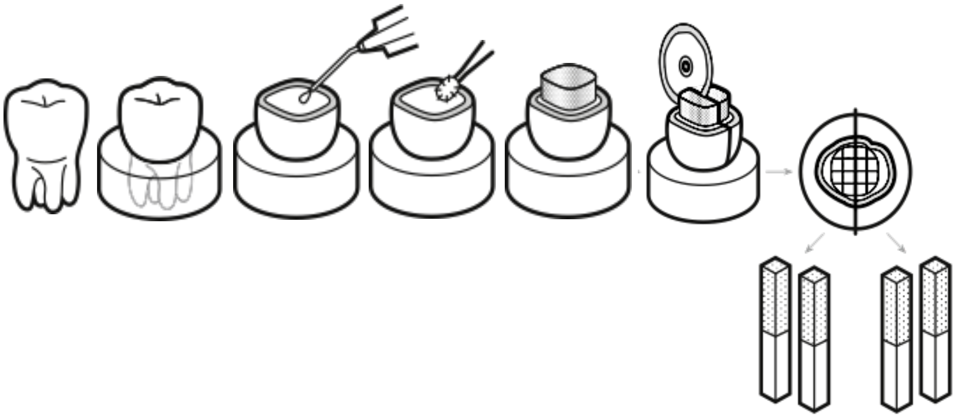


Figure 24: Schematic illustrating the successive steps of tooth mounting and bonding [519].

- All fractured portions were fixed to the aluminum stubs and observed under an optical numeric microscope (Keyence, Osaka, Japan) at 150× magnification to recognize the failure mode in each specimen. To understand why bonding fails, the researcher must need first to define the ways the failure can occur. There are two options for failure analysis:

    - Estimate area-% per failure mode ('Adhesive at interface', 'Cohesive in composite', 'Cohesive in bonding', 'Cohesive in dentin') per micro-sample. As an alternative, employ image analysis for semi-quantitative measurement (time-consuming).

  - Categorize micro-specimens based on their failure mode ('Adhesive at interface', 'Cohesive in composite', 'Cohesive in bonding', 'Cohesive in dentin', 'Mixed involving interfacial de-bonding') [519]. The latter was applied in this thesis (Fig. 25).

-

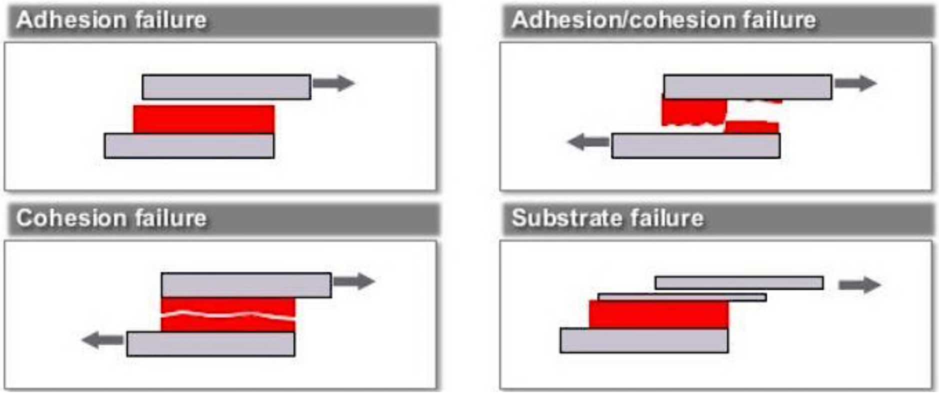


Figure 25: Representative images of the failure mode after the bond strength test.

- The specimens were viewed using a Quanta 250 FEG scanning electron microscopy (SEM) (FEI Company, Eindhoven, The Netherlands) operated at an accelerating voltage of 10 kV at different magnifications.

  - Micro-morphological analysis of the HL can be performed using either SEM, transmission electron microscopy (TEM), or confocal laser scanning microscopy.
  - Unlike traditional optical microscopy, SEM does not illuminate the specimen using visible light. A beam of electrons is generated to provide energy [528] (Fig. 26).

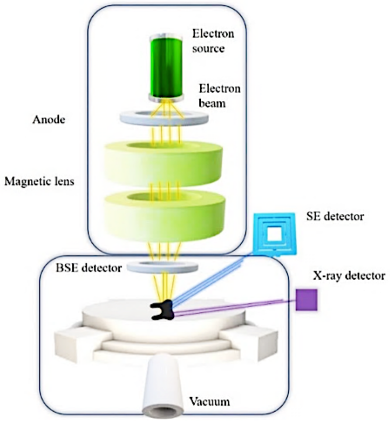


Figure 26: Principe of scanning electron microscopy [528].

Since electron waves are 10^5 times shorter in length than visible light waves, this approach allows for higher resolution photographs. The observer may obtain 10^7× magnification, while light microscopes are limited to a maximum magnification of 2000× [529]. The beam of electrons comes into contact with the specimen molecules, resulting in the release of energy [528].

  - The rationale of the use of SEM in this thesis is its frequent and essential use for investigations of tooth structure, and bonding mechanisms. It allows for a better understanding of complexity and 3D variations of the tooth structure [81,530].

- The wettability of adhesives was evaluated with an optical tensiometer (Biolin Scientific, Espoo, Finland) following a sessile drop method.

  - There are many factors which influence adhesion: wetting, substrate variations, dentin humidity, C-factor, teeth situation, and age of the patient (sclerotic dentin). Knowing that wettability of bonding system can differ from system to another, and knowing that there is a longstanding interest in the relation between the adhesion and BS. Although, the exact nature of the relation has not been elucidated, that said, practical experience with adhesive bonding has shown that an increase in the work of adhesion usually leads to an increase in the work of fracture. For ER adhesives, evidence was found about the relation between wettability and BS (higher wettability implies higher BS). However, there is no clear relationship between the CA of SE primer and BS [531].
  - Optimal wettability of solid surfaces is critical for adhesion. The spontaneous spread of a liquid on a solid surface is referred to as its wettability. In the case of dentin adhesives, high wettability indicates intimate adhesive-dentin contact, which leads to improved adherence. Adhesive wettability can be determined by measuring the CAs of adhesive drops on flat dental surfaces. The lower the CA, the higher the wettability [112,235].
  - The viscosity of the adhesive, surface roughness, and substrate heterogeneity all have an effect on the CA. Substrates with high wettability have more surface energy than the liquid's surface tension [532].
  - Adequate CA between the adherent and adhesive is necessary to provide adhesion [110]. Hence, the CA analysis was employed to analyze the wettability of the adhesives and how the application modality affects this wettability (Fig. 27).

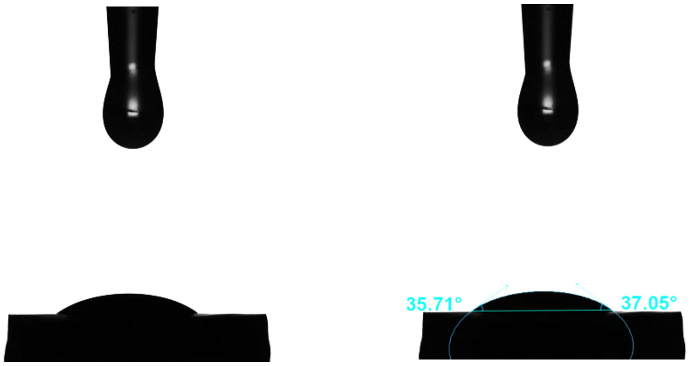


Figure 27: Principe of contact angle of an adhesive on the dentin surface.

- The solvent evaporation rate of each adhesive system used in this thesis was recorded with the protocols of different air-dry temperature (20°C, 40°C, and 60°C). This was done in an analytical balance (Mettler, type H6; Columbus, OH, USA; capacity to 160 g) (Fig. 28).

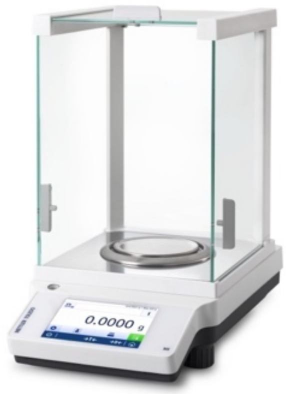


Figure 28: Analytical balance used to record the solvent evaporation rate.

- Solvent evaporation is typically achieved by agitating the adhesive over dentin/enamel surfaces, followed by solvent evaporation using compressed air. Fortunately, solvents must be removed when they have served their purpose because residual solvents have been shown to deteriorate the adhesive interface by interfering with resin polymerization and lowering mechanical characteristics [334,372,421,434].
- Manufacturers have added volatile solvents such as ethanol or acetone to dental adhesives to assist the mixing of hydrophilic and hydrophobic monomers and avoid phase separation between these elements [33]. Because these organic solvents demonstrate higher vapor pressure compared to water, they are considered to be crucial in facilitating the displacement of water from the demineralized dentin matrix; guaranteeing better monomer penetration into the micro- and nano-porosities left between the collagen fibrils and, therefore, strengthening resin micro-retention to dentin [7,9,33,112,174,209].
- The finding that resin-bonded dentin is not as adequately sealed as dentin covered with a smear layer raises questions about whether dental adhesives can ever properly seal dentin [533]. Attempts to evaporate solvents from resin-infiltrated dentin appear to leave nanometer-sized holes filled with water. It is envisaged that during dentin hybridization with hydrophilic monomers, all solvent and water will be entirely removed from the collagen interfibrillar gaps, ensuring optimum monomer infiltration/conversion. Further, it has been demonstrated that, among other parameters, water sorption of adhesives and resin-dentin interfaces is influenced by the existence of residual solvent inside these structures and the degree of adhesive hydrophilicity. Consequently, the presence of remaining solvent, along with the application of hydrophilic co-monomers on wet dentin, may undermine the criteria for complete sealing and long-term coupling between resin composites and resin-bonded dentin [435,534-536]. That being the case, solvent evaporation rate was used in this research.

This literature review highlights various strategies available to enhance the longevity of adhesive systems, such as extending light-curing time, prolonging application time, actively applying bonding agents, using multiple adhesive layers, prolonging air-drying, and utilizing warm air streams on the primer or adhesive. Consequently, clinicians should consider recommending techniques like ABT, MLA (with 2 layers or more), and warm air for solvent evaporation in their daily practice to improve BS of adhesive systems to dentin. However, the absence of a specific protocol for achieving stable and optimal adhesion remains a challenge in dental practice. Therefore, these modalities (ABT, MLA, and warm air) are chosen for their demonstrated effectiveness in enhancing BS, as indicated by previous studies. Moreover, they are modified (using different application modalities: PA, AA, CV, and CVM; employing different layer applications: single active application (A) and triple adhesive layer application including Active–Passive–Passive (APP); Active–Active–Passive (AAP); and Active–Active–Active (AAA); and implementing protocols for air-dry temperatures of 20 °C, 40 °C, and 60 °C) in this thesis.

1.10. Conclusions

Adhesive agents have advanced beyond technique simplicity, and their current progress is prompted by versatility. To aid decision-making, general dentists ought to remain up-to-the-minute on the ever-changing adhesive agents. Adhesive dental agents are commonly classified into three categories: ER, SE, and UAs. ER adhesives are available in three-step and two-step varieties, whilst SE adhesives are available in two-step and one-step versions. The pH of SE adhesives has a considerable effect on their bonding ability. UAs provide versatility by allowing dentists to choose an application method (ER, SE, or selective-etch) dependent on the substrate and clinical scenario. ER adhesives generally have high bond effectiveness. They still demand cautious technique and may be sensitive to dentin moisture levels. SE adhesives are popular among clinicians due to their superior efficiency and lessened method sensitivity. UAs offer an array of benefits of both processes, combining the advantages of ER and SE adhesives. However, the efficiency of UAs on dental hard tissues and indirect restorative materials is material dependent, as some adhesives are not intended to adhere to all types of restorative materials.

Recognizing each category's features and limitations is crucial for successful bonding and dental restorations. Ongoing adhesive research and enhanced performance will help to advance the field of adhesive dentistry. As a result of that, the practitioner needs to stay bang up-to-date.

Supplementary, companies have been making continuing progress in the development of innovative dentin adhesives with the goal of easing the process and improving clinical outcomes, which correlates to their stability with time and BS efficiency. Even though simplicity of adhesive systems has been linked to a loss of effectiveness, efforts have been made to advance the chemistry of the latest adhesives.

It is unclear if adhesives have reached a clinical performance level that can still be enhanced, particularly given the established higher efficiency of gold-standard adhesives. Perhaps clinicians are unaware that it has achieved a success rate exceeding 90% of what can be achieved with dental adhesion. To clinically differentiate adhesives in terms of bonding implementation, a substantially longer follow-up is now required to detect differences in their clinical outcomes across the most recent adhesive generations, even when compared to previous gold-standard multi-step adhesives. The new adhesive solutions can also be ascribed to their capacity to reduce or eliminate postoperative sensitivity, improve marginal seal, reduce microleakage, and increase resin flow into the fissure. The evolution of functional monomers with a strong and stable chemical affinity to HAp is unquestionably a beneficial direction in the pursuit of enhancing dentin adhesion.

The challenge lies in the absence of a gold-standard approach for achieving stable and optimal adhesion of adhesive systems to dentin. Moreover, numerous researchers have proposed various methods to enhance BS. Importantly, the rationale behind this thesis was to evaluate modalities for achieving superior and prolonged adhesion of resin composite to dentin, ultimately aiming to develop cost-effective, easy-to-use, and quick-to-place approaches for adhesive systems.

1.11. References

1. Van Meerbeek, B.; Peumans, M.; Poitevin, A.; Mine, A.; Van Ende, A.; Neves, A.; De Munck, J. Relationship between bond-strength tests and clinical outcomes. *Dent. Mater*. **2010**, *26*, e100-21. doi:10.1016/j.dental.2009.11.148.
2. Cardoso, M.V.; de Almeida Neves, A.; Mine, A.; Coutinho, E.; Van Landuyt, K.; De Munck, J.; Van Meerbeek, B. Current aspects on bonding effectiveness and stability in adhesive dentistry. *Aust. Dent. J.* **2011**, *56*, 31-44. doi:10.1111/j.1834-7819.2011.01294.x.
3. Perdigão, J. Current perspectives on dental adhesion: (1) Dentin adhesion - not there yet. *Jpn. Dent. Sci. Rev.* **2020**, *56*, 190-207. doi:10.1016/j.jdsr.2020.08.004.
4. Breschi, L.; Maravic, T.; Cunha, S.R.; Comba, A.; Cadenaro, M.; Tjäderhane, L.; Pashley, D.H.; Tay, F.R.; Mazzoni, A. Dentin bonding systems: From dentin collagen structure to bond preservation and clinical applications. *Dent. Mater.* **2018**, *34*, 78-96.
5. Paken, G.; Çömlekoğlu, M.E.; Sonugelen, M. Detection of the hybrid layer biodegradation initiation factor with a scanning electron microscope. *Microsc. Res. Tech*. **2021**, *84*, 2166-2175. doi:10.1002/jemt.23771.
6. Takamizawa, T.; Imai, A.; Hirokane, E.; Tsujimoto, A.; Barkmeier, W.W.; Erickson, R.L.; Latta, M.A.; Miyazaki, M. SEM observation of novel characteristic of the dentin bond interfaces of universal adhesives. *Dent. Mater.* **2019**, *35*, 1791-1804. doi:10.1016/j.dental.2019.10.006.
7. Bourgi, R.; Hardan, L.; Rivera-Gonzaga, A.; Cuevas-Suárez, C.E. Effect of warm-air stream for solvent evaporation on bond strength of adhesive systems: A systematic review and meta-analysis of in vitro studies. *Int. J. Adhes. Adhes*. **2021**, *105*, 102794. doi:10.1016/j.ijadhadh.2021.102794.
8. Frassetto, A.; Breschi, L.; Turco, G.; Marchesi, G.; Di Lenarda, R.; Tay, F.R.; Pashley, D.H.; Cadenaro, M. Mechanisms of degradation of the hybrid layer in adhesive dentistry and therapeutic agents to improve bond durability--A literature review. *Dent. Mater.* **2016**, *32*, e41-53. doi:10.1016/j.dental.2015.11.007.
9. Sofan, E.; Sofan, A.; Palaia, G.; Tenore, G.; Romeo, U.; Migliau, G. Classification review of dental adhesive systems: From the IV generation to the universal type. *Ann. Stomatol.* (Roma) **2017**, *8*, 1-17. doi:10.11138/ads/2017.8.1.001.
10. Pashley, D.H.; Tay, F.R.; Breschi, L.; Tjäderhane, L.; Carvalho, R.M.; Carrilho, M.; Tezvergil-Mutluay, A. State of the art etch-and-rinse adhesives. *Dent. Mater*. **2011**, *27*, 1-16. doi:10.1016/j.dental.2010.10.016.
11. Moszner, N.; Hirt, T. New polymer-chemical developments in clinical dental polymer materials: Enamel-dentin adhesives and restorative composites. *J. Polym. Sci. Part A Polym. Chem.* **2012**, *50*, 4369-4402. doi:10.1002/pola.26258.
12. Vermelho, P.M.; Reis, A.F.; Ambrosano, G.M.; Giannini, M. Adhesion of multimode adhesives to enamel and dentin after one year of water storage. *Clin. Oral Investig.* **2017**, *21*, 1707-1715. doi:10.1007/s00784-016-1966-1.
13. Yoshihara, K.; Nagaoka, N.; Hayakawa, S.; Okihara, T.; Yoshida, Y.; Van Meerbeek, B. Chemical interaction of glycero-phosphate dimethacrylate (GPDM) with hydroxyapatite and dentin. *Dent. Mater.* **2018**, *34*, 1072-1081. doi:10.1016/j.dental.2018.04.003.
14. Van Meerbeek, B.; Yoshihara, K.; Yoshida, Y.; Mine, A.; De Munck, J.; Van Landuyt, K.L. State of the art of self-etch adhesives. *Dent. Mater.* **2011**, *27*, 17-28. doi:10.1016/j.dental.2010.10.023.
15. Arandi, N.Z. The Classification and Selection of Adhesive Agents; an Overview for the General Dentist. *Clin. Cosmet. Investig. Dent*. **2023**, *15*, 165-180. doi:10.2147/CCIDE.S425024.
16. Hurtado, A.; Fuentes, V.; Cura, M.; Tamayo, A.; Ceballos, L. Long-Term In Vitro Adhesive Properties of Two Universal Adhesives to Dentin. *Materials* **2023**, *16*, 3458. doi:10.3390/ma16093458.
17. Dressano, D.; Salvador, M.V.; Oliveira, M.T.; Marchi, G.M.; Fronza, B.M.; Hadis, M.; Palin, W.M.; Lima, A.F. Chemistry of novel and contemporary resin-based dental adhesives. *J. Mech. Behav. Biomed. Mater.* **2020**, *110*, 103875. doi:10.1016/j.jmbbm.2020.103875.

18. Yiu, C.K.; Pashley, E.L.; Hiraishi, N.; King, N.M.; Goracci, C.; Ferrari, M.; Carvalho, R.M.; Pashley, D.H.; Tay, F.R. Solvent and water retention in dental adhesive blends after evaporation. *Biomaterials* **2005**, *26*, 6863-6872. doi:10.1016/j.biomaterials.2005.05.011.
19. Al-Salamony, H.; Naguib, E.A.; Hamza, C.S.; Younis, S.H. The Effect of Warm Air Solvent Evaporation on Microtensile Bond Strength of Two Different Self-Etch Adhesives to Dentin (In Vitro Study). *Sylwan* **2020**, *164*, 479.
20. Ferreira, J.C.; Pires, P.T.; Azevedo, A.F.; Oliveira, S.A.; Melo, P.R.; Silva, M.J. Influence of solvents and composition of etch-and-rinse and self-etch adhesive systems on the nanoleakage within the hybrid layer. *J. Contemp. Dent. Pract.* **2013**, *14*, 691-699. doi:10.5005/jp-journals-10024-1386.
21. Chimeli, T.B.; D'Alpino, P.H.; Pereira, P.N.; Hilgert, L.A.; Di Hipólito, V.; Garcia, F.C. Effects of solvent evaporation on water sorption/solubility and nanoleakage of adhesive systems. *J. Appl. Oral Sci.* **2014**, *22*, 294-301. doi:10.1590/1678-775720130653.
22. El-Askary, F.S.; Van Noort, R. Effect of air-drying pressure and distance on microtensile bond strength of a self-etching adhesive. *J. Adhes. Dent.* **2011**, *13*, 147-153. doi:10.3290/j.jad.a18782.
23. Cadenaro, M.; Maravic, T.; Comba, A.; Mazzoni, A.; Fanfoni, L.; Hilton, T.; Ferracane, J.; Breschi, L. The role of polymerization in adhesive dentistry. *Dent. Mater.* **2019**, *35*, e1-e22. doi:10.1016/j.dental.2018.11.012.
24. Klein-Junior, C.A.; Sobieray, K.; Zimmer, R.; Portella, F.F.; Reston, E.G.; Marinowic, D.; Hosaka, K. Effect of heat treatment on cytotoxicity and polymerization of universal adhesives. *Dent. Mater. J.* **2020**, *39*, 970-975. doi:10.4012/dmj.2019-103.
25. Hardan, L.; Bourgi, R.; Kharouf, N.; Mancino, D.; Zarow, M.; Jakubowicz, N.; Haikel, Y.; Cuevas-Suárez, C.E. Bond Strength of Universal Adhesives to Dentin: A Systematic Review and Meta-Analysis. *Polymers* **2021**, *13*, 814. doi:10.3390/polym13050814.
26. Ekambaram, M.; Yiu, C.K.Y.; Matinlinna, J.P. An overview of solvents in resin-dentin bonding. *Int. J. Adhes. Adhes.* **2015**, *57*, 22-33. doi:10.1016/j.ijadhadh.2014.10.001.
27. Carvalho, C.N.; Lanza, M.D.S.; Dourado, L.G.; Carvalho, E.M.; Bauer, J. Impact of Solvent Evaporation and Curing Protocol on Degree of Conversion of Etch-and-Rinse and Multimode Adhesives Systems. *Int. J. Dent.* **2019**, *2019*, 5496784. doi:10.1155/2019/5496784.
28. Moritake, N.; Takamizawa, T.; Ishii, R.; Tsujimoto, A.; Barkmeier, W.W.; Latta, M.A.; Miyazaki, M. Effect of Active Application on Bond Durability of Universal Adhesives. *Oper. Dent.* **2019**, *44*, 188-199. doi:10.2341/17-384-L.
29. Jang, J.H.; Jeon, B.K.; Mo, S.Y.; Park, M.; Choi, D.; Choi, K.K.; Kim, D.S. Effect of various agitation methods on adhesive layer formation of HEMA-free universal dentin adhesive. *Dent. Mater. J.* **2019**, *38*, 101-106. doi:10.4012/dmj.2018-031.
30. Perdigão, J.; Araujo, E.; Ramos, R.Q.; Gomes, G.; Pizzolotto, L. Adhesive dentistry: Current concepts and clinical considerations. *J. Esthet. Restor. Dent.* **2021**, *33*, 51-68. doi:10.1111/jerd.12692.
31. Chowdhury, A.F.M.A.; Saikaew, P.; Alam, A.; Sun, J.; Carvalho, R.M.; Sano, H. Effects of Double Application of Contemporary Self-Etch Adhesives on Their Bonding Performance to Dentin with Clinically Relevant Smear Layers. *J. Adhes. Dent.* **2019**, *21*, 59-66. doi:10.3290/j.jad.a41986.
32. Ito, S.; Tay, F.R.; Hashimoto, M.; Yoshiyama, M.; Saito, T.; Brackett, W.W.; Waller, J.L.; Pashley, D.H. Effects of multiple coatings of two all-in-one adhesives on dentin bonding. *J. Adhes. Dent.* **2005**, *7*, 133-141.
33. Van Meerbeek, B.; Yoshihara, K.; Van Landuyt, K.; Yoshida, Y.; Peumans, M. From Buonocore's Pioneering Acid-Etch Technique to Self-Adhering Restoratives. A Status Perspective of Rapidly Advancing Dental Adhesive Technology. *J. Adhes. Dent.* **2020**, *22*, 7-34.
34. Yoshida, Y.; Nagakane, K.; Fukuda, R.; Nakayama, Y.; Okazaki, M.; Shintani, H.; Inoue, S.; Tagawa, Y.; Suzuki, K.; De Munck, J.; Van Meerbeek, B. Comparative study on adhesive performance of functional monomers. *J. Dent. Res.* **2004**, *83*, 454-458. doi:10.1177/154405910408300604.
35. Zheng, H.; Shi, Y.; Bi, L.; Zhang, Z.; Zhou, Z.; Shao, C.; Cui, D.; Cheng, X.; Tang, R.; Pan, H.; Wu, Z.; Fu, B. Dual Functions of MDP Monomer with De- and Remineralizing Ability. *J. Dent. Res*. **2022**, *101*, 1172–1180.
36. Yoshihara, K.; Yoshida, Y.; Hayakawa, S.; Nagaoka, N.; Irie, M.; Ogawa, T.; Van Landuyt, K.L.; Osaka, A.; Suzuki, K.; Minagi, S.; Van Meerbeek, B. Nanolayering of phosphoric acid ester monomer on enamel and dentin. *Acta Biomater.* **2011**, *7*, 3187-3195. doi:10.1016/j.actbio.2011.04.026.
37. Ferreira-Barbosa, I.; Araújo-Pierote, J.J.; Rodrigues de Menezes, L.; Trazzi-Prieto, L.; Frazão-Câmara, J.V.; Sgarbosa de Araújo-Matuda, L.; Marchi, G.M.; Maffei Sartini-Paulillo, L.A.; Pimenta de Araujo, C.T. Effect of

Alternative Solvent Evaporation Techniques on Mechanical Properties of Primer-Adhesive Mixtures. *Acta Odontol. Latinoam.* **2020**, *33*, 135–142.

38. Ogura, Y.; Shimizu, Y.; Shiratsuchi, K.; Tsujimoto, A.; Takamizawa, T.; Ando, S.; Miyazaki, M. Effect of warm air-drying on dentin bond strength of single-step self-etch adhesives. *Dent. Mater. J.* **2012**, *31*, 507-513. doi:10.4012/dmj.2011-258.
39. Marsiglio, A.A.; Almeida, J.C.; Hilgert, L.A.; D'Alpino, P.H.; Garcia, F.C. Bonding to dentin as a function of air-stream temperatures for solvent evaporation. *Braz. Oral Res.* **2012**, *26*, 280-287. doi:10.1590/s1806-83242012000300016.
40. Bourgi, R.; Kharouf, N.; Cuevas-Suárez, C.E.; Lukomska-Szymanska, M.; Kharma, K.; Moussa, F.H.; Metlej, M.; Haikel, Y.; Hardan, L. Warm Air Delivery in Adhesive Application: Effect on Bonding Performance and Morphological Outcomes. *Biomimetics* **2024**, *9*, 194. doi:10.3390/biomimetics9040194.
41. 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**, *107*, 2121-2131. doi:10.1002/jbm.b.34305.
42. Tanaka, R.; Shibata, Y.; Manabe, A.; Miyazaki, T. Mineralization potential of polarized dental enamel. *PLoS One* **2009**, *4*, e5986.
43. Ahmed, G.M.; Abouauf, E.A.; AbuBakr, N.; Dörfer, C.E.; El-Sayed, K.F. Tissue engineering approaches for enamel, dentin, and pulp regeneration: an update. *Stem Cells Int.* **2020**, *2020*, 5734539.
44. Purk, J.H. Morphologic and structural analysis of material-tissue interfaces relevant to dental reconstruction. In *Material-tissue Interfacial Phenomena*; Woodhead Publishing: Sawston, UK, **2017**; pp. 205-229.
45. Bedran-Russo, A.; Leme-Kraus, A.A.; Vidal, C.M.P.; Teixeira, E.C. An Overview of Dental Adhesive Systems and the Dynamic Tooth-Adhesive Interface. *Dent. Clin. North Am.* **2017**, *61*, 713-731. doi:10.1016/j.cden.2017.06.001.
46. Desoutter, A.; Felbacq, D.; Gergely, C.; Varga, B.; Bonnet, L.; Etienne, P.; Vialla, R.; Cuisinier, F.; Salehi, H.; Rousseau, E.; Rufflé, B. Properties of dentin, enamel and their junction, studied with Brillouin scattering and compared to Raman microscopy. *Arch. Oral Biol.* **2023**, *152*, 105733.
47. Sui, T.; Dluhoš, J.; Li, T.; Zeng, K.; Cernescu, A.; Landini, G.; Korsunsky, A.M. Structure-Function Correlative Microscopy of Peritubular and Intertubular Dentine. *Materials (Basel)* **2018**, *11*, 1493. doi:10.3390/ma11091493.
48. Van Landuyt, K.L.; Snauwaert, J.; De Munck, J.; Peumans, M.; Yoshida, Y.; Poitevin, A.; Coutinho, E.; Suzuki, K.; Lambrechts, P.; Van Meerbeek, B. Systematic review of the chemical composition of contemporary dental adhesives. *Biomaterials* **2007**, *28*, 3757-3785.
49. Moszner, N.; Salz, U.; Zimmermann, J. Chemical aspects of self-etching enamel-dentin adhesives: a systematic review. *Dent. Mater.* **2005**, *21*, 895-910. doi:10.1016/j.dental.2005.05.001.
50. Xu, C.; Wang, Y. Chemical composition and structure of peritubular and intertubular human dentine revisited. *Arch. Oral Biol.* **2012**, *57*, 383-391. doi:10.1016/j.archoralbio.2011.09.008.
51. Yoshihara, K.; Yoshida, Y.; Nagaoka, N.; Hayakawa, S.; Okihara, T.; De Munck, J.; Maruo, Y.; Nishigawa, G.; Minagi, S.; Osaka, A.; Van Meerbeek, B. Adhesive interfacial interaction affected by different carbon-chain monomers. *Dent. Mater.* **2013**, *29*, 888-897. doi:10.1016/j.dental.2013.05.006.
52. Chiba, A.; Zhou, J.; Nakajima, M.; Tan, J.; Tagami, J.; Scheffel, D.L.; Hebling, J.; Agee, K.A.; Breschi, L.; Grégoire, G.; Jang, S.S.; Tay, F.R.; Pashley, D.H. The effects of ethanol on the size-exclusion characteristics of type I dentin collagen to adhesive resin monomers. *Acta Biomater.* **2016**, *33*, 235-241. doi: 10.1016/j.actbio.2016.01.040.
53. Marshall, G.W. Jr; Marshall, S.J.; Kinney, J.H.; Balooch, M. The dentin substrate: structure and properties related to bonding. *J. Dent.* **1997**, *25*, 441-458. doi: 10.1016/s0300-5712(96)00065-6.
54. Masarwa, N.; Mohamed, A.; Abou-Rabii, I.; Abu Zaghlan, R.; Steier, L. Longevity of Self-etch Dentin Bonding Adhesives Compared to Etch-and-rinse Dentin Bonding Adhesives: A Systematic Review. *J. Evid Based Dent Pract.* **2016**, *16*, 96-106. doi: 10.1016/j.jebdp.2016.03.003.
55. Nakabayashi, N.; Kojima, K.; Masuhara, E. The promotion of adhesion by the infiltration of monomers into tooth substrates. *J. Biomed Mater Res.* **1982**, *16*, 265-273. doi: 10.1002/jbm.820160307.
56. H S Delgado, A.; Belmar Da Costa, M.; Polido, M.C.; Mano Azul, A.; Sauro, S. Collagen-depletion strategies in dentin as alternatives to the hybrid layer concept and their effect on bond strength: a systematic review. *Sci. Rep.* **2022**, *12*, 13028. doi: 10.1038/s41598-022-17371-0.
57. Simmer, J. P.; Hu, J. C.-C. Dental enamel formation and its impact on clinical dentistry. *J. Dent. Educ.* **2001**, *65*, 896-905.

58. Wilmers, J.; Bargmann, S. Nature's design solutions in dental enamel: Uniting high strength and extreme damage resistance. *Acta Biomater.* **2020**, *107*, 1-24.
59. Akasapu, A.; Hegde, U.; Murthy, P.S. Enamel surface morphology: An ultrastructural comparative study of anterior and posterior permanent teeth. *J. Microsc. Ultrastruct.* **2018**, *6*, 160-164.
60. Tjäderhane, L.; Nascimento, F.D.; Breschi, L.; Mazzoni, A.; Tersariol, I.L.; Geraldeli, S.; Tezvergil-Mutluay, A.; Carrilho, M.R.; Carvalho, R.M.; Tay, F.R.; Pashley, D.H. Optimizing dentin bond durability: control of collagen degradation by matrix metalloproteinases and cysteine cathepsins. *Dent. Mater.* **2013**, 29, 116-135.
61. Tjäderhane, L.; Carrilho, M.R.; Breschi, L.; Tay, F.R.; Pashley, D.H. Dentin basic structure and composition—an overview. *Endod. Topics.* **2009**, *20*, 3-29.
62. Mazzoni, A.; Breschi, L.; Carrilho, M.; Nascimento, F.D.; Orsini, G.; Ruggeri Jr, A.; Gobbi, P.; Manzoli, L.; Tay, F.R.; Pashley, D.H.; Tjäderhane, L. A review of the nature, role, and function of dentin non-collagenous proteins. Part II: enzymes, serum proteins, and growth factors. *Endod. Topics.* **2009**, *21*, 19-40.
63. Lodish, H.; Berk, A.; Zipursky, S.L. Collagen: The Fibrous Proteins of the Matrix. In *Molecular Cell Biology*; W.H. Freeman & Co. Ltd.: New York, NY, USA, **2000**.
64. Bella, J.; Brodsky, B.; Berman, H.M. Hydration structure of a collagen peptide. *Structure* ***1995***, *3*, 893-906.
65. Toroian, D.; Lim, J.E.; Price, P.A. The size exclusion characteristics of type I collagen: implications for the role of noncollagenous bone constituents in mineralization. *J. Biol. Chem.* ***2007***, *282*, 22437-22447.
66. Nakabayashi, N.; Pashley, D.H. Hybridization Of Dental Hard Tissues. *Quintessence Publishing:* Batavia, IL, USA, ***1998***.
67. Tjäderhane, L. Dentin bonding: can we make it last? *Oper. Dent.* **2015,** *40*, 4-18.
68. Vaidyanathan, T.K.; Vaidyanathan, J. Recent advances in the theory and mechanism of adhesive resin bonding to dentin: A critical review. *J. Biomed. Mater. Res. B Appl. Biomater.* **2009**, 88, 558-578.
69. Salz, U.; Zimmermann, J.; Zeuner, F.; Moszner, N. Hydrolytic stability of self-etching adhesive systems. *J. Adhes. Dent.* **2005**, 7, 107-116.
70. Illev, G.; Hardan, L.; Kassis, C.; Bourgi, R.; Cuevas-Suárez, C.E.; Lukomska-Szymanska, M.; Mancino, D.; Haikel, Y.; Kharouf, N. Shelf life and storage conditions of universal adhesives: A literature review. *Polymers* **2021**, 13, 2708.
71. Spencer, P.; Ye, Q.; Park, J.; Topp, E.M.; Misra, A.; Marangos, O.; Wang, Y.; Bohaty, B.S.; Singh, V.; Sene, F.; Eslick, J. Adhesive/dentin interface: the weak link in the composite restoration. *Ann. Biomed. Eng.* **2010**, *38*, 1989-2003.
72. Bertassoni, L.E.; Orgel, J.P.; Antipova, O.; Swain, M.V. The dentin organic matrix–limitations of restorative dentistry hidden on the nanometer scale. *Acta Biomater.* **2012**, *8*, 2419-2433.
73. Xu, Q.; Torres, J.E.; Hakim, M.; Babiak, P.M.; Pal, P.; Battistoni, C.M.; Nguyen, M.; Panitch, A.; Solorio, L.; Liu, J.C. Collagen-and hyaluronic acid-based hydrogels and their biomedical applications. *Mater. Sci. Eng. R Rep.* **2021**, *146*, 100641.
74. Saikaew, P.; Sattabanasuk, V.; Harnirattisai, C.; Chowdhury, A.F.; Carvalho, R.; Sano, H. Role of the smear layer in adhesive dentistry and the clinical applications to improve bonding performance. *Jpn. Dent. Sci. Rev.* **2022**, *58*, 59-66.
75. Chowdhury, A.F.M.A.; Islam, R.; Alam, A.; Matsumoto, M.; Yamauti, M.; Carvalho, R.M.; et al. Variable Smear Layer and Adhesive Application: The Pursuit of Clinical Relevance in Bond Strength Testing. *Int. J. Mol. Sci.* **2019**, *20*, 5381.
76. Eick, J.D.; Wilko, R.A.; Anderson, C.H.; Sorensen, S.E. Scanning electron microscopy of cut tooth surfaces and identification of debris by use of the electron microprobe. *J. Dent. Res.* **1970**, *49*, 1359-1368.
77. Zheng, S. Effect of different smear layers on the bonding performance and durability of four adhesive systems. *Chin. J. Tissue Eng. Res.* **2020**, *24*, 517-523.
78. Pashley, D.H.; Livingston, M.J.; Greenhill, J.D. Regional resistances to fluid flow in human dentine in vitro. *Arch. Oral Biol.* **1978**, *23*, 807-810.
79. Terry, D.; Trajtenberg, C.; Blatz, M.; Leinfelder, K. A Review of Dental Tissue Microstructure, Biomodification, and Adhesion. *Funct. Esthet. Restor. Dent.* **2008**, *2*, 10-17.
80. Saikaew, P.; Matsumoto, M.; Sattabanasuk, V.; Harnirattisai, C.; Carvalho, R.M.; Sano, H. Ultra-morphological characteristics of dentin surfaces after different preparations and treatments. *Eur. J. Oral Sci.* **2020**, *128*, 246-254.

81. Eick, J.D.; Cobb, C.M.; Chappell, R.P.; Spencer, P.; Robinson, S.J. The dentinal surface: its influence on dentinal adhesion. Part I. *Quintessence Int.* **1991**, *22*.
82. Łukomska-Szymańska, Monika.; Sokołowski, Jerzy.; Łapińska, Barbara. Current views on adhesive bonding systems. *J. Stomatol.* **2017**, *70*, 384-393.
83. Retief DH, Denys FR. Retief, D.H.; Denys, F.R. Adhesion to enamel and dentin. *Am. J. Dent.* **1989**, *2*, 133-144.
84. Eick, J.D. Smear layer—Materials surface. *Proc. Finn. Dent. Soc.* **1992**, *88 (Suppl. 1)*, 225-242.
85. Perinka, L.; Sano, H.; Hosoda, H. Dentin thickness, hardness, and Ca-concentration vs bond strength of dentin adhesives. *Dent. Mater.* **1992**, *8*, 229-233.
86. Watanabe, I.; Nakabayashi, N.; Pashley, D.H. Bonding to ground dentin by a Phenyl-P self-etching primer. *J. Dent. Res.* **1994**, *73*, 1212-1220.
87. Sano, H.; Shono, T.; Sonoda, H.; Takatsu, T.; Ciucchi, B.; Carvalho, R.; Pashley, D.H. Relationship between surface area for adhesion and tensile bond strength—Evaluation of a micro-tensile bond test. *Dent. Mater.* **1994**, *10*, 236-240.
88. Saikaew, P.; Chowdhury, A.F.; Fukuyama, M.; Kakuda, S.; Carvalho, R.M.; Sano, H. The effect of dentin surface preparation and reduced application time of adhesive on bonding strength. *J. Dent.* **2016**, *47*, 63-70.
89. Oliveira, S.S.; Pugach, M.K.; Hilton, J.F.; Watanabe, L.G.; Marshall, S.J.; Marshall, G.W., Jr. The influence of the dentin smear layer on adhesion: A self-etching primer vs. a total-etch system. *Dent. Mater.* **2003**, *19*, 758–767.
90. Suyama, Y.; Lührs, A.K.; De Munck, J.; Mine, A.; Poitevin, A.; Yamada, T.; Van Meerbeek, B.; Cardoso, M.V. Potential smear layer interference with bonding of self-etching adhesives to dentin. *J. Adhes. Dent.* **2013**, *15*, 317-324.
91. Van Landuyt, K.L.; Mine, A.; De Munck, J.; Jaecques, S.; Peumans, M.; Lambrechts, P.; Van Meerbeek, B. Are one-step adhesives easier to use and better performing? Multifactorial assessment of contemporary one-step self-etching adhesives. *J. Adhes. Dent.* **2009**, *11*, 175-190.
92. Taschner, M.; Kümmerling, M.; Lohbauer, U.; Breschi, L.; Petschelt, A.; Frankenberger, R. Effect of double-layer application on dentin bond durability of one-step self-etch adhesives. *Oper. Dent.* **2014**, *39*, 416-426.
93. Erhardt, M.C.; Osorio, R.; Pisani-Proenca, J.; Aguilera, F.S.; Osorio, E.; Breschi, L.; Toledano, M. Effect of double layering and prolonged application time on MTBS of water/ethanol-based self-etch adhesives to dentin. *Oper. Dent.* **2009**, *34*, 571-577.
94. Sattabanasuk, V.; Vachiramon, V.; Qian, F.; Armstrong, S.R. Resin-dentin bond strength as related to different surface preparation methods. *J. Dent.* **2007**, *35*, 467-475.
95. Buonocore, M.G. A simple method of increasing the adhesion of acrylic filling materials to enamel surfaces. *J. Dent. Res.* **1955**, *34*, 849-853.
96. Mokeem, L.S.; Garcia, I.M.; Balhaddad, A.A.; Cline, K.; Rakovsky, G.; Collares, F.M.; Melo, M.A. Dental Adhesives: State-of-the-Art, Current Perspectives, and Promising Applications. *Adhes. Biomed. Appl.* **2023**, 2, 253-277.
97. Rizk, S. Principles of Adhesion to Tooth Structure. *Biomater. J.* **2023**, *2*, 10-30.
98. Porto, I.C.; Lôbo, T.D.; Rodrigues, R.F.; Lins, R.B.; da Silva, M.A. Insight into the development of versatile dentin bonding agents to increase the durability of the bonding interface. *Front. Dent. Med.* **2023**, *4*, 1127368.
99. Christensen, G.J. Bonding to dentin and enamel: where does it stand in 2005? *J. Am. Dent. Assoc.* **2005**, *136*, 1299-1302.
100. Scotti, N.; Cavalli, G.; Gagliani, M.; Breschi, L. New adhesives and bonding techniques: Why and when? *Int. J. Esthet. Dent*. **2017**, *12*, 524-535.
101. Alla, R.K. Composite Resins (Tooth colored restorative materials) in Dental Materials Science, Jaypee Brothers Medical Publishers (P) Ltd., New Delhi, India, **2013**; 132-148.
102. Anusavice, K.J.; Shen, C.; Ralph Rawls, H. Bonding and bonding agents; in *Phillip's Science of Dental Materials*: *12th edition,* Elsevier Saunders: Philadelphia, PA, USA, **2012**; pp. 258-284.
103. Latta, M.A.; Barkmeier, W.W. Dental adhesives in contemporary restorative dentistry. *DCNA* **1998**, *42*, 567-577.
104. Perdigao, J.; Swift Jr, E.J.; Walter, R. Fundamental concepts of enamel and dentin adhesion. In *Sturdevant's Art and Science of Operative Dentistry*, 6th ed.; Heymann, H., Swift, E.J., Jr., Eds.; Elsevier/Mosby: St. Louis, MO, USA, **2012**; pp. 114-135.

105. Anusavice, K.J. Structure of matter and principles of adhesion. In *Philip's Science of Dental Materials*, 11th ed.; Saunders: St. Louis, MO, USA, **2003**; pp. 21-40.
106. Anusavice, K.J.; Shen, C.; Rawls, H.R. (Eds.) *Phillips' Science of Dental Materials;* Elsevier Health Sciences: Amsterdam, The Netherlands, ***2012***.
107. Navyasri, K.; Alla, R.K.; Vineeth, G.; Suresh Sajjan, M.C. An overview of dentin bonding agents. *Int. J. Dent. Mater.* **2019**, *1*, 60-67.
108. Pazinatto, F.B.; Marquezini, L., Jr; Atta, M.T. Influence of temperature on the spreading velocity of simplified-step adhesive systems. *J. Esthet. Restor. Dent.* **2006**, *18*, 38-46.
109. Von Fraunhofer, J. Adhesion and Cohesion. *Int. J. Dent.* **2012**, *2012*, 951324.
110. Rosales-Leal, J.I.; Osorio, R.; Holgado-Terriza, J.A.; Cabrerizo-Vílchez, M.A.; Toledano, M. Dentin wetting by four adhesive systems. *Dent. Mater.* **2001**, *17*, 526-532.
111. Hisamatsu, N.; Atsuta, M.; Matsumura, H. Effect of silane primers and unfilled resin bonding agents on repair bond strength of a prosthodontic microfilled composite. *J. Oral. Rehabil.* **2002**, *29*, 644-648.
112. Balkaya, H.; Demirbuğa, S. Evaluation of six different one-step universal adhesive systems in terms of dentin bond strength, adhesive interface characterization, surface tension, contact angle, degree of conversion and solvent evaporation after immediate and delayed use. *J. Esthet. Restor. Dent.* **2023**, *35*, 479-492.
113. Szalóki, M.; Szabó, Z.; Martos, R.; Csík, A.; Szőllősi, G.J.; Hegedűs, C. The Surface Free Energy of Resin-Based Composite in Context of Wetting Ability of Dental Adhesives. *Appl. Sci.* **2023**, *13*, 12061.
114. Shamly, M.; Nasim, I. Evaluation of wettability of hesperidin incorporated dentin adhesive-an in vitro study. *J. Popul. Ther. Clin. Pharmacol.* **2023**, *30*, 425-432.
115. Ruyter, I.E. The chemistry of adhesive agents. *Oper. Dent.* **1992**, *5*, 32-43.
116. Van Meerbeek, B.; Lambrechts, P.; Inokoshi, S.; Braem, M.; Vanherle, G. Factors affecting adhesion to mineralized tissues. *Oper. Dent.* **1992**, *5*, 111-124.
117. Pashley, D.H.; Horner, J.A.; Brewer, P.D. Interactions of conditioners on the dentin surface. *Oper. Dent.* **1992**, *5*, 137-150.
118. Schüpbach, P.; Krejci, I.; Lutz, F. Dentin bonding: effect of tubule orientation on hybrid-layer formation. *Eur. J. Oral Sci.* **1997**, *105*, 344-352.
119. Yoshikawa, T.; Sano, H.; Burrow, M.F.; Tagami, J.; Pashley, D.H. Effects of dentin depth and cavity configuration on bond strength. *J. Dent. Res.* **1999**, *78*, 898-905.
120. Suzuki, T.; Finger, W.J. Dentin adhesives: site of dentin vs. bonding of composite resins. *Dent. Mater.* **1988**, *4*, 379-383.
121. Schiltz-Taing, M.; Wang, Y.; Suh, B.; Brown, D.; Chen, L. Effect of tubular orientation on the dentin bond strength of acidic self-etch adhesives. *Oper. Dent.* **2011**, *36*, 86-91.
122. Botelho, M.P.J.; Isolan, C.P.; Schwantz, J.K.; Lopes, M.B.; Moraes, R.R. Rubbing time and bonding performance of one-step adhesives to primary enamel and dentin. *J. Appl. Oral. Sci.* **2017**, *25*, 523-532.
123. Falacho, R.I.; Melo, E.A.; Marques, J.A.; Ramos, J.C.; Guerra, F.; Blatz, M.B. Clinical in-situ evaluation of the effect of rubber dam isolation on bond strength to enamel. *J. Esthet. Restor. Dent.* **2023**, *35*, 48-55.
124. Dabbagh, S.; Hardan, L.; Kassis, C.; Bourgi, R.; Devoto, W.; Zarow, M.; Jakubowicz, N.; Ghaleb, M.; Kharouf, N.; Dabbagh, M.; Arbildo-Vega, H.I. Effect of intraoral humidity on dentin bond strength of two universal adhesives: an in vitro preliminary study. *Coatings* **2022**, *12*, 712.
125. Jacquot, B.; Durand, J.C.; Farge, P.; Valcarcel, J.; Deville de Périère, D.; Cuisinier, F. Influence of temperature and relative humidity on dentin and enamel bonding: a critical review of the literature. Part 1. Laboratory studies. *J. Adhes. Dent.* **2012**, *14*, 433-446.
126. Plasmans, P.J.; Creugers, N.H.; Hermsen, R.J.; Vrijhoef, M.M. Intraoral humidity during operative procedures. *J. Dent.* **1994**, *22*, 89-91.
127. Choi, A.N.; Lee, J.H.; Son, S.A.; Jung, K.H.; Kwon, Y.H.; Park, J.K. Effect of Dentin Wetness on the Bond Strength of Universal Adhesives. *Materials (Basel).* **2017**, *10*, 1224.
128. Moll, K.; Haller, B. Effect of intrinsic and extrinsic moisture on bond strength to dentine. *J. Oral. Rehabil.* **2000**, *27*, 150-165.
129. Paul, S.J.; Leach, M.; Rueggeberg, F.A.; Pashley, D.H. Effect of water content on the physical properties of model dentine primer and bonding resins. *J. Dent.* **1999**, *27*, 209-214.
130. Plasmans, P.J.; Reukers, E.A.; Vollenbrock-Kuipers, L.; Vollenbrock, H.R. Air humidity: a detrimental factor in dentine adhesion. *J. Dent.* **1993**, *21*, 228-233.

131. Sinjari, B.; Rexhepi, I.; Santilli, M.; D'addazio, G.; Chiacchiaretta, P.; Di Carlo, P.; Caputi, S. The Impact of COVID-19 Related Lockdown on Dental Practice in Central Italy—Outcomes of A Survey. *Int. J. Environ. Res. Public Health* **2020**, *17*, 5780**.**
132. Frankenberger, R.; Van Meerbeek, B. Editorial: Rubber-dam—A blessing not only in the COVID-19 era. *J. Adhes. Dent.* **2021**, *23*, 3.
133. Wang, Y.; Li, C.; Yuan, H.; Wong, M.C.; Zou, J.; Shi, Z.; Zhou, X. Rubber dam isolation for restorative treatment in dental patients. *Cochrane Database Syst. Rev.* **2016**, *9*, CD009858.
134. Abuzenada, B.M. Attitude of dental students towards the rubber dam use in operative dentistry. *J. Pharm. Bioallied. Sci.* **2021**, *13*, 637.
135. Dokania, R.; Varshney, S.; Verma, P.; Sahoo, S.K. Cross-Sectional Evaluation of Dentists Knowledge and Awareness towards Rubber Dam Usage in Pediatric Dental Procedures: An Original Study. *J. Adv. Med. Dent. Sci. Res.* **2019**, *7*, 121-4.
136. Nikolaenko, S.A.; Lohbauer, U.; Roggendorf, M.; Petschelt, A.; Dasch, W.; Frankenberger, R. Influence of c-factor and layering technique on microtensile bond strength to dentin. *Dent. Mater.* **2004**, *20*, 579-585.
137. Singh, T.V.; Patil, J.P.; Raju, R.C.; Venigalla, B.S.; Jyotsna, S.V.; Bhutani, N. Comparison of Effect of C-Factor on Bond Strength to Human Dentin Using Different Composite Resin Materials. *J. Clin. Diagn. Res.* **2015**, *9*, 88-91.
138. Yoshikawa, T.; Burrow, M.F.; Tagami, J. The effects of bonding system and light curing method on reducing stress of different C-factor cavities. *J. Adhes. Dent.* **2001**, *3*, 177-183.
139. Marques, M.S.; Kenshima, S.; Muench, A.; Ballester, R.Y.; Rodrigues Filho, L.E. Effect of the C-factor and dentin preparation method in the bond strength of a mild self-etch adhesive. *Oper. Dent.* **2009**, *34*, 452-459.
140. Yoshikawa, T.; Sadr, A.; Tagami, J. Effects of C-factor on bond strength to floor and wall dentin. *Dent. Mater. J.* **2016**, *35*, 918-922.
141. Perdigão, J. Dentin bonding-variables related to the clinical situation and the substrate treatment. *Dent Mater.* **2010**, *26*, 24-37.
142. Tay, F.R.; Pashley, D.H. Resin bonding to cervical sclerotic dentin: a review. *J. Dent.* **2004**, *32*, 173-196.
143. Florescu, A.; Efrem, I.C.; Haidoiu, C.; Hertzog, R.; Bîcleşanu, F.C. Microscopy comparative evaluation of the SE systems adhesion to normal and sclerotic dentin. *Rom. J. Morphol. Embryol.* **2015**, *56*, 1051-1056.
144. Hedge, J. Sclerotic dentin: clinical implications in restorative dentistry. *J. Dent.* **2011**, *1*, 5-6.
145. Al-Abd Al, M.A.; Al-Badr, R.J.; Abbas, M.S. Modern Adhesive Dentistry: A review of literatures. *Med. J. Ahl al-Bayt Univ.* **2023**, *2*, 6-13.
146. Cadenaro, M.; Josic, U.; Maravić, T.; Mazzitelli, C.; Marchesi, G.; Mancuso, E.; Breschi, L.; Mazzoni, A. Progress in dental adhesive materials. *J. Dent. Res.* **2023**, *102*, 254-262.
147. Muñoz, M.A.; Luque, I.; Hass, V.; Reis, A.; Loguercio, A.D.; Bombarda, N.H.C. Immediate bonding properties of universal adhesives to dentine. *J. Dent.* **2013**, *41*, 404-411.
148. Garg, N.; Garg, A. *Textbook of Operative Dentistry.* Boydell & Brewer Ltd.: Martlesham, UK, **2010**.
149. Hobson, R.S.; McCabe, J.F. Relationship between enamel etch characteristics and resin-enamel bond strength. *Br. Dent. J.* **2002**, *192*(8), 463-468.
150. Barnhart, E.C.; Campbell, P.M.; Noureldin, A.; Julien, K.; Buschang, P.H. The quality of etched enamel in different regions and tooth types and its significance in bonding and the development of white spot lesions. *Angle. Orthod.* **2021**, *91*, 576-582.
151. Kharouf, N.; Reitzer, F.; Ashi, T.; Daras, N.; Haikel, Y.; Mancino, D. Effectiveness of etching with phosphoric acid when associated with rubbing technique. *J. Stomatol.* **2021**, *74*, 16-21.
152. Talal, A.; Nasim, H.M.; Khan, A.S. Enamel etching and dental adhesives. In *Advanced Dental Biomaterials*; Woodhead Publishing: Sawston, UK, **2019;** pp. 229-253.
153. Aljifan, M.K.; Alshehri, A.M.; Alharbi, R.M.; Al Alhareth, M.S.; Alharbi, Z.A.; Alamri, S.M.; Alshahrani, N.S.; Alyamani, A.E.; Alzahrani, A.A.; Alqarni, A.A.; Al Joaithen, M.S. An Overview of Dentin Conditioning and Its Effect on Bond Strength. *Int. J. Community Med. Public Health.* **2023**, *10*, 371-375
154. Kharouf, N.; Mancino, D.; Naji-Amrani, A.; Eid, A.; Haikel, Y.; Hemmerle, J. Effectiveness of Etching by Three Acids on the Morphological and Chemical Features of Dentin Tissue. *J. Contemp. Dent. Pract.* **2019**, *20,* 915-919.
155. Majidinia, S.; Ghavamnasiri, M.; Bagheri, M.; Hajizadeh, H.; Namazikhah, M.S. Effect of different conditioning protocols on the adhesion of a glass ionomer cement to dentin. *J. Contemp. Dent. Pract.* **2009**, *10*, 9-16.

156. Eliades, G.; Palaghias, G.; Vougiouklakis, G. Effect of acidic conditioners on dentin morphology, molecular composition and collagen conformation in situ. *Dent. Mater.* **1997**, *13*, 24-33.
157. Atalay, C.; Uslu, A.; Yazici, A.R. Does laser etching have an effect on application mode of a universal adhesive?—A microleakage and scanning electron microscopy evaluation. *Microsc. Res. Tech.* **2021**, *84*, 125-132.
158. Sulieman, M. An overview of the use of lasers in general dental practice: 2. Laser wavelengths, soft and hard tissue clinical applications. *Dent. Update.* **2005**, *32*, 286-288.
159. Gutknecht, N.; Apel, C.; Schäfer, C.; Lampert, F. Microleakage of composite fillings in Er, Cr: YSGG laser-prepared class II cavities. *Lasers Surg. Med.* **2001**, *28*, 371-374.
160. Andrade, A.M.; Moura, S.K.; Reis, A.; Loguercio, A.D.; Garcia, E.J.; Grande, R.H. Evaluating resin-enamel bonds by microshear and microtensile bond strength tests: effects of composite resin. *J. Appl. Oral. Sci.* **2010**, *18*, 591-598.
161. Pires, P.T.; Ferreira, J.C.; Oliveira, S.A.; Azevedo, Á.F.; Dias, W.R.; Melo, P.R. Shear bond strength and SEM morphology evaluation of different dental adhesives to enamel prepared with ER: YAG laser. *Contemp. Clin. Dent.* **2013**, *4*, 20-26.
162. Üşümez, S.; Orhan, M.; Üşümez, A. Laser etching of enamel for direct bonding with an Er, Cr: YSGG hydrokinetic laser system. *Am. J. Orthod. Dentofacial. Orthop.* **2002**, *122*, 649-656.
163. Labunet, A.; Tonea, A.; Kui, A.; Sava, S. The use of laser energy for etching enamel surfaces in dentistry—a scoping review. *Materials* **2022**, *15*, 1988.
164. Sasaki, L.H.; Lobo, P.D.; Moriyama, Y.; Watanabe, I.S.; Villaverde, A.B.; Tanaka, C.S.; Moriyama, E.H.; Brugnera Jr, A. Tensile bond strength and SEM analysis of enamel etched with Er: YAG laser and phosphoric acid: a comparative study in vitro. *Braz. Dent. J.* **2008**, *19*, 57-61.
165. Salman, S.Q.; Hussein, B.M. Topographical Analysis of Human Enamel after Phosphoric Acid Etching and Er, Cr: YSGG Laser Irradiation. *J. Lasers Med. Sci.* **2023**, *14*, e68.
166. Odian, G. *Principles of Polymerization*. Wiley-Interscience: New York, NY, USA, **2004**.
167. Peutzfeldt, A. Resin composites in dentistry: the monomer systems. *Eur. J. Oral Sci.* **1997**, *105*, 97-116.
168. Nishiyama, N.; Suzuki, K.; Yoshida, H.; Teshima, H.; Nemoto, K. Hydrolytic stability of methacrylamide in acidic aqueous solution. *Biomaterials* **2004**, *25*, 965-969.
169. Bowen, R.L.; Bennett, P.S.; Groh, R.J.; Farahani, M.; Eichmiller, E.C. New surface-active comonomer for adhesive bonding. *J. Dent. Res.* **1996**, *75*, 606-10.
170. Imazato, S.; Russell, R.R.; McCabe, J.F. Antibacterial activity of MDPB polymer incorporated in dental resin. *J. Dent.* **1995**, *23*, 177-181.
171. Tay, F.R.; Pashley, D.H. Have dentin adhesives become too hydrophilic?. *J. Can. Dent. Assoc.* **2003**, *69*, 726-731.
172. Alex, G. Universal adhesives: the next evolution in adhesive dentistry? *Compend. Contin. Educ. Dent.* **2015**, *36*, 15-40.
173. Nakabayashi, N.; Takarada, K. Effect of HEMA on bonding to dentin. *Dent. Mater.* **1992**, *8*, 125-130.
174. Van Landuyt, K.L.; De Munck, J.; Snauwaert, J.; Coutinho, E.; Poitevin, A.; Yoshida, Y.; Inoue, S.; Peumans, M.; Suzuki, K.; Lambrechts, P.V.; Van Meerbeek, B. Monomer-solvent phase separation in one-step self-etch adhesives. *J. Dent. Res.* **2005**, *84*, 183-188.
175. da Silva, T.S.P.; de Castro, R.F.; Magno, M.B.; Maia, L.C.; Silva E Souza, M.H.D. Júnior. Do HEMA-free adhesive systems have better clinical performance than HEMA-containing systems in noncarious cervical lesions? A systematic review and meta-analysis. *J. Dent.* **2018**, *74*, 1-14.
176. Wiertelak-Makała, K.; Szymczak-Pajor, I.; Bociong, K.; Śliwińska, A. Considerations about Cytotoxicity of Resin-Based Composite Dental Materials: A Systematic Review. *Int. J. Mol. Sci.* **2023**, *25*, 152.
177. Spreafico, D.; Semeraro, S.; Mezzanzanica, D.; Re, D.; Gagliani, M.; Tanaka, T.; et al. The Effect of the Air-Blowing Step on the Technique Sensitivity of Four Different Adhesive Systems. *J. Dent.* **2006**, *34*, 237-244.
178. Van Landuyt, K.L.; Snauwaert, J.; Peumans, M.; De Munck, J.; Lambrechts, P.; Van Meerbeek, B. The Role of HEMA in One-Step Self-Etch Adhesives. *Dent. Mater.* **2008**, *24*, 1412-1419.
179. Hussain, L.A.; Dickens, S.H.; Bowen, R.L. Shear Bond Strength of Experimental Methacrylated Beta-Cyclodextrin-Based Formulations. *Biomaterials* **2005**, *26*, 3973-3979.
180. Burrow, M.F.; Tyas, M.J. Comparison of Two All-in-One Adhesives Bonded to Non-Carious Cervical Lesions – Results at 3 Years. *Clin. Oral. Investig.* **2012**, *16*, 1089-1094.

181. Moretto, S.G.; Russo, E.M.A.; Carvalho, R.C.R.; De Munck, J.; Van Landuyt, K.; Peumans, M.; et al. 3-Year Clinical Effectiveness of One-Step Adhesives in Non-Carious Cervical Lesions. *J. Dent.* **2013**, *41*, 675-682.
182. Scotti, N.; Comba, A.; Gambino, A.; Manzon, E.; Breschi, L.; Paolino, D.; et al. Influence of Operator Experience on Non-Carious Cervical Lesion Restorations: Clinical Evaluation with Different Adhesive Systems. *Am. J. Dent.* **2016**, *29*, 33-38.
183. Hafer, M.; Jentsch, H.; Haak, R.; Schneider, H. A Three-Year Clinical Evaluation of a One-Step Self-Etch and a Two-Step Etch-and-Rinse Adhesive in Non-Carious Cervical Lesions. *J. Dent.* **2015**, *43*, 350-361.
184. Yoshihara, K.; Nagaoka, N.; Okihara, T.; Kuroboshi, M.; Hayakawa, S.; Maruo, Y.; Nishigawa, G.; De Munck, J.; Yoshida, Y.; Van Meerbeek, B. Functional Monomer Impurity Affects Adhesive Performance. *Dent. Mater.* **2015**, *31*, 1493-1501.
185. Suh, W.K.; Kim, K.M.; Kwon, J.S. Changes in Adhesive Strength and pH of Dental Universal Adhesive in Accordance with Varying Proportions of 10-MDP. *Korean J. Dent. Mater.* **2023**, *50*, 281-292.
186. Yoshida, Y.; Yoshihara, K.; Nagaoka, N.; Hayakawa, S.; Torii, Y.; Ogawa, T.; Osaka, A.; Van Meerbeek, B. Self-Assembled Nano-Layering at the Adhesive Interface. *J. Dent. Res.* **2012**, *91*, 376-381.
187. Yoshihara, K.; Yoshida, Y.; Nagaoka, N.; Fukegawa, D.; Hayakawa, S.; Mine, A.; Nakamura, M.; Minagi, S.; Osaka, A.; Suzuki, K.; Van Meerbeek, B. Nano-Controlled Molecular Interaction at Adhesive Interfaces for Hard Tissue Reconstruction. *Acta Biomater.* **2010**, *6*, 3573-3582.
188. Nurrohman, H.; Nakashima, S.; Takagaki, T.; Sadr, A.; Nikaido, T.; Asakawa, Y.; Uo, M.; Marshall, S. J.; Tagami, J. Immobilization of Phosphate Monomers on Collagen Induces Biomimetic Mineralization. *BioMed. Mater. Eng*. **2015**, *25*, 89-99.
189. Teshima, I. Degradation of 10-Methacryloyloxydecyl Dihydrogen Phosphate. *J. Dent. Res.* **2010**, *89*, 1281-1286.
190. Wagner, A.; Wendler, M.; Petschelt, A.; Belli, R.; Lohbauer, U. Bonding Performance of Universal Adhesives in Different Etching Modes. *J. Dent.* **2014**, *42*, 800-807.
191. Muñoz, M.A.; Sezinando, A.; Luque-Martinez, I.; Szesz, A.L.; Reis, A.; Loguercio, A.D.; et al. Influence of a Hydrophobic Resin Coating on the Bonding Efficacy of Three Universal Adhesives. *J. Dent.* **2014**, *42*, 595-602.
192. Zhou, J.; Wurihan; Shibata, Y.; Tanaka, R.; Zhang, Z.; Zheng, K.; et al. Quantitative/Qualitative Analysis of Adhesive-Dentin Interface in the Presence of 10-Methacryloyloxydecyl Dihydrogen Phosphate. *J. Mech. Behav. Biomed. Mater.* **2019**, *92*, 71-78.
193. Feitosa, V.P.; Pomacóndor-Hernández, C.; Ogliari, F.A.; Leal, F.; Correr, A.B.; Sauro, S. Chemical Interaction of 10-MDP (Methacryloyloxy- Decyl-Dihydrogen-Phosphate) in Zinc-Doped Self-Etch Adhesives. *J. Dent.* **2014**, *42*, 359-365.
194. Yaguchi, T. Layering Mechanism of MDP-Ca Salt Produced in Demineralization of Enamel and Dentin Apatite. *Dent. Mater.* **2017**, *33*, 23-32.
195. Fujita Nakajima, K.; Nikaido, T.; Arita, A.; Hirayama, S.; Nishiyama, N. Demineralization Capacity of Commercial 10-Methacryloyloxydecyl Dihydrogen Phosphate-Based All-in-One Adhesive. *Dent. Mater.* **2018**, *34*, 1555-1565.
196. Yoshihara, K.; Hayakawa, S.; Nagaoka, N.; Okihara, T.; Yoshida, Y.; Van Meerbeek, B. Etching Efficacy of Self-Etching Functional Monomers. *J. Dent. Res.* **2018**, *97*, 1010-1016.
197. Putzeys, E.; Duca, R.C.; Coppens, L.; Vanoirbeek, J.; Godderis, L.; Van Meerbeek, B.; et al. In-Vitro Transdentinal Diffusion of Monomers from Adhesives. *J. Dent.* **2018**, *75*, 91-97.
198. Fehrenbach, J.; Isolan, C.P.; Münchow, E.A. Is the Presence of 10-MDP Associated to Higher Bonding Performance for Self-Etching Adhesive Systems? A Meta-Analysis of In Vitro Studies. *Dent. Mater.* **2021**, *37*, 1463-1485. doi: 10.1016/j.dental.2021.08.014.
199. Jin, X.; Han, F.; Wang, Q.; Yuan, X.; Zhou, Q.; Xie, H.; Niu, L.; Chen, C. The Roles of 10-Methacryloyloxydecyl Dihydrogen Phosphate and Its Calcium Salt in Preserving the Adhesive-Dentin Hybrid Layer. *Dent. Mater.* **2022**, *38*, 1194-1205.
200. de Oliveira, R.P.; de Paula, B.L.F.; Alencar, C.M.; Alves, E.B.; Silva, C.M. A Randomized Clinical Study of the Performance of Self-Etching Adhesives Containing HEMA and 10-MDP on Non-Carious Cervical Lesions: A 2-Year Follow-Up Study. *J. Dent.* **2023**, *130*, 104407. doi: 10.1016/j.jdent.2022.104407.
201. Koike, K.; Takamizawa, T.; Aoki, R.; Shibasaki, S.; Ishii, R.; Sai, K.; Kamimoto, A.; Miyazaki, M. Comparison of Dentin Bond Durability in Different Adhesive Systems Containing Glycerol-Phosphate Dimethacrylate (GPDM) Functional Monomers under Long-Term Water Storage. *Int. J. Adhes. Adhes.* **2023**, *124*, 103366.

202. Cuevas-Suárez, C.E.; Ramos, T.S.; Rodrigues, S.B.; Collares, F.M.; Zanchi, C.H.; Lund, R.G.; et al. Impact of Shelf-Life Simulation on Bonding Performance of Universal Adhesive Systems. *Dent. Mater.* **2019**, *35*, 204-219.
203. Feitosa, V.P.; Sauro, S.; Ogliari, F. A.; Stansbury, J. W.; Carpenter, G. H.; Watson, T. F.; Sinhoreti, M. A.; Correr, A.B. The Role of Spacer Carbon Chain in Acidic Functional Monomers on the Physicochemical Properties of Self-Etch Dental Adhesives. *J. Dent.* **2014**, *42*, 565-574.
204. Dentsply Sirona, PrimeBond active_Scientific Compendium_EN.pdf; **2016**.
205. Carrilho, E.; Cardoso, M.; Marques Ferreira, M.; Marto, C.M.; Paula, A.; Coelho, A.S. 10-MDP Based Dental Adhesives: Adhesive Interface Characterization and Adhesive Stability—A Systematic Review. *Mater.* **2019**, *12*, 790.
206. Chen, Y.; Tay, F.R.; Lu, Z.; Chen, C.; Qian, M.; Zhang, H.; et al. Dipentaerythritol Penta-Acrylate Phosphate—An Alternative Phosphate Ester Monomer for Bonding of Methacrylates to Zirconia. *Sci. Rep.* **2016**, *6*, 39542.
207. Hoshika, S.; Kameyama, A.; Suyama, Y.; De Munck, J.; Sano, H.; Van Meerbeek, B. GPDM- and 10-MDP-based Self-etch Adhesives Bonded to Bur-cut and Uncut Enamel - "Immediate" and "Aged" μTBS. *J. Adhes. Denti.* **2018**, *20*, 113–120.
208. Papadogiannis, D.; Dimitriadi, M.; Zafiropoulou, M.; Gaintantzopoulou, M.D.; Eliades, G. Universal Adhesives: Setting Characteristics and Reactivity with Dentin. *Materials (Basel)* **2019**, *12*, 1720.
209. Irmak, Ö.; Baltacıoğlu, İ.H.; Ulusoy, N.; Bağış, Y.H. Solvent Type Influences Bond Strength to Air or Blot-Dried Dentin. *BMC Oral Health* **2016**, *16*, 77.
210. Nihi, F.M.; Fabre, H.S.; Garcia, G.; Fernandes, K.B.; Ferreira, F.B.; Wang, L. In Vitro Assessment of Solvent Evaporation from Commercial Adhesive Systems Compared to Experimental Systems. *Braz. Dent. J.* **2009**, *20*, 396-402.
211. Reis, A.F.; Oliveira, M.T.; Giannini, M.; De Goes, M.F.; Rueggeberg, F.A. The Effect of Organic Solvents on One-Bottle Adhesives Bond Strength to Enamel and Dentin. *Oper. Dent.* **2003**, *28*, 700-706.
212. Pashley, D.H.; Carvalho, R.M.; Tay, F.R.; Agee, K.A.; Lee, K.W. Solvation of Dried Dentin Matrix by Water and Other Polar Solvents. *Am. J. Dent.* **2002**, *15*, 97-102.
213. Forman, D.L.; McLeod, R.R.; Shah, P.K.; Stansbury, J.W. Evaporation of Low-Volatility Components in Polymeric Dental Resins. *Dent. Mater.* **2015**, *31*, 1090-1099.
214. Joshi, D.R.; Adhikari, N. An Overview on Common Organic Solvents and Their Toxicity. *J. Pharm. Res. Int.* **2019**, *28*, 1-8.
215. Reis, A.; Loguercio, A.D. A 36-Month Clinical Evaluation of Ethanol/Water and Acetone-Based Etch-and-Rinse Adhesives in Non-Carious Cervical Lesions. *Oper. Dent.* **2009**, *34*, 384-391.
216. Elkassas, D.; Taher, H.A.; Elsahn, N.; Hafez, R.; El-Badrawy, W. Effect of the Number of Applications of Acetone-Based Adhesives on Microtensile Bond Strength and the Hybrid Layer. *Oper. Dent.* **2009**, *34*, 688-696.
217. Miyazaki, M.; Oshida, Y.; Xirouchaki, L. Dentin Bonding System. Part I: Literature Review. *Bio-Med. Mater. Eng.* **1996**, *6*, 15-31.
218. Gwinnett, A.J. Chemistry of the Adhesive Bond. In *Fundamentals of Operative Dentistry: A Contemporary Approach*; Summitt, J.B., Robbins, J.W., Schwartz, R.S., Eds.; Quintessence Publishing Co., Ltd.: Batavia, IL, USA, **2001**; pp. 183-200.
219. Cardoso, P.D.; Lopes, G.C.; Vieira, L.C.; Baratieri, L.N. Effect of Solvent Type on Microtensile Bond Strength of a Total-Etch One-Bottle Adhesive System to Moist or Dry Dentin. *Oper. Dent.* **2005**, *30*, 376.
220. Manso, A.P.; Marquezini Jr, L.; Silva, S.M.; Pashley, D.H.; Tay, F.R.; Carvalho, R.M. Stability of Wet Versus Dry Bonding with Different Solvent-Based Adhesives. *Dent. Mater.* **2008**, *24*, 476-482.
221. Bourgi, R.; Hardan, L.; Cuevas-Suárez, C.E.; Scavello, F.; Mancino, D.; Kharouf, N.; Haikel, Y. The Use of Warm Air for Solvent Evaporation in Adhesive Dentistry: A Meta-Analysis of In Vitro Studies. *J. Funct. Biomater.* **2023**, *14*, 285.
222. Simões, D.M.; Basting, R.T.; Amaral, F.L.; Turssi, C.P.; França, F.M. Influence of Chlorhexidine and/or Ethanol Treatment on Bond Strength of an Etch-and-Rinse Adhesive to Dentin: An In Vitro and In Situ Study. *Oper. Dent.* **2014**, *39*, 64-71.
223. Cadenaro, M.; Breschi, L.; Rueggeberg, F.A.; Suchko, M.; Grodin, E.; Agee, K.; Di Lenarda, R.; Tay, F.R.; Pashley, D.H. Effects of Residual Ethanol on the Rate and Degree of Conversion of Five Experimental Resins. *Dent. Mater.* **2009**, *25*, 621-628.
224. Ye, Q.; Spencer, P.; Wang, Y.; Misra, A. Relationship of Solvent to the Photopolymerization Process, Properties, and Structure in Model Dentin Adhesives. *J. Biomed. Mater. Res. Part A* **2007**, *80*, 342-350.

225. Malacarne-Zanon, J.; Pashley, D.H.; Agee, K.A.; Foulger, S.; Alves, M.C.; Breschi, L.; Cadenaro, M.; Garcia, F.P.; Carrilho, M.R. Effects of Ethanol Addition on the Water Sorption/Solubility and Percent Conversion of Comonomers in Model Dental Adhesives. *Dent. Mater.* **2009**, *25*, 1275-1284.
226. Massaro, H.; Zambelli, L.F.; Britto, A.A.; Vieira, R.P.; Ligeiro-de-Oliveira, A.P.; Andia, D.C.; Oliveira, M.T.; Lima, A.F. Solvent and HEMA Increase Adhesive Toxicity and Cytokine Release from Dental Pulp Cells. *Materials* **2019**, *12*, 2750.
227. Yevenes, I.H.; Fuentes, M.V.; Cury, J.A.; Reis, A.; Loguercio, A.D. Chemical Stability of Two Dentin Single-Bottle Adhesives as a Function of Solvent Loss. *Rev. Odonto Ciênc*. **2008**, *23*, 220–224.
228. Grégoire, G.; Sharrock, P.; Delannée, M.; Delisle, M.B. Depletion of Water Molecules During Ethanol Wet-Bonding with Etch and Rinse Dental Adhesives. *Mater. Sci. Eng. C.* **2013**, *33*, 21-27.
229. Agee, K.A.; Prakki, A.; Abu-Haimed, T.; Naguib, G.H.; Nawareg, M.A.; Tezvergil-Mutluay, A.; Scheffel, D.L.; Chen, C.; Jang, S.S.; Hwang, H.; Brackett, M. Water Distribution in Dentin Matrices: Bound vs. Unbound Water. *Dent. Mater.* **2015**, *31*, 205-216.
230. Van Meerbeek, B.; Yoshida, Y.; Lambrechts, P.; Vanherle, G.; Duke, E.S.; Eick, J.D.; et al. A TEM Study of Two Water-Based Adhesive Systems Bonded to Dry and Wet Dentin. *J. Dent. Res.* **1998**, *77*, 50-59.
231. Tay, F.R.; Pashley, D.H. Aggressiveness of Contemporary Self-Etching Systems: I: Depth of Penetration Beyond Dentin Smear Layers. *Dent. Mater.* **2001**, *17*, 296-308.
232. Tay, F.R.; Gwinnett, J.A.; Wei, S.H. Relation Between Water Content in Acetone/Alcohol-Based Primer and Interfacial Ultrastructure. *J. Dent.* **1998**, *26*, 147-156.
233. Bossardi, M.; Piva, E.; Isolan, C.P.; Münchow, E.A. One-Year Bonding Performance of One-Bottle Etch-and-Rinse Adhesives to Dentin at Different Moisture Conditions. *J. Adhes. Sci. Technol.* **2020**, *34*, 686-694.
234. De Oliveira Barros, L.; Apolonio, F.M.; Loguercio, A.D.; Aragao Saboia, V.D. Resin-Dentin Bonds of Etch-and-Rinse Adhesives to Alcohol-Saturated Acid-Etched Dentin. *J. Adhes. Dent.* **2013**, *15*, 333-340.
235. Grégoire, G.; Dabsie, F.; Dieng-Sarr, F.; Akon, B.; Sharrock, P. Solvent Composition of One-Step Self-Etch Adhesives and Dentine Wettability. *J. Dent.* **2011**, *39*, 30-39.
236. Orellana, N.; Ramírez, R.; Roig, M.; Giner, L.; Mercade, M.; Durán, F.; Herrera, G. Comparative Study of the Microtensile Bond Strength of Three Different Total Etch Adhesives with Different Solvents to Wet and Dry Dentin. (In Vitro Test). *Acta Odontol. Latinoam.* **2009**, *22*, 47-56.
237. Al-Nabulsi, M.; Daud, A.; Yiu, C.; Omar, H.; Sauro, S.; Fawzy, A.; et al. Co-Blend Application Mode of Bulk Fill Composite Resin. *Materials (Basel)* **2019**, *12*, 2504.
238. Riddick, J.; Bunger, W.B.; Sakano, T.K. Techniques of Chemistry. In *Organic Solvents*, 4th ed.; John Wiley and Sons: New York, NY, USA, **1985**; Volume 2, p. 196.
239. Daubert, T.E. Physical and Thermodynamic Properties of Pure Chemicals: Data Compilation. In *Design Institute for Physical Property Data (DIPPR)*: New York, NY, USA, **1989**.
240. Kumagai, R.Y.; Hirata, R.; Pereira, P.N.R.; Reis, A.F. Moist vs Over-Dried Etched Dentin: FE-SEM/TEM and Bond Strength Evaluation of Resin-Dentin Interfaces Produced by Universal Adhesives. *J. Esthet. Restor. Dent.* **2020**, *32*, 325-332.
241. de Solventes, C.A. Adhesive Systems: Considerations about Solvents. *Int. J. Odontostomat.* **2009**, *3*, 119-124.
242. de Geus, J.L.; Maran, B.M.; Cabral, K.A.; Dávila-Sánchez, A.; Tardem, C.; Barceleiro, M.O.; Heintze, S.D.; Reis, A.; Loguercio, A.D. Clinical Performance of Filled/Nanofilled Versus Nonfilled Adhesive Systems in Noncarious Cervical Lesions: A Systematic Review and Meta-Analysis. *Oper. Dent.* **2021**, *46*, E34-E59.
243. Sano, H.; Takatsu, T.; Ciucchi, B.; Russell, C.M.; Pashley, D.H. Tensile Properties of Resin-Infiltrated Demineralized Human Dentin. *J. Dent. Res.* **1995**, *74*, 1093-1102.
244. Ferracane, J.L.; Hilton, T.J. Polymerization Stress–Is It Clinically Meaningful? *Dent. Mater.* **2016**, *32*, 1-10.
245. Frankenberger, R.; Lopes, M.; Perdigão, J.; Ambrose, W.W.; Rosa, B.T. The Use of Flowable Composites as Filled Adhesives. *Dent. Mater.* **2002**, *18*, 227-238.
246. Labella, R.; Lambrechts, P.; Van Meerbeek, B.; Vanherle, G. Polymerization Shrinkage and Elasticity of Flowable Composites and Filled Adhesives. *Dent. Mater.* **1999**, *15*, 128-137.
247. Perdigão, J.; Lambrechts, P.; Van Meerbeek, B.; Braem, M.; Yildiz, E.; Yücel, T.; Vanherle, G. The Interaction of Adhesive Systems with Human Dentin. *Am. J. Dent.* **1996**, *9*, 167-173.
248. van Dijken, J.W. A Prospective 8-Year Evaluation of a Mild Two-Step Self-Etching Adhesive and a Heavily Filled Two-Step Etch-and-Rinse System in Non-Carious Cervical Lesions. *Dent. Mater.* **2010**, *26*, 940-946.

249. Belli, R.; Kreppel, S.; Petschelt, A.; Hornberger, H.; Boccaccini, A.R.; Lohbauer, U. Strengthening of Dental Adhesives via Particle Reinforcement. *J. Mech. Behav. Biomed. Mater.* **2014**, *37*, 100-108.
250. Peumans, M.; De Munck, J.; Mine, A.; Van Meerbeek, B. Clinical Effectiveness of Contemporary Adhesives for the Restoration of Non-Carious Cervical Lesions. A Systematic Review. *Dent. Mater.* **2014**, *30*, 1089-1103.
251. Tay, F.R.; Moulding, K.M.; Pashley, D.H. Distribution of Nanofillers from a Simplified-Step Adhesive in Acid-Conditioned Dentin. *J. Adhes. Dent.* **1999**, *1*, 103-117.
252. Tay, F.R.; Pashley, D.H.; Yiu, C.; Cheong, C.; Hashimoto, M.; Itou, K.; Yoshiyama, M.; King, N.M. Nanoleakage Types and Potential Implications: Evidence from Unfilled and Filled Adhesives with the Same Resin Composition. *Am. J. Dent.* **2004**, *17*, 182-190.
253. Schmalz, G.; Hickel, R.; van Landuyt, K.L.; Reichl, F.X. Nanoparticles in Dentistry. *Dent. Mater.* **2017**, *33*, 1298-1314.
254. Giannini, M.; Liberti, M.S.; Arrais, C.A.; Reis, A.F.; Mettenburg, D.; Rueggeberg, F.A. Influence of Filler Addition, Storage Medium and Evaluation Time on Biaxial Flexure Strength and Modulus of Adhesive Systems. *Acta Odontol. Scand.* **2012**, *70*, 478-484.
255. Giannini, M.; Mettenburg, D.; Arrais, C.A.; Rueggeberg, F.A. The Effect of Filler Addition on Biaxial Flexure Strength and Modulus of Commercial Dentin Bonding Systems. *Quintessence Int.* **2011**, *42*, e39-e43.
256. Lee, Y.; Pinzon, L.M.; O'Keefe, K.L.; Powers, J.M. Effect of Filler Addition on the Bonding Parameters of Dentin Bonding Adhesives Bonded to Human Dentin. *Am. J. Dent.* **2006**, *19*, 23.
257. Kaaden, C.; Powers, J.M.; Friedl, K.H.; Schmalz, G. Bond Strength of Self-Etching Adhesives to Dental Hard Tissues. *Clin. Oral. Investig.* **2002**, *6*, 155-160.
258. Jang, J.H.; Kim, H.Y.; Shin, S.M.; Lee, C.O.; Kim, D.S.; Choi, K.K.; Kim, S.Y. Clinical Effectiveness of Different Polishing Systems and Self-Etch Adhesives in Class V Composite Resin Restorations: Two-Year Randomized Controlled Clinical Trial. *Oper. Dent.* **2017**, *42*, 19-29.
259. Perdigão, J.; Dutra-Corrêa, M.; Saraceni, C.H.; Ciaramicoli, M.T.; Kiyan, V.H.; Queiroz, C.S. Randomized Clinical Trial of Four Adhesion Strategies: 18-Month Results. *Oper. Dent.* **2012**, *37*, 3-11.
260. Guchait, A.; Saxena, A.; Chattopadhyay, S.; Mondal, T. Influence of Nanofillers on Adhesion Properties of Polymeric Composites. *ACS Omega* **2022**, *7*, 3844-3859.
261. Conde, M.C.; Zanchi, C.H.; Rodrigues-Junior, S.A.; Carreno, N.L.; Ogliari, F.A.; Piva, E. Nanofiller Loading Level: Influence on Selected Properties of an Adhesive Resin. *J. Dent.* **2009**, *37*, 331-335.
262. Amin, F.; Fareed, M.A.; Zafar, M.S.; Khurshid, Z.; Palma, P.J.; Kumar, N. Degradation and Stabilization of Resin-Dentine Interfaces in Polymeric Dental Adhesives: An Updated Review. *Coatings* **2022**, *12*, 1094.
263. Van Meerbeek, B.; De Munck, J.; Yoshida, Y.; Inoue, S.; Vargas, M.; Vijay, P., et al. Buonocore Memorial Lecture. Adhesion to Enamel and Dentin: Current Status and Future Challenges. *Oper. Dent.* **2003**, *28*, 215-235.
264. Tavares, F.V.; Maciel, C.M.; Watanabe, M.U.; Vieira-Junior, W.F.; França, F.M.; Turssi, C.P.; Basting, R.T. Influence of Adhesive Systems Containing Different Functional Monomers on the Longevity of Bond Strength at Different Dentin Depths. *Int. J. Adhes. Adhes.* **2024**, *132*, 103723.
265. Yurevna, C.V. Adhesive Systems and Their Classification. *J. Mod. Educ. Achiev.* **2023**, *8*, 198-201.
266. Sauro, S.; Pashley, D.H. Strategies to Stabilize Dentine-Bonded Interfaces through Remineralizing Operative Approaches – State of The Art. *Int. J. Adhes. Adhes.* **2016**, *69*, 39-57.
267. Breschi, L.; Mazzoni, A.; Ruggeri, A.; Cadenaro, M.; Di Lenarda, R.; De Stefano Dorigo, E. Dental Adhesion Review: Aging and Stability of the Bonded Interface. *Dent. Mater.* **2008**, *24*, 90-101.
268. Moodley, D.; Grobler, S.R. Dentine Bonding Agents – A Review of Adhesion to Dentine. *SADJ* **2002**, *57*, 234-238.
269. Tay, F.R.; Gwinnett, A.J.; Wei, S.H. The Overwet Phenomenon: An Optical, Micromorphological Study of Surface Moisture in the Acid-Conditioned, Resin-Dentin Interface. *Am. J. Dent.* **1996**, *9*, 43-48.
270. Kanca, J. Wet Bonding: Effect of Drying Time and Distance. *Am. J. Dent.* **1996**, *9*, 273-276.
271. De Goes, M.F.; Pachane, G.C.; García-Godoy, F. Resin Bond Strength with Different Methods to Remove Excess Water from the Dentin. *Am. J. Dent.* **1997**, *10*, 298-301.
272. Costa, D.M.; Somacal, D.C.; Borges, G.A.; Spohr, A.M. Bond Capability of Universal Adhesive Systems to Dentin in Self-Etch Mode after Short-Term Storage and Cyclic Loading. *Open Dent. J.* **2017**, *11*, 276-283.
273. Breschi, L.; Prati, C.; Gobbi, P.; Pashley, D.; Mazzoti, G.; Teti, G., et al. Immunohistochemical Analysis of Collagen Fibrils within the Hybrid Layer: A FEISEM Study. *Oper. Dent.* **2004**, *29*, 538-546.

274. Tani, C.; Finger, W.J. Effect of Smear Layer Thickness on Bond Strength Mediated by Three All-in-One Self-Etching Priming Adhesives. *J. Adhes. Dent.* **2002**, *4*, 283-289.
275. Li, F.; Zhang, L.; Weir, M.D.; Cheng, L.; Zhang, K.; Xu, H.H.K. Understanding the Chemistry and Improving the Durability of Dental Resin-Dentin Bonded Interface. In *Material-Tissue Interfacial Phenomena*; Woodhead Publishing: Sawston, UK, **2017**, 147-180.
276. Cuevas-Suárez, C.E.; da Rosa, W.L.O.; Lund, R.G.; da Silva, A.F.; Piva, E. Bonding Performance of Universal Adhesives: An Updated Systematic Review and Meta-Analysis. *J. Adhes. Dent.* **2019**, *21*, 7-26.
277. Sezinando, A. Looking for the Ideal Adhesive – A Review. *Rev. Port. Estomatol.* **2014**, *55*, 194-206.
278. Alex, G. Adhesive Considerations in the Placement of Direct Composite Restorations. *Oral Health* **2008**, *98*, 109-119.
279. Fabianelli, A.; Vichi, A.; Kugel, G.; Ferrari, M. Influence of Self-Etching-Priming Bonding Systems on Sealing Ability of Class II Restorations: Leakage and SEM Evaluations. Paper presented at annual meeting of the International Association for Dental Research, Washington, D.C., USA, 5-8 April **2000.**
280. Lührs, A.K.; Guhr, S.; Schilke, R.; Borchers, L.; Geurtsen, W.; Günay, H. Shear Bond Strength of Self-Etch Adhesives to Enamel with Additional Phosphoric Acid Etching. *Oper. Dent.* **2008**, *33*, 155-162.
281. Manuja, N.; Nagpal, R.; Pandit, I.K. Dental Adhesion: Mechanism, Techniques, and Durability. *J. Clin. Pediatr. Dent.* **2012**, *36*, 223-234.
282. Yaseen, S.M.; Subba Reddy, V.V. Comparative Evaluation of Shear Bond Strength of Two Self-Etching Adhesives (Sixth and Seventh Generation) on Dentin of Primary and Permanent Teeth: An In Vitro Study. *J. Indian Soc. Pedod. Prev. Dent.* **2009**, *27*, 33-38.
283. Chersoni, S.; Suppa, P.; Grandini, S.; Goracci, C.; Monticelli, F.; Yiu, C.; et al. In Vivo and In Vitro Permeability of One-Step Self-Etch Adhesives. *J. Dent. Res.* **2004**, *83*, 459-464.
284. Chersoni, S.; Suppa, P.; Breschi, L.; Ferrari, M.; Tay, F.R.; Pashley, D.H.; et al. Water Movement in the Hybrid Layer after Different Dentin Treatments. *Dent. Mater.* **2004**, *20*, 796-803.
285. Sanares, A.M.E.; Itthagarun, A.; King, N.M.; Tay, F.R.; Pashley, D.H. Adverse Surface Interactions Between One-Bottle Light-Cured Adhesives and Chemical-Cured Composites. *Dent. Mater.* **2001**, *17*, 542-556. doi:10.1016/S0109-5641(01)00016-1.
286. Tay, F.R.; Suh, B.I.; Pashley, D.H.; Prati, C.; Chuang, S.-F.; Li, F. Factors Contributing to the Incompatibility Between Simplified-Step Adhesives and Self-Cured or Dual-Cured Composites. Part II. Single-Bottle, Total-Etch Adhesive. *J. Adhes. Dent.* **2003**, *5*, 91-105.
287. Suh, B.; Feng, L.; Pashley, D.; Tay, F. Factors Contributing to the Incompatibility Between Simplified-Step Adhesives and Chemically-Cured or Dual-Cured Composites. Part III. Effect of Acidic Resin Monomers. *J. Adhes. Dent.* **2003**, *5*, 267-282.
288. Tay, F.R.; Pashley, D.; Yiu, C.; Sanares, A.M.E.; Wei, S.H.Y. Factors Contributing to the Incompatibility Between Simplified-Step Adhesives and Chemically-Cured or Dual-Cured Composites. Part I. Single-Step Self-Etching Adhesive. *J. Adhes. Dent.* **2003**, *5*, 27-40.
289. Ñaupari-Villasante, R.; Matos, T.P.; de Albuquerque, E.G.; Warol, F.; Tardem, C.; Calazans, F.S.; Poubel, L.A.; Reis, A.; Barceleiro, M.O.; Loguercio, A.D. Five-Year Clinical Evaluation of Universal Adhesive Applied Following Different Bonding Techniques: A Randomized Multicenter Clinical Trial. *Dent. Mater.* **2023**, *39*, 586-594.
290. Isolan, C.P.; Valente, L.L.; Münchow, E.A.; Basso, G.R.; Pimentel, A.H.; Schwantz, J.K.; da Silva, A.V.; Moraes, R.R. Bond Strength of a Universal Bonding Agent and Other Contemporary Dental Adhesives Applied on Enamel, Dentin, Composite, and Porcelain. *Appl. Adhes. Sci.* **2014**, *2*, 25.
291. Tang, C.; Mercelis, B.; Yoshihara, K.; Peumans, M.; Van Meerbeek, B. Does the Universal Adhesive's Film Thickness Affect Dentin-Bonding Effectiveness? *Clin. Oral. Investig.* **2024**, *28*, 150.
292. Yamanaka, A.; Mine, A.; Matsumoto, M.; Hagino, R.; Yumitate, M.; Ban, S.; Ishida, M.; Miura, J.; Van Meerbeek, B.; Yatani, H. Back to the Multi-Step Adhesive System: A Next-Generation Two-Step System with Hydrophobic Bonding Agent Improves Bonding Effectiveness. *Dent. Mater. J.* **2021**, *40*, 928-933.
293. Wang, L.; Bai, X.; Liu, Y.; Islam, R.; Hoshika, S.; Sano, H.; Yang, F. The Effect of an Extra Hydrophobic Resin Layer on the Bond Strength and Durability of One-Step Universal Adhesives Used as a Primer. *J. Dent.* **2023**, *135*, 104568.

294. Tang, C.; Ahmed, M.H.; Yao, C.; Mercelis, B.; Yoshihara, K.; Peumans, M.; Van Meerbeek, B. Experimental Two-Step Universal Adhesives Bond Durably in a Challenging High C-Factor Cavity Model. *Dent. Mater.* **2023**, *39*, 70-85.
295. Cuevas-Suárez, C.E.; de Oliveira da Rosa, W.L.; Vitti, R.P.; da Silva, A.F.; Piva, E. Bonding Strength of Universal Adhesives to Indirect Substrates: A Meta-Analysis of In Vitro Studies. *J. Prosthodont.* **2020**, *29*, 298-308.
296. Schittly, E.; Bouter, D.; Le Goff, S.; Degrange, M.; Attal, J.P. Compatibility of Five Self-Etching Adhesive Systems with Two Resin Luting Cements. *J. Adhes. Dent.* **2010**, *12*, 137-142.
297. Suh, B.I. *Principles of Adhesive Dentistry: A Theoretical and Clinical Guide for Dentists*; Aegis Publications LLC: Newtown, PA, USA, **2013.**
298. Suh, B.I. Universal Adhesives: The Evolution of Adhesive Solutions Continues. *Compend. Contin. Educ. Dent.* **2014**, *35*, 278.
299. Brkanović, S.; Sever, E.K.; Vukelja, J.; Ivica, A.; Miletić, I.; Krmek, S.J. Comparison of Different Universal Adhesive Systems on Dentin Bond Strength. *Materials* **2023**, *16*, 1530.
300. Lima, R.B.W.; Silva, A.F.; da Rosa, W.L.; Piva, E.; Duarte, R.M.; De Souza, G.M. Bonding Efficacy of Universal Resin Adhesives to Zirconia Substrates: Systematic Review and Meta-Analysis. *J. Adhes. Dent.* **2023**, *25*, 51-62. doi:10.3290/J.JAD.B3868649.
301. Dos Santos, R.A.; de Lima, E.A.; Mendonça, L.S.; de Oliveira, J.E.; Rizuto, A.V.; de Araújo Silva Tavares, Á.F.; Braz da Silva, R. Can universal adhesive systems bond to zirconia?. *J. Esthet. Restor. Dent.* **2019**, *31*, 589-594.
302. de Lucena Pereira, L.; Campos, F.; Dal Piva, A.M.; Gondim, L.D.; de Assunção Souza, R.O.; Oezcan, M. Can application of universal primers alone be a substitute for airborne-particle abrasion to improve adhesion of resin cement to zirconia. *J. Adhes. Dent.* **2015**, *17*, 169-174.
303. Amaral, M.; Belli, R.; Cesar, P.F.; Valandro, L.F.; Petschelt, A.; Lohbauer, U. The Potential of Novel Primers and Universal Adhesives to Bond to Zirconia. *J. Dent.* **2014**, *42*, 90-98. doi:10.1016/j.jdent.2013.11.004.
304. Makishi, P.; André, C.B.; Silva, J.P.L.E.; Bacelar-Sá, R.; Correr-Sobrinho, L.; Giannini, M. Effect of Storage Time on Bond Strength Performance of Multimode Adhesives to Indirect Resin Composite and Lithium Disilicate Glass Ceramic. *Oper. Dent.* **2016**, *41*, 541-551. doi:10.2341/15-187-L.
305. Lima, R.B.; Muniz, I.D.; Murillo-Gómez, F.; de Andrade, A.K.; Duarte, R.M.; de Souza, G.M. Effect of universal adhesives and self-etch ceramic primers on bond strength to glass-ceramics: A systematic review and meta-analysis of in vitro studies. *J. Prosthet. Dent.* **2024**, *131*, 392-402.
306. Kim, Y.R.; Kim, J.H.; Son, S.A.; Park, J.K. Effect of Silane-Containing Universal Adhesives on the Bonding Strength of Lithium Disilicate. *Materials* **2021**, *14*, 3976. doi:10.3390/ma14143976.
307. Kalavacharla, V.K.; Lawson, N.C.; Ramp, L.C.; Burgess, J.O. Influence of Etching Protocol and Silane Treatment with a Universal Adhesive on Lithium Disilicate Bond Strength. *Oper. Dent.* **2015**, *40*, 372-378. doi:10.2341/14-116-L.
308. Tsujimoto, A.; Shimatani, Y.; Nojiri, K.; Barkmeier, W.W.; Markham, M.D.; Takamizawa, T.; Latta, M.A.; Miyazaki, M. Influence of surface wetness on bonding effectiveness of universal adhesives in etch-and-rinse mode. *Eur. J. Oral Sci.* **2019**, *127*, 162-169.
309. Alex, G. Preparing Porcelain Surfaces for Optimal Bonding. *Compend. Contin. Educ. Dent.* **2008**, *29*, 324-336.
310. Awad, M.M.; Albedaiwi, L.; Almahdy, A.; Khan, R.; Silikas, N.; Hatamleh, M.M.; Alkhtani, F.M.; Alrahlah, A. Effect of universal adhesives on microtensile bond strength to hybrid ceramic. *BMC Oral Health* **2019**, *19*, 178.
311. Alin, W.; Ferracane, J. Resin-based cements used in dentistry. In Handbook of Oral Biomaterials; Pan Stanford Publishing Pte. Ltd.: Singapore, **2014**; pp. 213–254.
312. Yoshihara, K.; Nagaoka, N.; Sonoda, A.; Maruo, Y.; Makita, Y.; Okihara, T.; Irie, M.; Yoshida, Y.; Van Meerbeek, B. Effectiveness and stability of silane coupling agent incorporated in 'universal' adhesives. *Dent. Mater.* **2016**, *32*, 1218-1225.
313. Tsujimoto, A.; Fischer, N.G.; Barkmeier, W.W.; Latta, M.A. Bond Durability of Two-Step HEMA-Free Universal Adhesive. *J. Funct. Biomater.* **2022**, *13*, 134.
314. Katsuki, S.; Takamizawa, T.; Yokoyama, M.; Sai, K.; Tamura, T.; Ishii, R.; Kamimoto, A.; Miyazaki, M. Influence of Bonding Agent Application Method on the Dentin Bond Durability of a Two-Step Adhesive Utilizing a Universal-Adhesive-Derived Primer. *Eur. J. Oral Sci.* **2022**, *130*, e12868.

315. Takamizawa, T.; Hirokane, E.; Sai, K.; Ishii, R.; Aoki, R.; Barkmeier, W.W.; Latta, M.A.; Miyazaki, M. Bond Durability of a Two-Step Adhesive with a Universal-Adhesive-Derived Primer in Different Etching Modes Under Different Degradation Conditions. *Dent. Mater. J.* **2023**, *42*, 121-132.
316. Takamizawa, T.; Barkmeier, W.W.; Tsujimoto, A.; Berry, T.P.; Watanabe, H.; Erickson, R.L.; Latta, M.A.; Miyazaki, M. Influence of different etching modes on bond strength and fatigue strength to dentin using universal adhesive systems. *Dent. Mater*. **2016**, *32*, e9–e21.
317. Triani, F.; Pereira da Silva, L.; Ferreira Lemos, B.; Domingues, J.; Teixeira, L.; Manarte-Monteiro, P. Universal Adhesives: Evaluation of the Relationship Between Bond Strength and Application Strategies—A Systematic Review and Meta-Analyses. *Coatings* **2022**, *12*, 1501. doi:10.3390/coatings12101501.
318. Da Rosa, W.L.D.O.; Piva, E.; Da Silva, A.F. Bond Strength of Universal Adhesives: A Systematic Review and Meta-Analysis. *J. Dent.* **2015**, *43*, 765-776. doi:10.1016/j.jdent.2015.04.003.
319. Pongprueksa, P.; Miletic, V.; De Munck, J.; Brooks, N.R.; Meersman, F.; Nies, E.; et al. Effect of Evaporation on the Shelf Life of a Universal Adhesive. *Oper. Dent.* **2014**, *39*, 500-507.
320. Sundfeld, R.H.; da Silva, A.M.J.D.; Croll, T.P.; de Oliveira, C.H.; Briso, A.L.F.; de Alexandre, R.S.; et al. The Effect of Temperature on Self-Etching Adhesive Penetration. *Compend. Contin. Educ. Dent.* **2006**, *27*, 552-556, 581.
321. Antoniazzi, B.F.; Nicoloso, G.F.; Lenzi, T.L.; Soares, F.Z.; Rocha, R.D.O. Selective Acid Etching Improves the Bond Strength of Universal Adhesive to Sound and Demineralized Enamel of Primary Teeth. *J. Adhes. Dent.* **2016**, *18*, 311-316.
322. Chang, B.J.; Lawson, N.C.; Burgess, J.O. Effect of Adhesive Coats and Solvents on Bond Strength. *J. Dent. Res.* **2015**, *94*, 3385.
323. Elkaffas, A.A.; Hamama, H.H.; Mahmoud, S.H.; Fawzy, A.S. Effect of Acid Etching on Dentin Bond Strength of Ultra-Mild Self-Etch Adhesives. *Int. J. Adhes. Adhes.* **2020**, *99*, 102567.
324. Burke, F.T.; Mackenzie, L. Bonding to Dentine: An Update on Universal Adhesives. *Dent. Update* **2021**, *48*, 620-631.
325. Loguercio, A.D.; Muñoz, M.A.; Luque-Martinez, I.; Hass, V.; Reis, A.; Perdigão, J. Does Active Application of Universal Adhesives to Enamel in Self-Etch Mode Improve Their Performance? *J. Dent.* **2015**, *43*, 1060-1070.
326. e Siqueira, F.S.; Pinto, T.F.; Carvalho, E.M.; Bauer, J.; Gonçalves, L.M.; Szesz, A.L.; Reis, A.; Cardenas, A.F.; Loguercio, A.D. Influence of Dentinal Moisture on the Properties of Universal Adhesives. *Int. J. Adhes. Adhes.* **2020**, *101*, 102633.
327. Chen, C.; Niu, L.N.; Xie, H.; Zhang, Z.Y.; Zhou, L.Q.; Jiao, K.; Chen, J.H.; Pashley, D.H.; Tay, F.R. Bonding of universal adhesives to dentine—Old wine in new bottles? *J. Dent*. **2015**, *43*, 525-536.
328. Burke, F.T.; Sands, P.; Crisp, R.J. A practice-based clinical evaluation of a novel two-bottle dentine adhesive system. *Dent. Update* **2022**, *49*, 112-116.
329. Van de Sande, F.H.; Collares, K.; Correa, M.B.; Cenci, M.S.; Demarco, F.F.; Opdam, N.J.M. Restoration Survival: Revisiting Patients' Risk Factors through a Systematic Literature Review. *Oper. Dent*. **2016**, *41*, S7–S26.
330. Frankenberger, R.; Tay, F.R.; Self-etch, Bonding. Self-etch, total-etch, and selective enamel etch adhesives in clinical dentistry. *Oper. Dent.* **2021**, *46*, E330-E345.
331. Malaquias, P.; da Silva, L.P.; Lemos, B.F.; Domingues, J.; Teixeira, L.; Monteiro, P.M. Universal adhesives and dual-cured core buildup composite material: adhesive properties. *J. Appl. Oral Sci.* **2020**, *28*, e20200121.
332. Gutiérrez, M.F.; de Assis, D.R.; Fugolin, A.P.; Scheffel, D.L.; Giannini, M.; Reis, A.; Loguercio, A.D. Effect of self-curing activators and curing protocols on adhesive properties of universal adhesives bonded to dual-cured composites. *Dent. Mater.* **2017**, *33*, 775-787.
333. Lawson, N.C.; Robles, A.; Fu, C.; Lin, C.P.; Sawlani, K.; Burgess, J.O. Two-year clinical trial of a universal adhesive in total-etch and self-etch mode in non-carious cervical lesions. *J. Dent.* **2016**, *51*, 78-83.
334. Luque-Martinez, I.V.; Perdigão, J.; Muñoz, M.A.; Sezinando, A.; Reis, A.; Loguercio, A.D. Effects of solvent evaporation time on immediate adhesive properties of universal adhesives to dentin. *Dent. Mater.* **2014**, *30*, 1126-1135.
335. De Munck, J.; Mine, A.; Poitevin, A.; Van Ende, A.; Cardoso, M.V.; Van Landuyt, K.L.; Peumans, M.; Van Meerbeek, B. Meta-analytical review of parameters involved in dentin bonding. *J. Dent. Res.* **2012**, *91*, 351-357.

336. Dreweck, F.D.; Burey, A.; de Oliveira Dreweck, M.; Fernandez, E.; Loguércio, A.D.; Reis, A. Challenging the concept that OptiBond FL and Clearfil SE bond in NCCLs are gold standard adhesives: a systematic review and meta-analysis. *Oper. Dent.* **2021**, *46*, E276-E295.
337. van Dijken, J.W.; Pallesen, U. Long-term dentin retention of etch-and-rinse and self-etch adhesives and a resin-modified glass ionomer cement in non-carious cervical lesions. *Dent. Mater.* **2008**, *24*, 915-922.
338. Peumans, M.; De Munck, J.; Van Landuyt, K.; Van Meerbeek, B. Thirteen-year randomized controlled clinical trial of a two-step self-etch adhesive in non-carious cervical lesions. *Dent. Mater.* **2015**, *31*, 308-314.
339. Reis, A.; Loguercio, A.D.; Favoreto, M.; Chibinski, A.C. Some myths in dentin bonding: an evidence-based perspective. *J. Dent. Res.* **2023**, *102*, 376-382.
340. Zald, H.S. The Effect of Primer Application Modifications on the Bond Strength of 4th Generation Adhesive Bonding Agents (Doctoral dissertation, Uniformed Services University of the Health Sciences).
341. Wang, R.; Shi, Y.; Li, T.; Pan, Y.; Cui, Y.; Xia, W. Adhesive interfacial characteristics and the related bonding performance of four self-etching adhesives withdifferent functional monomers applied to dentin. *J. Dent.* **2017**, *62*, 72-80.
342. Vinagre, A.; Ramos, J.; Marques, F.; Chambino, A., Messias, A., Mata, A. Randomized clinical trial of five adhesive systems in occlusal restorations: One-year results. *Dent. Mater. J.* **2020**, *39*, 397-406.
343. Nicola, C.; Sava, S.; Dudea, D.; Bondor, C.I.; Şoancă, A.; Colceriu, L.; Alb, C. Influence of adhesive systems composition on dual-cured resin cements. *J. Optoelectron. Biomed. Mater.* **2009**, *1*, 331-337.
344. Lukomska-Szymanska, M.; Zarzycka, B.; Zurawska-Olszewska, J.; Olbert-Sieroszewska, V.; Sokolowski, K.; Sokolowski, J. Antibacterial activity of eight dentine bonding systems. *IOSR J. Dent. Med. Sci.* **2014**, *13*, 48-54.
345. Lapinska, B.; Konieczka, M.; Zarzycka, B.; Sokolowski, K.; Grzegorczyk, J.; Lukomska-Szymanska, M. Flow cytometry analysis of antibacterial effects of universal dentin bonding agents on *Streptococcus mutans*. *Molecules* **2019**, *24*, 532.
346. Polydorou, O.; Rogatti, P.; Bolek, R.; Wolkewitz, M.; Kümmerer, K.; Hellwig, E. Elution of monomers from three different bonding systems and their antibacterial effect. *Odontology* **2013**, *101*, 170-176.
347. Peumans, M.; De Munck, J.; Van Landuyt, K.L.; Poitevin, A.; Lambrechts, P.; Van Meerbeek, B. A 13-year clinical evaluation of two three-step etch-and-rinse adhesives in non-carious class-V lesions. *Clin. Oral. Investig.* **2012**, *16*, 129-137.
348. Wilder, A.D., Jr.; Swift, E.J., Jr.; Heymann, H.O.; Ritter, A.V.; Sturdevant, R., Jr.; Bayne, S.C. A 12-year clinical evaluation of a three-step dentin adhesive in noncarious cervical lesions. *J. Am. Dent. Assoc.* **2009**, 140, 526-535.
349. Walter, R.; Swift, E.J., Jr.; Boushell, L.W.; Braswell, K. Enamel and dentin bond strengths of a new self-etch adhesive system. *J. Esthet. Restor. Dent.* **2011**, *23*, 390-396.
350. Magne, P.; So, W.-S.; Cascione, D. Immediate dentin sealing supports delayed restoration placement. *J. Prosthet. Dent.* **2007**, *98*, 166-174.
351. Carvalho, A.O.; Bacelar-Sá, R.; Wodevotzky, O.; Ambrosano, G.M.B.; Magne, P.; Giannini, M. Bond strength and micromorphology of resin-dentin interface of etch-and-rinse dentin bonding agents after 1-year of water storage. *Appl. Adhes. Sci.* **2016**, *4*, 1.
352. Magne, P. Immediate dentin sealing: a fundamental procedure for indirect bonded restorations. *J. Esthet. Restor. Dent.* **2005**, *17*, 144-152.
353. de Carvalho, M.A.; Lazari-Carvalho, P.C.; Polonial, I.F.; de Souza, J.B.; Magne, P. Significance of immediate dentin sealing and flowable resin coating reinforcement for unfilled/lightly filled adhesive systems. *J. Esthet. Restor. Dent.* **2021**, *33*, 88-98.
354. Peumans, M.; De Munck, J.; Van Landuyt, K.L.; Poitevin, A.; Lambrechts, P.; Van Meerbeek, B. Eight-year clinical evaluation of a 2-step self-etch adhesive with and without selective enamel etching. *Dent. Mater.* **2010**, *26*, 1176-1184.
355. Peumans, M.; De Munck, J.; Van Landuyt, K.; Lambrechts, P.; Van Meerbeek, B. Five-year clinical effectiveness of a two-step self-etching adhesive. *J. Adhes. Dent.* **2007**, *9*, 7-10.
356. Valsan, D.; Bhaskaran, S.; Mathew, J.; Hari, K.; Joy, J. Comparative Evaluation of the Bonding Efficacy of Multimode Adhesive, Two-Step Self-Etch Adhesive, and a Total-Etch System to Pulpal Floor Dentin–An In vitro Study. *Contemp. Clin. Dent.* **2023**, *14*, 104-108.
357. Sensi, L.G.; Lopes, G.C.; Monteiro, S., Jr.; Baratieri, L.N.; Vieira, L.C. Dentin bond strength of self-etching primers/adhesives. *Oper. Dent.* **2005**, *30*, 63-68.

358. Takahashi, A.; Sato, Y.; Uno, S.; Pereira, P.N.; Sano, H. Effects of mechanical properties of adhesive resins on bond strength to dentin. *Dent. Mater.* **2002**, *18*, 263-268.
359. Montes, M.A.; de Goes, M.F.; da Cunha, M.R.; Soares, A.B. A morphological and tensile bond strength evaluation of an unfilled adhesive with low-viscosity composites and a filled adhesive in one and two coats. *J. Dent.* **2001**, 29, 435-441.
360. Tuncer, S.; Tekce, N.; Pashaev, D.; Demirci, M.; Baydemir, C. Short-and long-term bond strengths of a gold standard two-step self-etch adhesive system to dentin: a preliminary study. *J. Istanbul Univ. Fac. Dent.* **2015**, 49, 1-7.
361. Sato, K.; Hosaka, K.; Takahashi, M.; Ikeda, M.; Tian, F.; Komada, W.; Nakajima, M.; Foxton, R.; Nishitani, Y.; Pashley, D.H.; Tagami, J. Dentin Bonding Durability of Two-step Self-etch Adhesives with Improved of Degree of Conversion of Adhesive Resins. *J. Adhes. Dent.* **2017**, *19*, 31-37.
362. Bourgi, R.; Kharouf, N.; Cuevas-Suárez, C.E.; Lukomska-Szymańska, M.; Devoto, W.; Kassis, C.; Hasbini, O.; Mancino, D.; Haikel, Y.; Hardan, L. Effect of Modified Triple-Layer Application on the Bond Strength of Different Dental Adhesive Systems to Dentin. *J. Funct. Biomater.* **2023**, *14*, 522.
363. Esteves, C.M.; Ota-Tsuzuki, C.; Reis, A.F.; Rodrigues, J.A. Antibacterial Activity of Various Self-etching Adhesive Systems Against Oral Streptococci. *Oper. Dent.* **2010**, *35*, 448-453.
364. Brandt, P.D.; Botha, F.S.; de Wet, F.A. Antibacterial properties of five bonding agents. *SADJ* **2008**, *63*, 448-451.
365. Imazato, S.; Ehara, A.; Torii, M.; Ebisu, S. Antibacterial activity of dentine primer containing MDPB after curing. *J. Dent.* **1998**, *26*, 267-271.
366. Sesen Uslu, Y.; Arıcan Alpay, B.; Sesen, P.; Özyürek, T. Preventive Effects of Laser Irradiation and Dentin Bonding Agent Application on Tooth Discoloration Induced by Mineral Trioxide Aggregate. *Materials* **2024**, *17*, 1015.
367. Mahdhaoui, K.; Fournier, B.; Derbanne, M.A. Unbound monomers do diffuse through the dentin barrier. *Dent. Mater.* **2017**, *33*, 743-751.
368. Tian, F.C.; Wang, X.Y.; Huang, Q.; Niu, L.N.; Mitchell, J.; Zhang, Z.Y.; Prananik, C.; Zhang, L.; Chen, J.H.; Breshi, L.; Pashley, D.H. Effect of nanolayering of calcium salts of phosphoric acid ester monomers on the durability of resin-dentin bonds. *Acta Biomater.* **2016**, *38*, 190-200.
369. Siddarth, B.; Aileni, K.R.; Rachala, M.R.; Dasari, A.K.; Mallepally, J.P.; Thadisina, P.R.; Navab, S. Comparative evaluation and influence of new Optibond eXTRa self-etch universal adhesive and conventional transbond XT on shear bond strength of orthodontic brackets—an in vitro study. *J. Orthod. Sci.* **2022**, *11*, 43.
370. Han, F.; Dai, S., Yang, J.; Shen, J.; Liao, M.; Xie, H.; Chen, C. Glycerol phosphate dimethacrylate: An alternative functional phosphate ester monomer to 10-methacryloyloxydecyl dihydrogen phosphate for enamel bonding. *ACS Omega* **2020**, *5*, 24826-24837.
371. Peumans, M.; Kanumilli, P.; De Munck, J.; Van Landuyt, K.; Lambrechts, P.; Van Meerbeek, B. Clinical effectiveness of contemporary adhesives: a systematic review of current clinical trials. *Dent. Mater.* **2005**, *21*, 864-881.
372. Almusa, A.; Delgado, A.H.S.; Ashley, P.; Young, A.M. Determination of Dental Adhesive Composition throughout Solvent Drying and Polymerization Using ATR-FTIR Spectroscopy. *Polymers (Basel)* **2021**, 13, 3886.
373. Aung, S. S. M. P.; Takagaki, T.; Ikeda, M.; Tagami, J. Ultra-morphological Studies on Enamel-Universal Adhesive Interface. *J. Dent.* **2021**, *104*, 103527.
374. Besic, E.; Norstedt, S. Shear Bond Strength of Composite to Dentine with Various Adhesive Systems. **2023**.
375. Latif, A.R.; Vorobyeva, Y.B.; Malysheva, D.D.; Kovalevsky, A.M. Laboratory study and clinical application of adhesive marginal fit of dental hard tissue restorations. *Russ. J. Dent.* **2022**, *26*, 487-95.
376. Staxrud, F.; Valen, H. Potential of "Universal" Bonding Agents for Composite Repair. *Biomater. Investig. Dent.* **2022**, *9*, 41-46.
377. Bourgi, R.; Daood, U.; Bijle, M.N.; Fawzy, A.; Ghaleb, M.; Hardan, L. Reinforced universal adhesive by ribose crosslinker: A novel strategy in adhesive dentistry. *Polymers* **2021**, *13*, 704.
378. Fabião, A.D.M.; Fronza, B.M.; André, C.B.; Cavalli, V.; Giannini, M. Microtensile dentin bond strength and interface morphology of different self-etching adhesives and universal adhesives applied in self-etching mode. *J. Adhes. Sci. Technol*. **2020**, *35*, 1-10.
379. Ahmed, M.H.; Yao, C.; Van Landuyt, K.; Peumans, M.; Van Meerbeek, B. Extra Bonding Layer Compensates Universal Adhesive's Thin Film Thickness. *J. Adhes. Dent*. **2020**, *22*, 483-501.

380. Tichy, A.; Hosaka, K.; Abdou, A.; Nakajima, M.; Tagami, J. Degree of Conversion Contributes to Dentin Bonding Durability of Contemporary Universal Adhesives. *Oper. Dent*. **2020**, 45, 556-566.
381. Sugimura, R.; Tsujimoto, A.; Hosoya, Y.; Fischer, N.G.; Barkmeier, W.W.; Takamizawa, T.; Latta, M.A.; Miyazaki, M. Surface moisture influence on etch-and-rinse universal adhesive bonding. *Am. J. Dent*. **2019**, *32*, 33-38.
382. de Almeida, R.A.; Lima, S.N.; Nassif, M.V.; Mattos, N.H.; de Matos, T.P.; de Jesus Tavarez, R.R.; Cardenas, A.F.; Bandeca, M.C.; Loguercio, A.D. Eighteen-month clinical evaluation of a new universal adhesive applied in the "no-waiting" technique: A randomized clinical trial. *Clin. Oral. Investig*. **2023**, 27, 151-63.
383. Hardan, L.; Orsini, G.; Bourgi, R.; Cuevas-Suárez, C.E.; Nicastro, M.; Lazarescu, F.; Filtchev, D.; Cornejo-Ríos, E.; Zamarripa-Calderón, J.E.; Sokolowski, K. Effect of Active Bonding Application after Selective Dentin Etching on the Immediate and Long-Term Bond Strength of Two Universal Adhesives to Dentin. *Polymers* **2022**, *14*, 1129.
384. Saeed, N.A.; Tichy, A.; Kuno, Y.; Hosaka, K.; Tagami, J.; Nakajima, M. Effect of Surface Moisture on Bur-Cut Dentin on Bonding of HEMA-Free and HEMA-Containing Universal Adhesives with or without Methacrylamide Monomer. *J. Adhes. Dent*. **2021**, *23*, 327-334.
385. Ruschel, V.C.; Stolf, S.C.; Shibata, S.; Chung, Y.; Boushell, L.W.; Baratieri, L.N.; Walter, R. Three-year clinical evaluation of universal adhesives in non-carious cervical lesions. *Am. J. Dent*. **2019**, *32*, 223-228.
386. Lopes, L.S.; Calazans, F.S.; Hidalgo, R.; Buitrago, L.L.; Gutierrez, F.; Reis, A.; Loguercio, A.D.; Barceleiro, M.O. Six-month follow-up of cervical composite restorations placed with a new universal adhesive system: a randomized clinical trial. *Oper. Dent*. **2016**, *41*, 465-480.
387. Barceleiro, M.O.; Lopes, L.S.; Tardem, C.; Calazans, F.S.; Matos, T.P.; Reis, A.; Calixto, A.L.; Loguercio, A.D. Thirty-six-month follow-up of cervical composite restorations placed with an MDP-free universal adhesive system using different adhesive protocols: a randomized clinical trial. *Clin. Oral. Investig*. **2022**, *26*, 4337-4350.
388. Ahmed, M.H.; De Munck, J.; Van Landuyt, K.; Peumans, M.; Yoshihara, K.; Van Meerbeek, B. Do universal adhesives benefit from an extra bonding layer? *J. Adhes. Dent*. **2019**, *21*, 117-132.
389. Gutierrez, M.F.; Bermudez, J.; Davila-Sanchez, A.; Alegria-Acevedo, L.F.; Mendez-Bauer, L.; Hernandez, M.; Astorga, J.; Reis, A.; Loguercio, A.D.; Farago, P.V.; Fernandez, E. Zinc oxide and copper nanoparticles addition in universal adhesive systems improve interface stability on caries-affected dentin. *J. Mech. Behav. Biomed. Mater*. **2019**, *100*, 103366.
390. Burrer, P.; Dang, H.; Par, M.; Attin, T.; Taubock, T.T. Effect of over-etching and prolonged application time of a universal adhesive on dentin bond strength. *Polymers (Basel)* **2020**, *12*, 2902.
391. Zhang, Z.Y.; Tian, F.C.; Niu, L.N.; Ochala, K.; Chen, C.; Fu, B.P.; Wang, X.Y.; Pashley, D.H.; Tay, F.R. Defying ageing: An expectation for dentine bonding with universal adhesives? *J. Dent.* **2016**, *45*, 43-52.
392. Serafim, M.F.D.; Leal, A.M.A.; Bauer, J.; Gomes, I.A.; Carneiro, K.G.K. Effect of an hydrophobic layer on a universal adhesive. *RGO-Revista Gaúcha de Odontologia* **2018**, 66, 339-344.
393. Albuquerque, M.; Pegoraro, M.; Mattei, G.; Reis, A.; Loguercio, A.D. Effect of double-application or the application of a hydrophobic layer for improved efficacy of one-step self-etch systems in enamel and dentin. *Oper. Dent*. **2008**, *33*, 564-570.
394. Roggendorf, M.J.; Krämer, N.; Appelt, A.; Naumann, M.; Frankenberger, R. Marginal quality of flowable 4-mm base vs. conventionally layered resin composite. *J. Dent*. **2011**, *39*, 643-647.
395. Van Meerbeek, B.; Willems, G.; Celis, J.P.; Roos, J.R.; Braem, M.; Lambrechts, P.; Vanherle, G. Assessment by nano-indentation of the hardness and elasticity of the resin-dentin bonding area. *J. Dent. Res.* **1993**, *72*, 1434-1442.
396. van den Breemer, C.; Özcan, M.; Cune, M.S.; Ayres, A.A.; Van Meerbeek, B.; Gresnigt, M. Effect of Immediate Dentin Sealing and Surface Conditioning on the Microtensile Bond Strength of Resin-based Composite to Dentin. *Oper. Dent.* **2019**, *44*, 289-298.
397. Van Landuyt, K.L.; Peumans, M.; De Munck, J.; Lambrechts, P.; Van Meerbeek, B. Extension of a one-step self-etch adhesive into a multi-step adhesive. *Dent. Mater.* **2006**, *22*, 533-544.
398. Yamada, M.; Miyazaki, M.; Moore, B.K. Influence of interchanging adhesive resins and self-etching primers on the mechanical properties of adhesive resins. *Oper. Dent.* **2004**, *29*, 532-537.
399. Sartori, N.; Peruchi, L.D.; Guimarães, J.C.; Silva, S.B.; Monteiro Jr, S.; Baratieri, L.N., et al. Clinical effectiveness of a hydrophobic coating used in conjunction with a one-step self-etch adhesive: an 18-month evaluation. *Oper. Dent.* **2013**, *38*, 249-257.

400. Mahdan, M.H.; Nakajima, M.; Foxton, R.M.; Tagami, J. Combined effect of smear layer characteristics and hydrostatic pulpal pressure on dentine bond strength of HEMA-free and HEMA-containing adhesives. *J. Dent.* **2013**, *41*, 861-871.
401. Perdigão, J.; Muñoz, M. A.; Sezinando, A.; Luque-Martinez, I. V.; Staichak, R.; Reis, A.; Loguercio, A. D. Immediate Adhesive Properties to Dentin and Enamel of a Universal Adhesive Associated with a Hydrophobic Resin Coat. *Oper. Dent.* **2014**, *39*, 489-499.
402. Ermis, R.B.; Ugurlu, M.; Ahmed, M.H.; Van Meerbeek, B. Universal Adhesives Benefit from an Extra Hydrophobic Adhesive Layer When Light Cured Beforehand. *J. Adhes. Dent.* **2019**, *21*, 179-188.
403. Hardan, L.; Bourgi, R.; Cuevas-Suárez, C.E.; Devoto, W.; Zarow, M.; Monteiro, P.; Jakubowicz, N.; Zoghbi, A.E.; Skaba, D.; Mancino, D.; Kharouf, N. Effect of different application modalities on the bonding performance of adhesive systems to dentin: a systematic review and meta-analysis. *Cells* **2023**, *12*, 190.
404. Huang, X.; Pucci, C.R.; Luo, T.; Breschi, L.; Pashley, D.H.; Niu, L.; Tay, F.R. No-Waiting Dentine Self-Etch Concept—Merit or Hype. *J. Dent.* **2017**, *62*, 54-63.
405. Peutzfeldt, A.; Vigild, M.A. Survey of the Use of Dentin-Bonding Systems in Denmark. *Dent. Mater.* **2001**, *17*, 211-216.
406. Peutzfeldt, A.; Asmussen, E. Adhesive Systems: Effect on Bond Strength of Incorrect Use. *J. Adhes. Dent.* **2002**, *4*, 233-242.
407. Liu, Y.; Liu, Q.; Yu, Q.S., Wang, Y. Non-thermal Atmospheric Plasmas in Dental Restoration. *J. Dent. Res.* **2016**, *95*, 496-505.
408. Ayres, A.P.; Bonvent, J.J.; Mogilevych, B.; Soares, L.E.S.; Martin, A.A.; Ambrosano, G.M.; Nascimento, F.D.; Van Meerbeek, B.; Giannini, M. Effect of non-thermal atmospheric plasma on the dentin-surface topography and composition and on the bond strength of a universal adhesive. *Eur. J. Oral Sci.* **2018**, *126*, 53-65.
409. Han, G.J.; Kim, J.H., Chung, S.N., Chun, B.H., Kim, C.K., Seo, D.G., Son, H.H., Cho, B.H. Effects of non-thermal atmospheric pressure pulsed plasma on the adhesion and durability of resin composite to dentin. *Eur. J. Oral Sci.* **2014**, *122*, 417-423
410. Chen, M.; Zhang, Y.; Sky Driver, M.; Caruso, A.N.; Yu, Q.; Wang, Y. Surface modification of several dental substrates by non-thermal, atmospheric plasma brush. *Dent. Mater.* **2013**, *29*, 871-880.
411. Zhang, Y.; Yu, Q.; Wang, Y. Non-thermal atmospheric plasmas in dental restoration: Improved resin adhesive penetration. *J. Dent.* **2014**, *42*, 1033-1042.
412. Ritts, A.C.; Li, H.; Yu, Q.; Xu, C.; Yao, X.; Hong, L.; Wang, Y. Dentin surface treatment using a non-thermal argon plasma brush for interfacial bonding improvement in composite restoration. *Eur. J. Oral Sci.* **2010**, *118*, 510-516
413. Kim, J.-H.; Han, G.-J.; Kim, C.-K.; Oh, K.-H.; Chung, S.-N.; Chun, B.-H.; Cho, B.-H. Promotion of adhesive penetration and resin bond strength to dentin using non-thermal atmospheric pressure plasma. *Eur. J. Oral Sci.* **2016**, *124*, 89-95.
414. Chen, M.; Zhang, Y.; Dusevich, V.; Liu, Y.; Yu, Q.; Wang, Y. Non-thermal atmospheric plasma brush induces HEMA grafting onto dentin collagen. *Dent. Mater.* **2014**, *30*, 1369-1377.
415. Sampaio, P.C.P.; de Kruly, P.C.; Ribeiro, C.C.; Hilgert, L.A.; Pereira, P.N.R.; Scaffa, P.M.C.; Di Hipólito, V.; D'Alpino, P.H.P.; Garcia, F.C.P. Comparative bonding ability to dentin of a universal adhesive system and monomer conversion as functions of extended light curing times and storage. *J. Mech. Behav. Biomed. Mater.* **2017**, *75*, 41-49.
416. Tay, F.R.; Pashley, D.H.; Kapur, R.R.; Carrilho, M.R.O.; Hur, Y.B.; Garrett, L.V.; Tay, K.C.Y. Bonding BisGMA to Dentin—a Proof of Concept for Hydrophobic Dentin Bonding. *J. Dent. Res.* **2007**, *86*, 1034-1039.
417. Shin, T.P.; Yao, X.; Huenergardt, R.; Walker, M.P.; Wang, Y. Morphological and chemical characterization of bonding hydrophobic adhesive to dentin using ethanol wet bonding technique. *Dent. Mater.* **2009**, *25*, 1050-1057.
418. Sauro, S.; Toledano, M.; Aguilera, F.S.; Mannocci, F.; Pashley, D.H.; Tay, F.R.; Watson, T.F.; Osorio, R. Resin–dentin bonds to EDTA-treated vs. acid-etched dentin using ethanol wet-bonding. Part II: Effects of mechanical cycling load on microtensile bond strengths. *Dent. Mater.* **2011**, 27, 563-572.
419. Li, F.; Liu, X.Y.; Zhang, L.; Kang, J.J.; Chen, J.H. Ethanol-wet bonding technique may enhance the bonding performance of contemporary etch-and-rinse dental adhesives. *J. Adhes. Dent.* **2012**, *14*, 113.

420. Basting, R.T.; Bridi, E.C.; Basting, R.T. Wet-bonding technique with ethanol may reduce protease activity in dentin-resin interface following application of universal adhesive system. *J. Clin. Exp. Dent.* **2023**, *15*, e403-e410.
421. Faria-e-Silva, A.L.; Araujo, J.E.; Rocha, G.P.; de Oliveira, A.S.; de Moraes, R.R. Solvent content and dentin bond strengths using water-wet, ethanol-wet and deproteinization bonding techniques. *Acta. Odontol. Scand.* **2013**, *71*, 710-715.
422. Zhao, S.; Zhu, Z.; Yu, J.; Yao, C.; Yu, M.; Yang, H.; Huang, C. Enhancing dentin bonding quality through Acetone wet-bonding technique: a promising approach. *Front. Bioeng. Biotechnol.* **2023**, *11*, 1309503.
423. Zecin-Deren, A.; Sokolowski, J.; Szczesio-Wlodarczyk, A.; Piwonski, I.; Lukomska-Szymanska, M.; Lapinska, B. Multi-Layer Application of Self-Etch and Universal Adhesives and the Effect on Dentin Bond Strength. *Molecules* **2019**, *24*, 345.
424. Gallo, J.R.; Comeaux, R.; Haines, B.; Xu, X.; Burgess, J.O. Shear bond strength of four filled dentin bonding systems. *Oper. Dent.* **2001**, *26*, 44-47.
425. Choi, K.K.; Condon, J.R.; Ferracane, J.L. The effects of adhesive thickness on polymerization contraction stress of composite. *J. Dent. Res.* **2000**, *79*, 812-817.
426. Kim, J. S.; Cho, B. H.; Lee, I. B.; Um, C. M.; Lim, B. S.; Oh, M. H.; Chang, C. G.; Son, H. H. Effect of the Hydrophilic Nanofiller Loading on the Mechanical Properties and the Microtensile Bond Strength of an Ethanol-Based One-Bottle Dentin Adhesive. *J. Biomed. Mater. Res. Part B Appl. Biomater.* **2005**, *72*, 284-291.
427. Fujiwara, S.; Takamizawa, T.; Barkmeier, W. W.; Tsujimoto, A.; Imai, A.; Watanabe, H.; Erickson, R. L.; Latta, M. A.; Nakatsuka, T.; Miyazaki, M. Effect of Double-Layer Application on Bond Quality of Adhesive Systems. *J. Mech. Behav. Biomed. Mater.* **2018**, *77*, 501-509.
428. Hashimoto, M.; De Munck, J.; Ito, S.; Sano, H.; Kaga, M.; Oguchi, H.; Van Meerbeek, B.; Pashley, D. H. In Vitro Effect of Nanoleakage Expression on Resin-Dentin Bond Strengths Analyzed by Microtensile Bond Test, SEM/EDX, and TEM. *Biomaterials* **2004**, *25*, 5565-5574.
429. Hardan, L.; Lukomska-Szymanska, M.; Zarow, M.; Cuevas-Suárez, C. E.; Bourgi, R.; Jakubowicz, N.; Sokolowski, K.; D'Arcangelo, C. One-Year Clinical Aging of Low Stress Bulk-Fill Flowable Composite in Class II Restorations: A Case Report and Literature Review. *Coatings* **2021**, *11*, 504.
430. Fu, J.; Saikaew, P.; Kawano, S.; Carvalho, R. M.; Hannig, M.; Sano, H.; Selimovic, D. Effect of Air-Blowing Duration on the Bond Strength of Current One-Step Adhesives to Dentin. *Dent. Mater.* **2017**, *33*, 895-903.
431. Bail, M.; Malacarne-Zanon, J.; Silva, S.; Anauate-Netto, A.; Nascimento, F.; Amore, R.; Lewgoy, H.; Pashley, D.H.; Carrilho, M. Effect of Air-Drying on the Solvent Evaporation, Degree of Conversion and Water Sorption/Solubility of Dental Adhesive Models. *J. Mater. Sci. Mater. Med.* **2012**, *23*, 629-638.
432. Daronch, M.; Rueggeberg, F.A.; De Goes, M.; Giudici, R. Polymerization Kinetics of Pre-Heated Composite. *J. Dent. Res.* **2006**, *85*, 38-43.
433. Amaral, R.; Stanislawczuk, R.; Zander-Grande, C.; Gagler, D.; Reis, A.; Loguercio, A.D. Bond Strength and Quality of the Hybrid Layer of One-Step Self-Etch Adhesives Applied with Agitation on Dentin. *Oper. Dent.* **2010**, *35*, 211-219.
434. Reis, A.; Klein-Junior, C.A.; de Souza, F.C.; Stanislawczuk, R.; Loguercio, A.D. The Use of Warm Air Stream for Solvent Evaporation: Effects on the Durability of Resin-Dentin Bonds. *Oper. Dent.* **2010**, *35*, 29-36.
435. Klein-Junior, C.A.; Zander-Grande, C.; Amaral, R.; Stanislawczuk, R.; Garcia, E.J.; Baumhardt-Neto, R.; Meier, M.M.; Loguercio, A.D.; Reis, A. Evaporating Solvents with a Warm Air-Stream: Effects on Adhesive Layer Properties and Resin–Dentin Bond Strengths. *J. Dent.* **2008**, *36*, 618-625.
436. Moura, S.K.; Murad, C.G.; Reis, A.; Klein-Júnior, C.A.; Grande, R.H.M.; Loguercio, A.D. The Influence of Air Temperature for Solvent Evaporation on Bonding of Self-Etch Adhesives to Dentin. *Eur. J. Dent.* **2014**, *8*, 205-210.
437. Wambier, L.; Malaquias, T.; Wambier, D. S.; Patzlaff, R. T.; Bauer, J.; Loguercio, A. D.; Reis, A. Effects of Prolonged Light Exposure Times on Water Sorption, Solubility, and Cross-Linking Density of Simplified Etch-and-Rinse Adhesives. *J. Adhes. Dent.* **2014**, *16*, 229-234.
438. Ferreira, S.Q.; Costa, T.R.; Klein-Júnior, C.A.; Accorinte, M.D.; Meier, M.M.; Loguercio, A.D.; Reis, A. Improvement of Exposure Times: Effects on Adhesive Properties and Resin-Dentin Bond Strengths of Etch-and-Rinse Adhesives. *J. Adhes. Dent.* **2011**, *13*, 235-241.

439. Reis, A.; Ferreira, S.Q.; Costa, T.R.; Klein-Júnior, C.A.; Meier, M.M.; Loguercio, A.D. Effects of increased exposure times of simplified etch-and-rinse adhesives on the degradation of resin-dentin bonds and quality of the polymer network. *Eur. J. Oral Sci*. **2010**, *118*, 502–509.
440. Cadenaro, M.; Antoniolli, F.; Sauro, S.; Tay, F. R.; Di Lenarda, R.; Prati, C.; Biasotto, M.; Contardo, L.; Breschi, L. Degree of Conversion and Permeability of Dental Adhesives. *Eur. J. Oral Sci.* **2005**, *113*, 525-530.
441. Breschi, L.; Cadenaro, M.; Antoniolli, F.; Sauro, S.; Biasotto, M.; Prati, C.; Tay, F. R.; Di Lenarda, R. Polymerization Kinetics of Dental Adhesives Cured with LED: Correlation Between Extent of Conversion and Permeability. *Dent. Mater.* **2007**, *23*, 1066-1072.
442. Mills, R.W.; Uhl, A.; Jandt, K.D. Optical power outputs, spectra and dental composite depths of cure, obtained with blue light emitting diode (LED) and halogen light curing units (LCUs). *Br. Dent. J.* **2002**, *193*, 459-455.
443. Cadenaro, M.; Navarra, C. O.; Antoniolli, F.; Mazzoni, A.; Di Lenarda, R.; Rueggeberg, F. A.; Breschi, L. The Effect of Curing Mode on Extent of Polymerization and Microhardness of Dual-Cured, Self-Adhesive Resin Cements. *Am. J. Dent.* **2010**, *23*, 14-18.
444. Saikaew, P.; Fu, J.; Chowdhury, A.F.M.A.; Carvalho, R.M.; Sano, H. Effect of air-blowing time and long-term storage on bond strength of universal adhesives to dentin. *Clin. Oral. Investig.* **2019**, *23*, 2629-2635.
445. Ikeda, T.; De Munck, J.; Shirai, K.; Hikita, K.; Inoue, S.; Sano, H.; Lambrechts, P.; Van Meerbeek, B. Effect of Air-Drying and Solvent Evaporation on the Strength of HEMA-Rich versus HEMA-Free One-Step Adhesives. *Dent. Mater.* **2008**, *24*, 1316-1323.
446. Betancourt, D.E.; Baldion, P.A.; Castellanos, J.E. Resin-Dentin Bonding Interface: Mechanisms of Degradation and Strategies for Stabilization of the Hybrid Layer. *Int. J. Biomater.* **2019**, *2019*, 1-11.
447. Daood, U.; Tsoi, J. K. H.; Neelakantan, P.; Matinlinna, J. P.; Omar, H. A. K.; Al-Nabulsi, M.; Fawzy, A. S. In vitro Assessment of Ribose Modified Two-Step Etch-and-Rinse Dentine Adhesive. *Dent. Mater.* **2018**, *34*, 1175-1187.
448. Bourbia, M.; Ma, D.; Cvitkovitch, D.G.; Santerre, J.P.; Finer, Y. Cariogenic bacteria degrade dental resin composites and adhesives. *J. Dent. Res.* **2013**, *92*, 989-994.
449. Daood, U.; Yiu, C.K.; Niu, L.N.; Tay, F.R. Effect of a novel quaternary ammonium silane on dentin protease activities. *J. Dent.* **2017**, *58*, 19-27.
450. Zheng, P.; Chen, H. Evaluate the effect of different mmps inhibitors on adhesive physical properties of dental adhesives, bond strength and mmp substarte activity. *Sci. Rep.* **2017**, *7*, 4975.
451. Bali, P.; Kalaivanan, D.; Divater, V.; Logarani. Matrix metalloproteinases: A double-edged sword. *Dent. Med. Res.* **2016**, *4*, 3-8.
452. Zhou, W.; Liu, S.; Zhou, X.; Hannig, M.; Rupf, S.; Feng, J.; Peng, X.; Cheng, L. Modifying Adhesive Materials to Improve the Longevity of Resinous Restorations. *Int. J. Mol. Sci.* **2019**, *20*, 723.
453. Breschi, L.; Maravic, T.; Comba, A.; Cunha, S. R.; Loguercio, A. D.; Reis, A.; Hass, V.; Cadenaro, M.; Mancuso, E.; Mayer-Santos, E.; Niu, L.; Pashley, D. H.; Tay, F. R.; Mazzoni, A. Chlorhexidine Preserves the Hybrid Layer in vitro after 10-years Aging. *Dent. Mater.* **2020**, *36*, 672-680.
454. Lessa, F. C.; Nogueira, I.; Vargas, F. da S.; Spolidorio, D. M.; Hebling, J.; García-Godoy, F.; Costa, C. A. Direct and Transdentinal Antibacterial Activity of Chlorhexidine. *Am. J. Dent.* **2010**, *23*, 255-259.
455. Carvalho, C.; Fernandes, F. P.; Freitas, V. da P.; França, F. M.; Basting, R. T.; Turssi, C. P.; Amaral, F. L. Effect of Green Tea Extract on Bonding Durability of an Etch-and-Rinse Adhesive System to Caries-Affected Dentin. *J. Appl. Oral Sci.* **2016**, *24*, 211-217.
456. Tezvergil-Mutluay, A.; Agee, K. A.; Uchiyama, T.; Imazato, S.; Mutluay, M. M.; Cadenaro, M.; Breschi, L.; Nishitani, Y.; Tay, F. R.; Pashley, D. H. The Inhibitory Effects of Quaternary Ammonium Methacrylates on Soluble and Matrix-Bound MMPs. *J. Dent. Res.* **2011**, *90*, 535-540.
457. Mohammadi, Z.; Shalavi, S.; Jafarzadeh, H. Ethylenediaminetetraacetic acid in endodontics. *Eur. J. Dent.* **2013**, *7*, 135-142.
458. Perdigão, J.; Reis, A.; Loguercio, A.D. Dentin adhesion and MMPs: a comprehensive review. *J. Esthet. Restor. Dent.* **2013**, *25*, 219-241.
459. Maravić, T.; Comba, A.; Cunha, S. R.; Angeloni, V.; Cadenaro, M.; Visinitini, E.; Navarra, C. O.; Salgarello, S.; Breschi, L.; Mazzoni, A. Long-term Bond Strength and Endogenous Enzymatic Activity of a Chlorhexidine-Containing Commercially Available Adhesive. *J. Dent.* **2019**, *84*, 60-66.
460. Carvalho, R.M.; Manso, A.P.; Geraldeli, S.; Tay, F.R.; Pashley, D.H. Durability of bonds and clinical success of adhesive restorations. *Dent. Mater.* **2012**, *28*, 72-86.

461. Daood, U.; Sauro, S.; Pichika, M.R.; Omar, H.; Liang Lin, S.; Fawzy, A.S. Novel riboflavin/VE-TPGS modified universal dentine adhesive with superior dentine bond strength and self-crosslinking potential. *Dent. Mater.* **2020**, *36*, 145-156.
462. Hass, V.; Luque-Martinez, I. V.; Gutierrez, M. F.; Moreira, C. G.; Gotti, V. B.; Feitosa, V. P.; Koller, G.; Otuki, M. F.; Loguercio, A. D.; Reis, A. Collagen Cross-linkers on Dentin Bonding: Stability of the Adhesive Interfaces, Degree of Conversion of the Adhesive, Cytotoxicity and In Situ MMP Inhibition. *Dent. Mater.* **2016**, *32*, 732-741.
463. Parise Gré, C.; Pedrollo Lise, D.; Ayres, A. P.; De Munck, J.; Tezvergil-Mutluay, A.; Seseogullari-Dirihan, R.; Lopes, G. C.; Van Landuyt, K.; Van Meerbeek, B. Do Collagen Cross-linkers Improve Dentin's Bonding Receptiveness? *Dent. Mater.* **2018**, *34*, 1679-1689
464. Mazzoni, A.; Angeloni, V.; Apolonio, F. M.; Scotti, N.; Tjäderhane, L.; Tezvergil-Mutluay, A.; Di Lenarda, R.; Tay, F. R.; Pashley, D. H.; Breschi, L. Effect of Carbodiimide (EDC) on the Bond Stability of Etch-and-Rinse Adhesive Systems. *Dent. Mater.* **2013**, *29*, 1040-1047.
465. Bedran-Russo, A.K.; Yoo, K.J.; Ema, K.C.; Pashley, D.H. Mechanical properties of tannic-acid-treated dentin matrix. *J. Dent Res.* **2009**, 88, 807-811.
466. Cai, J.; Palamara, J.E.A.; Burrow, M.F. Effects of Collagen Crosslinkers on Dentine: A Literature Review. *Calcif Tissue Int.* **2018**, *102*, 265-279.
467. Bertolo, M.V.L.; Guarda, M.B.; Fronza, B.M.; Abuna, G.F.; Vitti, R.P.; Geraldeli, S.; Sinhoreti, M.A.C. Electric Current Effects on Bond Strength, Nanoleakage, Degree of Conversion and Dentinal Infiltration of Adhesive Systems. *J. Mech. Behav. Biomed. Mater.* **2021**, *119*, 104529.
468. Guarda, M.B.; Di Nizo, P.T.; Abuna, G.F.; Catelan, A.; Sinhoreti, M.A.C.; Vitti, R.P. Effect of Electric Current-Assisted Application of Adhesives on Their Bond Strength and Quality. *J. Adhes. Dent.* **2020**, *22*, 393-398.
469. Maciel, C.M.; da Rosa Rinhel, M.F.; Abuna, G.F.; Pacheco, R.R.; Baroudi, K.; Sinhoreti, M.A.C.; Vitti, R.P. Resin Composite Adhesion to Dentin Using Different Curing Lights and Adhesive Systems Applied under Electric Current. *Clin. Oral. Investig.* **2021**, *25*, 5181-5188.
470. Mena-Serrano, A.; Costa, T.R.; Patzlaff, R.T.; Loguercio, A.D.; Reis, A. Effect of sonic application mode on the resin-dentin bond strength and dentin permeability of self-etching systems. *J. Adhes. Dent.* **2014**, *16*, 435-440.
471. Bagis, B.; Turkaslan, S.; Vallittu, P.K.; Lassila, L.V. Effect of high frequency ultrasonic agitation on the bond strength of self-etching adhesives. *J. Adhes Dent.* **2009**, *11*, 369-374.
472. Breschi, L.; Mazzoni, A.; Pashley, D.H.; Pasquantonio, G.; Ruggeri, A.; Suppa, P.; Mazzotti, G.; Di Lenarda, R.; Tay, F. Electric-Current-Assisted Application of Self-Etch Adhesives to Dentin. *J. Dent. Res.* **2006**, *85*, 1092-1096.
473. Chen, H.; Fu, D.; Yang, H.; Liu, Y.; Huang, Y.; Huang, C. Optimization of Direct Currents to Enhance Dentine Bonding of Simplified One-step Adhesive. *Eur. J. Oral Sci.* **2014**, *122*, 286-292.
474. Pasquantonio, G.; Tay, F.R.; Mazzoni, A.; Suppa, P.; Ruggeri Jr, A.; Falconi, M.; Di Lenarda, R.; Breschi, L. Electric Device Improves Bonds of Simplified Etch-and-Rinse Adhesives. *Dent. Mater.* **2007**, *23*, 513-518.
475. Pashley, D.H.; Agee, K.A.; Carvalho, R.M.; Lee, K.-W.; Tay, F.R.; Callison, T.E. Effects of Water and Water-Free Polar Solvents on the Tensile Properties of Demineralized Dentin. *Dent. Mater.* **2003**, *19*, 347-352.
476. Taneja, S.; Kumari, M.; Bansal, S. Effect of saliva and blood contamination on the shear bond strength of fifth-, seventh-, and eighth-generation bonding agents: An in vitro study. *J. Conserv. Dent.* **2017**, *20*, 157-160.
477. Eiriksson, S.O.; Pereira, P.N.; Swift, E.J. Jr.; Heymann, H.O.; Sigurdsson, A. Effects of saliva contamination on resin-resin bond strength. *Dent. Mater.* **2004**, *20*, 37-44.
478. Veneziani, M. Adhesive restorations in the posterior area with subgingival cervical margins: new classification and differentiated treatment approach. *Eur. J. Esthet. Dent.* **2010**, *5*, 50-76.
479. Bourgi, R.; Cuevas-Suarez, C.E.; Devoto, W.; Monjarás-Ávila, A.J.; Monteiro, P.; Kharma, K.; Lukomska-Szymanska, M.; Hardan, L. Effect of contamination and decontamination methods on the bond strength of adhesive systems to dentin: A systematic review. *J. Esthet. Restor. Dent.* **2023**, *35*, 1218-1238.
480. Park, J.W.; Lee, K.C. The influence of salivary contamination on shear bond strength of dentin adhesive systems. *Oper. Dent-Univ. Wash.* **2004**, *29*, 437-442.
481. Xie, J.; Powers, J.; McGuckin, R. In vitro bond strength of two adhesives to enamel and dentin under normal and contaminated conditions. *Dent. Mater.* **1993**, *9*, 295-299.
482. Atalay, C.; Meral, E. Does rubbing of universal adhesive reduce the negative effect of saliva on adhesion? *J. Adhes. Dent.* **2021**, *23*, 57-65.

483. Darabi, F.; Tavangar, M.; Davalloo, R. Effect of different decontamination procedures from a saliva-contaminated cured bonding system (single bond). *Dent. Res. J.* **2012**, *9*, 399.
484. Kim, J.; Hong, S.; Choi, Y.; Park, S. The effect of saliva decontamination procedures on dentin bond strength after universal adhesive curing. *Restor. Dent. Endod.* **2015**, *40*, 299-305.
485. Elkassas, D.; Arafa, A. Assessment of post-contamination treatments affecting different bonding stages to dentin. *Eur. J. Dent.* **2016**, *10*, 327-332.
486. Chasqueira, A.F.; Luís, J.; Portugal, J. Effect of saliva decontamination protocol on the adhesion to dentin with a universal adhesive. *Med. Dent. Cir. Maxilofac.* **2019**, *60*, 51-58.
487. Hoorizad, M.; Heshmat, H.; Hosseini, T.A.; Kazemi, S.S.; Tabatabaei, S.F. Effect of hemostatic agent on microshear bond strength of total-etch and self-etch adhesive systems. *Dent. Res. J. (Isfahan).* **2019**, *16*, 361-365.
488. Van Schalkwyk, J.; Botha, F.; Van Der Vyver, P.; De Wet, F.; Botha, S. Effect of biological contamination on dentine bond strength of adhesive resins. *SADJ J South Afr Dent Assoc Tydskr Van Suid-Afr Tandheelkd Ver.* **2003**, *58*, 143-147.
489. Chang, S. W.; Cho, B. H.; Lim, R. Y.; Kyung, S. H.; Park, D. S.; Oh, T. S.; Yoo, H. M. Effects of Blood Contamination on Microtensile Bond Strength to Dentin of Three Self-etch Adhesives. *Oper. Dent.* **2010**, *35*, 330-336.
490. Fawzy, A.S.; Amer, M.A.; El-Askary, F.S. Sodium hypochlorite as dentin pretreatment for etch-and-rinse single-bottle and two-step self-etching adhesives: atomic force microscope and tensile bond strength evaluation. *J. Adhes. Dent.* **2008**, *10*, 135-144.
491. Tezvergil-Mutluay, A.; Mutluay, M.; Seseogullari-Dirihan, R.; Agee, K. A.; Key, W. O.; Scheffel, D. L.; Breschi, L.; Mazzoni, A.; Tjäderhane, L.; Nishitani, Y.; Tay, F. R.; Pashley, D. H. Effect of Phosphoric Acid on the Degradation of Human Dentin Matrix. *J. Dent. Res.* **2013**, *92*, 87-91.
492. Anil, A.; Sekhar, A.; Thomas, M.S.; Ginjupalli, K. Haemostatic agents on the shear bond strength of self-adhesive resin. *J. Clin. Exp. Dent.* **2015**, *7*, e356.
493. Ajami, A. A.; Kahnamoii, M. A.; Kimyai, S.; Oskoee, S. S.; Pournaghi-Azar, F.; Bahari, M.; Firouzmandi, M. Effect of Three Different Contamination Removal Methods on Bond Strength of a Self-etching Adhesive to Dentin Contaminated with an Aluminum Chloride Hemostatic Agent. *J. Contemp. Dent. Pract.* **2013**, *14*, 26-33.
494. Chaiyabutr, Y.; Kois, J. The effect of tooth-preparation cleansing protocol on the bond strength of self-adhesive resin cement to dentin contaminated with a hemostatic agent. *Oper. Dent.* **2011**, *36*, 18-26.
495. Bertoldi, C.; Monari, E.; Cortellini, P.; Generali, L.; Lucchi, A.; Spinato, S.; Zaffe, D. Clinical and Histological Reaction of Periodontal Tissues to Subgingival Resin Composite Restorations. *Clin. Oral. Investig.* **2020**, *24*, 1001-1011.
496. Nasim, H.; Lone, M. A.; Kumar, B.; Ahmed, N.; Farooqui, W. A.; Alsahhaf, A.; Alresayes, S.; Vohra, F.; Abduljabbar, T. Evaluation of Gingival Displacement, Bleeding, and Ease of Application for Polytetrafluoroethylene (PTFE) and Conventional Retraction Cord - A Clinical Trial. *Eur. Rev. Med. Pharmacol. Sci.* **2023**, *27*, 2222-223
497. Karaman, E.; Tuncer, D.; Toz, T.; Kusdemir, M.; Genc, G. The influence of blood and/or hemostatic agent contamination on Micro-TBS to dentin. *J. Adhes. Sci. Technol.* **2015**, *29*, 1295-1300.
498. Pucci, C. R.; Araújo, R. M.; Lacerda, A. J.; Souza, M. A.; Huhtala, M. F.; Feitosa, F. A. Effects of Contamination by Hemostatic Agents and Use of Cleaning Agent on Etch-and-Rinse Dentin Bond Strength. *Braz. Dent. J.* **2016**, *27*, 688-692.
499. Nair, P.; Hickel, R.; Ilie, N. Adverse effects of salivary contamination for adhesives in restorative dentistry. A literature review. *Am. J. Dent.* **2017**, *30*, 156-164.
500. Stape, T.H.S.; Wik, P.; Mutluay, M.M.; Al-Ani, A.A.S.; Tezvergil-Mutluay, A. Selective dentin etching: A potential method to improve bonding effectiveness of universal adhesives. *J. Mech. Behav. Biomed. Mater.* **2018**, *86*, 14-22.
501. Takamizawa, T.; Barkmeier, W. W.; Tsujimoto, A.; Endo, H.; Tsuchiya, K.; Erickson, R. L.; Latta, M. A.; Miyazaki, M. Influence of Pre-etching Times on Fatigue Strength of Self-etch Adhesives to Enamel. *J. Adhes. Dent.* **2016**, *18*, 501-511.
502. Kharouf, N.; Rapp, G.; Mancino, D.; Hemmerlé, J.; Haikel, Y.; Reitzer, F. Effect of Etching the Coronal Dentin with the Rubbing Technique on the Microtensile Bond Strength of a Universal Adhesive System. *Dent. Med. Probl.* **2019**, *56*, 343-348.

503. Stape, T. H. S.; Viita-Aho, T.; Sezinando, A.; Wik, P.; Mutluay, M.; Tezvergil-Mutluay, A. To Etch or Not to Etch, Part I: On the Fatigue Strength and Dentin Bonding Performance of Universal Adhesives. *Dent. Mater.* **2021**, *37*, 949-960.
504. Stape, T. H. S.; Viita-Aho, T.; Sezinando, A.; Seseogullari-Dirihan, R.; Eleftheriadi, E.; Mutluay, M.; Tezvergil-Mutluay, A. To Etch or Not to Etch, Part II: On the Hydrophobic-Rich Content and Fatigue Strength of Universal Adhesives. *Dent. Mater.* **2022**, *38*, 1419-1431.
505. Stape, T.H.; Mutluay, M.; Tezvergil-Mutluay, A. To etch or not to etch, Part III: On the hydrophobic-rich content and fatigue strength of universal adhesives after long-term ageing. *Dent. Mater.* **2024**, *40*, 44-52.
506. Velasquez, L.M.; Sergent, R.S.; Burgess, J.O.; Mercante, D.E. Effect of placement agitation and placement time on the shear bond strength of 3 self-etching adhesives. *Oper. Dent.* **2006**, *31*, 426-430.
507. Irmak, Ö.; Yaman, B. C.; Orhan, E. O.; Ozer, F.; Blatz, M. B. Effect of Rubbing Force Magnitude on Bond Strength of Universal Adhesives Applied in Self-Etch Mode. *Dent. Mater. J.* **2018**, *37*, 139-145.
508. Bourgi, R.; Hardan, L.; Cuevas-Suárez, C. E.; Devoto, W.; Kassis, C.; Kharma, K.; Harouny, R.; Ashi, T.; Mancino, D.; Kharouf, N.; Haikel, Y. Effectiveness of Different Application Modalities on the Bond Performance of Four Polymeric Adhesive Systems to Dentin. *Polymers* **2023**, *15*, 3924.
509. Tay, F.R.; Pashley, D.H. Guided tissue remineralisation of partially demineralised human dentine. *Biomaterials* **2008**, *29*, 1127-1137.
510. Tay, F.R.; Pashley, D.H. Biomimetic remineralization of resin-bonded acid-etched dentin. *J. Dent. Res.* **2009**, *88*, 719-724.
511. Daood, U.; Fawzy, A.S. Minimally invasive high-intensity focused ultrasound (HIFU) improves dentine remineralization with hydroxyapatite nanorods. *Dent. Mater.* **2020**, *36*, 456-467.
512. Almeida, G.; Marques, J.A.; Van Meerbeek, B.; Ramos, J.C.; Falacho, R.I. Particle abrasion as a pre-bonding dentin surface treatment: A scoping review. *J. Esthet. Restor. Dent.* **2024**, *36*, 746-760.
513. Ramos, R.Q.; Peumans, M.; Mercelis, B.; Ahmed, M.H.; Politano, G.; Lopes, G.C.; Van Meerbeek, B. Influence of airborne particle abrasion on dentin bonding effectiveness of a 2-step universal adhesive. *J. Dent.* **2024**, *144*, 104918.
514. Franca, F.M.G.; Santos, A.J.S.; Lovadino, J.R. Influence of air abrasion and Long-Term storage on the bond strength of Self-etching adhesives to dentin. *Oper. Dent.* **2007**, *32*, 217-224.
515. Motisuki, C.; Monti Lima, L.; Emi Sanabe, M.; Jacques, P.; Santos-Pinto, L. Evaluation of the microtensile bond strength of composite resin restoration in dentin prepared with different sizes of aluminum oxide particles, using the air abrasion system. *Minerva. Stomatol.* **2006**, *55*, 611-618.
516. Millar, J.R. Management of biofilm formation with Airflow in patients with fixed orthodontic appliances (Doctoral dissertation, University of Otago).
517. Eram, A.; Kr, R.V.; Chethan, K.N.; Keni, L.G.; Shetty, D.D.; Zuber, M.; Kumar, S.; Pradeep, S. Air-Abrasion in Dentistry: A Short Review of the Materials and Performance Parameters. *J. Biomed. Phys. Eng.* **2024**, *14*, 99.
518. Ilie, N.; Hilton, T. J.; Heintze, S. D.; Hickel, R.; Watts, D. C.; Silikas, N.; Stansbury, J. W.; Cadenaro, M.; Ferracane, J. L. Academy of Dental Materials guidance-Resin composites: Part I-Mechanical properties. *Dent. Mater.* **2017**, *33*, 880-894.
519. Armstrong, S.; Breschi, L.; Özcan, M.; Pfefferkorn, F.; Ferrari, M.; Van Meerbeek, B. Academy of Dental Materials guidance on in vitro testing of dental composite bonding effectiveness to dentin/enamel using micro-tensile bond strength (μTBS) approach. *Dent. Mater.* **2017**, *33*, 133-143.
520. El Mourad, A.M. Assessment of Bonding Effectiveness of Adhesive Materials to Tooth Structure using Bond Strength Test Methods: A Review of Literature. *Open. Dent.* **2018**, *12*, 664-678.
521. Armstrong, S.; Geraldeli, S.; Maia, R.; Raposo, L.H.; Soares, C.J.; Yamagawa, J. Adhesion to tooth structure: a critical review of "micro" bond strength test methods. *Dent. Mater.* **2010**, *26*, 50-62.
522. Wang, R.; Hass, V.; Wang, Y. Machine Learning Analysis of Microtensile Bond Strength of Dental Adhesives. *J. Dent. Res*. **2023**, *102*, 1022-1030.
523. Sood, A.; Ramarao, S.; Carounanidy, U. Influence of different crosshead speeds on diametral tensile strength of a methacrylate based resin composite: An in-vitro study. *J. Conserv. Dent.* **2015**, *18*, 214-217.
524. Hara, A.T.; Pimenta, L.A.; Rodrigues Jr., A.L. Influence of cross-head speed on resin-dentin shear bond strength. *Dent. Mater.* **2001**, *17*, 165-169.

525. Dao Luong, M.N.; Shimada, Y.; Turkistani, A.; Tagami, J.; Sumi, Y.; Sadr, A. Fractography of interface after microtensile bond strength test using swept-source optical coherence tomography. *Dent. Mater.* **2016**, *32*, 862-869.
526. Yamaguchi, K.; Miyazaki, M.; Takamizawa, T.; Tsubota, K.; Rikuta, A. Influence of crosshead speed on micro-tensile bond strength of two-step adhesive systems. *Dent. Mater.* **2006**, *22*, 420-425.
527. Salz, U.; Bock, T. Testing adhesion of direct restoratives to dental hard tissue-a review. *J. Adhes. Dent.* **2010**, *12*, 343-371.
528. Nawrocka, A.; Piwonski, I.; Sauro, S.; Porcelli, A.; Hardan, L.; Lukomska-Szymanska, M. Traditional microscopic techniques employed in dental adhesion research—applications and protocols of specimen preparation. *Biosensors* **2021**, *11*, 408.
529. Saghiri, M.A.; Asgar, K.; Lotfi, M.; Karamifar, K.; Saghiri, A.M.; Neelakantan, P.; Sheibaninia, A. Back-scattered and secondary electron images of scanning electron microscopy in dentistry: A new method for surface analysis. *Acta. Odontol. Scand.* **2012**, *70*, 603-609.
530. Ramic, B.D.; Drobac, M.R.; Stojanac, I.L.; Premovic, M.T.; Petrovic, L.M. The micromorphological characterization of adhesive bond in dentin different locations. *Microsc. Res. Tech.* **2018**, *81*, 33-37.
531. Aguilar-Mendoza, J.A.; Rosales-Leal, J.I.; Rodríguez-Valverde, M.A.; González-López, S.; Cabrerizo-Vílchez, M.A. Wettability and bonding of self-etching dental adhesives. Influence of the smear layer. *Dent. Mater.* **2008**, *24*, 994-1000.
532. Arhun, N.; Halacoglu, D.M.; Ozduman, Z.C.; Tuncer, D. Efficacy of multi-mode adhesive systems on dentin wettability and microtensile bond strength of resin composite. *J. Adhes. Sci. Technol.* **2018**, *32*, 2405-2418.
533. Nawareg, M.M.; Zidan, A.Z.; Zhou, J.; Chiba, A.; Tagami, J.; Pashley, D.H. Adhesive sealing of dentin surfaces in vitro: A review. *Am. J. Dent.* **2015**, *28*, 321-332.
534. Kameyama, A.; Haruyama, A.; Abo, H.; Kojima, M.; Nakazawa, Y.; Muramatsu, T. Influence of solvent evaporation on ultimate tensile strength of contemporary dental adhesives. *Appl. Adhes. Sci.* **2019**, *7*, 1-11.
535. Taguchi, K.; Hosaka, K.; Ikeda, M.; Kishikawa, R.; Foxton, R.; Nakajima, M.; Tagami, J. The effect of warm air-blowing on the microtensile bond strength of one-step self-etch adhesives to root canal dentin. *J. Prosthodont. Res.* **2018**, *62*, 330-336.
536. Yonekura, K.; Hosaka, K.; Tichy, A.; Taguchi, K.; Ikeda, M.; Thanatvarakorn, O.; Prasansuttiporn, T.; Nakajima, M.; Tagami, J. Air-blowing strategies for improving the microtensile bond strength of one-step self-etch adhesives to root canal dentin. *Dent. Mater. J.* **2020**, *39*, 892-899.

1.12. Publications of Chapter I

USJ 1875
Université Saint-Joseph de Beyrouth
Faculté de médecine dentaire
fmd

THE INTERNATIONAL ARAB
JOURNAL OF DENTISTRY

SCOPUS INDEXED

CERIFICATE OF ACCEPTANCE

The article entitled:

"Assessment of Clinical Performance of Universal Adhesives Versus Other Adhesive Systems: A Systematic Review and Meta-Analysis of Clinical Trials"

Authored by:

Rim Bourgi, Naji Kharouf, Carlos Enrique Cuevas-Suárez, Cynthia Kassis, Ana Josefina Monjaras-Avila, Mohammad Qaddomi, Sophie Abi Raad, Mohammed Al Hasani, Youssef Haikel, Louis Hardan

Has been accepted in "*International Arab Journal of Dentistry*" (ISNN:2218-0885) and will be published in Vol 15, issue 2, in November 2024.

applied sciences

MDPI

Review

A Literature Review of Adhesive Systems in Dentistry: Key Components and Their Clinical Applications

Rim Bourgi [1,2,*], Naji Kharouf [2,3], Carlos Enrique Cuevas-Suárez [4], Monika Lukomska-Szymanska [5], Youssef Haikel [2,3,6,†] and Louis Hardan [1,†]

[1] Department of Restorative Dentistry, School of Dentistry, Saint-Joseph University, Beirut 1107 2180, Lebanon; louis.hardan@usj.edu.lb
[2] Department of Biomaterials and Bioengineering, INSERM UMR_S 1121, University of Strasbourg, 67000 Strasbourg, France; dentistenajikharouf@gmail.com (N.K.); youssef.haikel@unistra.fr (Y.H.)
[3] Department of Endodontics and Conservative Dentistry, Faculty of Dental Medicine, University of Strasbourg, 67000 Strasbourg, France
[4] Dental Materials Laboratory, Academic Area of Dentistry, Autonomous University of Hidalgo State, San Agustín Tlaxiaca 42160, Mexico; cecuevas@uaeh.edu.mx
[5] Department of General Dentistry, Medical University of Lodz, 92-213 Lodz, Poland; monika.lukomska-szymanska@umed.lodz.pl
[6] Pôle de Médecine et Chirurgie Bucco-Dentaire, Hôpital Civil, Hôpitaux Universitaire de Strasbourg, 67000 Strasbourg, France
[*] Correspondence: rim.bourgi@net.usj.edu.lb; Tel.: +961-71455529
[†] These authors contributed equally to this work.

Abstract: The central aim of adhesive dentistry is to improve the compatibility between current adhesives and a range of substrates by employing diverse application techniques. Therefore, the overarching objective of this review is to offer a comprehensive analysis of dentin bonding systems, starting with an introduction to adhesion and a detailed overview of enamel and dentin structures, their histology, and the impact of dentin structure on resin–dentin bonding. It covers the mechanisms of resin–dentin bonding, including resin adhesive application, bonding mechanisms, and factors influencing efficacy. Further, this review explores the composition of resin adhesive systems, including acidic components, cross-linking monomers, solvents, and other critical elements. It also examines various adhesive strategies—etch-and-rinse, self-etch, and universal adhesives—highlighting their applications and advantages. The review extends to clinical applications of dental adhesion, including direct restorations, indirect restorations, and immediate dentin sealing (IDS), demonstrating the practical implications of adhesive systems in enhancing restoration longevity and performance. In conclusion, despite significant advancements, no gold-standard method for optimal adhesion exists. Each adhesive system has distinct strengths and limitations. The review emphasizes the importance of evaluating methods for achieving durable adhesion and staying current with technological advancements in adhesive systems. **Summary:** This review provides a thorough analysis of dentin bonding systems, delving into the structures and bonding mechanisms of both enamel and dentin. By exploring various adhesive systems and their components, it highlights the ongoing challenges in achieving optimal resin–dentin adhesion. The review also addresses the clinical applications of dental adhesion, including direct restorations, indirect restorations, and immediate dentin sealing (IDS), illustrating how different adhesive techniques impact clinical outcomes. It underscores the necessity for continuous innovation and assessment of adhesive systems to enhance long-term bonding effectiveness in clinical practice.

Keywords: adhesion; dental adhesive; dental bonding; dentin bonding agent; etch-and-rinse; self-etch; universal adhesive

check for updates

Citation: Bourgi, R.; Kharouf, N.; Cuevas-Suárez, C.E.; Lukomska-Szymanska, M.; Haikel, Y.; Hardan, L. A Literature Review of Adhesive Systems in Dentistry: Key Components and Their Clinical Applications. *Appl. Sci.* **2024**, *14*, 8111. https://doi.org/10.3390/app14188111

Academic Editor: Bruno Chrcanovic

Received: 11 August 2024
Revised: 27 August 2024
Accepted: 28 August 2024
Published: 10 September 2024

Journal of
Functional Biomaterials

MDPI

Review

The Use of Warm Air for Solvent Evaporation in Adhesive Dentistry: A Meta-Analysis of In Vitro Studies

Rim Bourgi [1,2], Louis Hardan [1,†], Carlos Enrique Cuevas-Suárez [3], Francesco Scavello [4,*], Davide Mancino [2,5,6], Naji Kharouf [2,5,*] and Youssef Haikel [2,5,6,†]

[1] Department of Restorative Dentistry, School of Dentistry, Saint-Joseph University, Beirut 1107 2180, Lebanon; rim.bourgi@net.usj.edu.lb (R.B.); louis.hardan@usj.edu.lb (L.H.)
[2] Department of Biomaterials and Bioengineering, INSERM UMR_S 1121, University of Strasbourg, 67000 Strasbourg, France; mancino@unistra.fr (D.M.); youssef.haikel@unistra.fr (Y.H.)
[3] Dental Materials Laboratory, Academic Area of Dentistry, Autonomous University of Hidalgo State, San Agustín Tlaxiaca 42160, Mexico; cecuevas@uaeh.edu.mx
[4] IRCCS Humanitas Research Hospital, 20089 Rozzano, Milan, Italy
[5] Department of Endodontics and Conservative Dentistry, Faculty of Dental Medicine, University of Strasbourg, 67000 Strasbourg, France
[6] Pôle de Médecine et Chirurgie Bucco-Dentaire, Hôpital Civil, Hôpitaux Universitaire de Strasbourg, 67000 Strasbourg, France
[*] Correspondence: francesco.scavello@humanitasresearch.it (F.S.); dentistenajikharouf@gmail.com (N.K.); Tel.: +33-66752-2841 (N.K.)
[†] These authors contributed equally to this work.

Abstract: Any excess solvent from dental adhesive systems must be eliminated prior to material photopolymerization. For this purpose, numerous approaches have been proposed, including the use of a warm air stream. This study aimed to investigate the effect of different temperatures of warm air blowing used for solvent evaporation on the bond strength of resin-based materials to dental and nondental substrates. Two different reviewers screened the literature in diverse electronic databases. In vitro studies recording the effect of warm air blowing to evaporate solvents of adhesive systems on the bond strength of resin-based materials to direct and indirect substrates were included. A total of 6626 articles were retrieved from all databases. From this, 28 articles were included in the qualitative analysis, and 27 remained for the quantitative analysis. The results of the meta-analysis for etch-and-rinse adhesives revealed that the use of warm air for solvent evaporation was statistically significantly higher ($p = 0.005$). For self-etch adhesives and silane-based materials, this effect was observed too ($p < 0.001$). The use of a warm air stream for solvent evaporation enhanced the bonding performance of alcohol-/water-based adhesive systems for dentin. This effect seems to be similar when a silane coupling agent is submitted to a heat treatment before the cementation of a glass-based ceramic.

Keywords: dentine; silane; solvent-based; total-etch; warm air

1. Introduction

Adhesive systems contain resin monomers with hydrophilic and hydrophobic characteristics, polymerization modulators, and a high concentration of solvents [1]. Organic solvents act as diluting agents that improve wetting and the infiltration of resin monomers into the dentinal surface [2]. It is crucial that any excess solvent must be eliminated from the dental substrate by means of air drying prior to the photopolymerization of the applied adhesive, in addition to allowing time between these two processes [3]. A presence of residual solvents might affect the polymerization of monomers and hinder the integrity of the bond, creating unwanted pathways for voids inside the adhesive interface and causing a decrease in the bond strength [4,5].

check for updates

Citation: Bourgi, R.; Hardan, L.; Cuevas-Suárez, C.E.; Scavello, F.; Mancino, D.; Kharouf, N.; Haikel, Y. The Use of Warm Air for Solvent Evaporation in Adhesive Dentistry: A Meta-Analysis of In Vitro Studies. *J. Funct. Biomater.* **2023**, *14*, 285. https://doi.org/10.3390/jfb14050285

Academic Editors: Ping Li, Guojiang Wan, Shulan Xu and An Li

Received: 20 April 2023
Revised: 15 May 2023
Accepted: 17 May 2023
Published: 20 May 2023

Chapter II: Protocols for the Different Application Modalities

2.1. Introduction

Regardless of the strategy used in adhesion procedures, including ER or SE adhesives, dentinal bond quality necessitates the creation of a structure called the HL, which is comprised of a demineralized layer of collagen fibrils reinforced by the solvated resin matrix [1]. The stability of the HL ultimately depends on each component's resistance to degradation, regardless of the adhesive layer thickness and/or tags' length [2]. Efforts to reach a durable resin-dentin bond have been made, embracing the mechanisms slowing down or halting the HL disorganization and degradation, perfecting the dental adhesive system manufacturing process, as well as evolving modalities for the protection of the HL [3].

Among the ER adhesives, OBFL (Kerr Co., Orange, CA, USA), an ER III adhesive, has been widely considered one of the gold-standards of multiple-bottle systems [4]. This adhesive incorporates a highly hydrophobic bonding agent, which includes GPDM, which can react chemically with HAp in the etched and primed enamel and dentin substrate to enhance bond resilience [5]. Subsequently, SE systems were initiated, abolishing the application of H_3PO_4 (on dentin) and the subsequent rinsing step [6]. Among the SE adhesives, CSE (Kuraray Noritake Dental, Tokyo, Japan) is documented as a gold-standard in this category; the primer and the adhesive of this system include 10-MDP, which reacts with Ca to generate a strong and stable bond, thus forming nano-layers of 10-MDP-Ca [7].

A conventional view of dental bonding by means of a faster application was recently introduced to the market [8]. A less sensitive technique with numerous application options is feasible for clinicians nowadays with the arrival of UAs [9]. These systems have three different modes of application: ER, SE, and selective-etch. They can also adhere to multiple substrates, including resin composites, zirconia, silica-based ceramics, and metals [10]. Evidence from a previous systematic review and meta-analysis suggested that the use of the SE adhesion approach with this new type of adhesive appears to be an optimal option that enhances the BS to the dentin structure [11].

Accordingly, one of the major goals of adhesive dentistry is guided by two main tendencies: the development of the next generation of dental adhesives based on UAs and overcoming their shortcomings. The second tendency is related to the improvement of the interaction of the already-existing adhesives with the different substrates by using different application techniques [12]. Thus, numerous methods have enhanced the bonding effectiveness of adhesive systems while sustaining their versatility and multi-functional characteristics; these include the application of an extra hydrophobic resin coat after adhesive application and a double-layer application technique (two layers and more). Furthermore, AA along with solvent evaporation for longer than 10 s may be recommended for improving the BS of the materials [12,13]. Moreover, using a warm air stream on the primer or the adhesive system is recommended for better bonding [14].

Standardized dentin BS assessments assist in quantifying the dentin bond performance of dental adhesives, comparing dentinal BS values between different products and conditions, screening bonding capability, and understanding the mechanism of bonding from a mechanical perspective. Yet, the nature of the reactions that occur between adhesives and the dentin substrate remains unclear, and because of that, qualitative and morphological evaluations are compulsory. SEM and TEM are examples of the aforementioned tests employed in bonding mechanism research [15]. However, the predominant technique is SEM due to its user friendliness. SEM can be obtained either in secondary mode [16] or in backscattered mode [17].

Bonding efficiently to organic and wet dentin is a baffling task in the era of adhesive dentistry. Sano et al., [18] stated that the μTBS could be better than the SBS test to consider the BS of an adhesive system, while another report described that the significant factor for BS is the bonding agent used, irrespective of the testing exemplary used [19]. For optimal adhesion, an adhesive must completely "wet" the surface to be bonded [20]. "Wetting" means that the adhesive flows and covers a surface to maximize the contact surface and the forces of attraction between the adhesive and this bonding surface. Wettability is generally based on the measurement of CA as primary data, which indicates the degree of wetting when a solid and a liquid interact. A small CA lower than 90° (<90°) corresponds to high wettability, while a large CA (>90°) corresponds to low wettability. The CA is defined as the angle formed by the intersection of the liquid adhesive-solid dentin interface [21].

Recently, a new device called Compo-Vibes (Smile Line, St-Imier, Switzerland) was launched for easier, faster, and more reliable composite modeling. This device generates micro-vibrations of 0.158 kHz or 158 Hz with a tolerance of approximately +/−15% for more precise composite applications, made possible by different tips. Additionally, a special brush, which has multiple functions, was attached to this device and used in this study for bonding applications. Till now, to the best of researcher knowledge, there have been no studies that have simultaneously compared the bonding effectiveness of four application modalities: PA (applying the adhesive without any agitation), AA (applying the adhesive with active agitation), CV (Smile Line, St-Imier, Switzerland) (applying the adhesive with the help of a Compo-Vibes (Smile Line, St-Imier, Switzerland) tip used as a brush for bonding), or CVM (Smile Line, St-Imier, Switzerland) using a micro-brush. Hence, this article aims to assess the bonding performance of four adhesive systems to dentin using various application modes: PA, AA, CV, and CVM. According to the null hypothesis, the application method has no effect on the: (i) immediate and long-term BS of the adhesive systems to dentin following the four modalities; and (ii) dentinal wettability following AA and PA.

2.2. Materials and Methods

2.2.1. Materials

In this study, the μTBS of four adhesive systems were analyzed considering different application modalities: (1) PA, applying the adhesive without any agitation; (2) AA, applying the adhesive with active agitation; and (3) CV (Smile Line, St-Imier, Switzerland), applying the adhesive with the help of a Compo-Vibes (Smile Line, St-Imier, Switzerland) brush for bonding (CV) or a (4) micro-brush (CVM). Two UAs, PBU (Dentsply DeTrey GmbH, Konstanz, Germany) and OBU (Kerr Co., Orange, CA, USA), one ER III adhesive, OBFL, and one SE II adhesive, CSE, were evaluated. The sample size was estimated based on a previous literature that evaluated the BS of an adhesive system using different application modalities in a comparative study design with 4 independent groups [22]. Using an α of 0.05, a power of 80%, and a two-sided test, the minimal sample size was 5 specimens in each group in order to detect a difference of 5 MPa among the tested groups.

The composition of the adhesive systems evaluated in this study is described in Table 3.

Material	pH	Composition *	Manufacturer	Material Application	Active Application According to the Manufacturer Instructions
Prime&Bond Universal/Mild universal adhesive	pH = 2.5	10-MDP, PENTA, isopropanol, water, photo-initiator, bi- and multifunctional acrylate	Dentsply DeTrey GmbH, Konstanz, Germany	Adhesive was applied using the self-etch technique. One layer of adhesive was applied according to the modalities tested in this study for 20 s, and then mild air-blowing was carried out for 5 s. Adhesive was light irradiated for 20 s.	“Keep Prime&Bond Universal slightly agitated for 20 s”.
OptiBond Universal/Universal adhesive	pH = 2.5–3.0	Acetone, HEMA, GDMA, ethanol, GPDM	Kerr Co., Orange, CA, USA	Adhesive was applied using the self-etch technique. One layer of adhesive was applied according to the modalities tested in this study for 20 s, and then mild air-blowing was carried out for 5 s. Adhesive was light irradiated for 20 s.	“Apply a generous amount of OptiBond Universal adhesive to the enamel/dentin surface. Scrub the surface with a brushing motion for 20 s”.
OptiBond FL/Three-step etch-and-rinse adhesive	pH = Primer: 1.9; Bonding: 6.9	Etchant: 37.5% H_3PO_4 Primer: HEMA, GPDM, MMEP, water, ethanol, CQ and BHT Adhesive: Bis-GMA, HEMA, GDMA, CQ, and filler (fumed SiO_2, barium aluminoborosilicat, Na_2SiF_6), coupling factor A174	Kerr Co., Orange, CA, USA	Etching for 15 s using a 37% phosphoric DENTOETCH acid (Itena Clinical, Paris, France). Rinsing with distilled water for 15–30 s. Air-drying for 15 s to obtain a moist dentin. One layer of primer and adhesive was applied according to the modalities tested in this study for 20 s. Mild air-blowing was carried out for 5 s after primer application and after adhesive application. In the case of the adhesive, this was light irradiated for 20 s.	“Apply material to the prepared enamel/dentin surfaces with a light scrubbing motion for 15 s”.
Clearfil SE Bond/Two-step self-etch adhesive	pH primer = 1.76 pH bond = 2	Primer: 10-MDP, HEMA, hydrophilic dimethacrylate, CQ, DEPT, water	Kuraray Noritake Dental Inc., Tokyo, Japan	One layer of acidic primer and adhesive was applied according to the modalities tested in this study for 20 s, and then mild air-blowing	“Not specified”.

	Bond: MDP, HEMA, Bis-GMA, hydrophobic dimethacrylate, CQ, DEPT, silanized colloidal silica	was carried out for 5 s after acidic primer and adhesive application. In the case of the adhesive, this was light irradiated for 20 s.

* Based on manufacturers' MSDS. 10-MDP = 10-methacryloyloxydecyl dihydrogen phosphate; PENTA = dipentaerythritol pentaacrylate phosphate; HEMA = hydroxy ethyl methacrylate; GDMA = glycerol-dimethacrylate; GPDM = glycero-phosphate dimethacrylate; MMEP = methacryloyloxy-ethyl-dihydrogen phosphate; CQ = camphorquinone; SiO_2 = silicon dioxide; Na_2SiF_6 = sodium hexafluorosilicate; BHT = butyl hydroxy toluene; Bis-GMA = bisphenol A-glycidyl methacrylate; DEPT = N,N-Diethyl-p-toluidine.

Table 3: Manufacturer and composition of the adhesives used.

Four groups based on the application modalities (PA, AA, CV, and CVM) were used. For PA, all adhesives tested were applied for 20 s and left undisturbed; for AA, all adhesives tested were applied with active agitation for 20 s. Further, for micro-vibration with CV and CVM, all adhesives tested were applied for 20 s with the Compo-Vibes (Smile Line, St-Imier, Switzerland) instrument (this could be possible with the help of the Compo-Vibes (Smile Line, St-Imier, Switzerland) brush used for bonding in this study (Fig. 29a) or by using a micro-brush (Fig. 29b)). It is important to note that for the CVM modality, a micro-brush was cut as shown in Fig. 29b. Furthermore, the red button on the handle allowed for micro-vibration of both CV and CVM modalities.

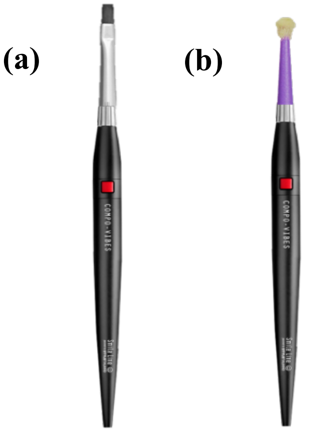


Figure 29: Representative images of the Compo-Vibes (Smile Line, St-Imier, Switzerland) instrument (an application modality could be possible with the help of the Compo-Vibes (Smile Line, St-Imier, Switzerland) brush in (a) used for bonding in this study or by using a micro-brush in (b)).

2.2.2. Bonding and Sample Preparations

Eighty sound human molars extracted for periodontal and orthodontic reasons were collected, cleansed of soft tissue, and stored in a 0.2% sodium azide solution at 4 °C for one month to inhibit microbial growth [23]. Upon the approval of the ethical committee of the faculty of dental medicine at the Saint-Joseph University of Beirut, Lebanon (FMD-221; ref.#USJ-2022-140), all these teeth were used for determining the research methodologies. For specimen preparation, the roots were sectioned, and their crowns were embedded in gypsum, permitting the buccal enamel surface to be visible. Afterward, the enamel surface was abraded by means of an orthodontic grinder (Essencedental, Araraquara, SP, Brazil) until exposure to a flat medium dentin surface. The exposed dentin was later wet-ground with P320 SiC for one-minute by means of a speed grinder-polisher (Buehler Ltd., Lake Bluff, IL, USA), under a water-cooling condition, at a motor speed of 70 rpm, for smear layer standardization and regulation. Then, the teeth were randomly distributed into four groups according to the adhesive systems. Subsequently, the specimens were divided into subgroups following the application modalities, totaling 16 subgroups (4 adhesive systems with 4 application techniques: AA, CV, CVM, and PA). Next, the evaporation of each applied adhesive system was carried out according to the instructions of the manufacturer.

All the bonding procedures were carried out by a single operator (RB) at room temperature and a constant relative humidity. After that, photo-activation was conducted during 20 s with a LED multiwave light-curing unit Curing Pen (Eighteeth, Changzhou, China) using an irradiance of 1000 mW/cm^2 [24,25,26], and resin composites (Reflectys, Itena Clinical, Paris, France) were applied in 3 increments of 2 mm each (A2 shade), and each layer was polymerized for 30 s with the same light-curing unit.

Following the bonding procedure and after immersion in distilled water at 37 °C for 24 h, the specimens were sectioned occluso-gingivally using a low-speed precision cutting machine (EXAKT Vertriebs GmbH, Norderstedt, Germany) into 1.0 mm × 1.0 mm composite-dentin beams. The μTBS was established in accordance with International Organization for Standardization (ISO)/ Technical Specification (TS) 11405, with the resin composite fashioning the upper half of the beam and the underlying dentin forming the lower half of the beam. From each tooth, approximately fourteen beams were acquired. Half of the specimens (7 beams/tooth = 35 beams for 5 teeth) were evaluated after 24 h of aging in distilled water at 37 °C, while the other half (7 beams/tooth = 35 beams for 5 teeth) were stored at 37 °C in distilled water and evaluated after 6 months of aging [27].

2.2.3. Micro-Tensile Bond Strength Testing

Bonded resin-dentin beams were attached to a Geraldeli's jig using cyanoacrylate glue (Zapit, Dental Ventures of North America, Corona, CA, USA), adapted to a universal testing machine (YLE GmbH Waldstraße, Bad König, Germany), and subjected to a tensile force until failure with a 1 mm/min crosshead speed and a 500 N load cell. Consequently, the cross-sectional area of each failed specimen was measured using a digital calliper with 0.01 mm of precision (Model CD-6BS Mitutoyo, Tokyo, Japan). By dividing the force at debonding [N] with the bonded surface area of the specimen [mm^2], the μTBS value was calculated and expressed in MPa. For each tooth, the results obtained from the seven beams examined were averaged, and the mean attained was then used for statistical determinations (n= 5) [27].

2.2.4. Failure Mode Analysis

All fractured portions were fixed to the aluminum stubs and observed under an optical numeric microscope (Keyence, Osaka, Japan) at 150× magnification to recognize the failure mode in each specimen. A VHX-5000 software was used to calculate the percentage of each area and to classify the type of failure as adhesive (the fracture site was within the adhesive), cohesive within composite, cohesive within dentin, or mixed (the fracture site extended into either the dentin or the resin composite). (Fig. 30).

Technique of area measurement using VHX-5000

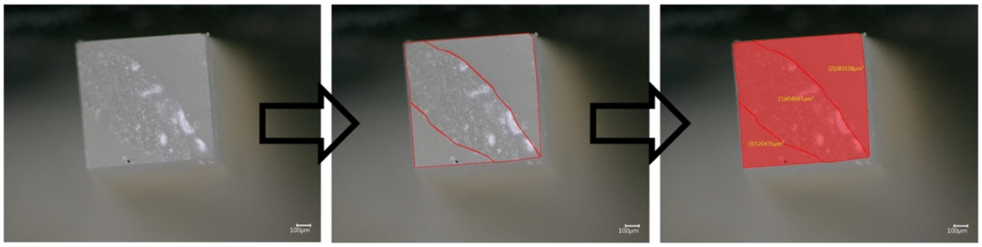


Figure 30: Representative images were obtained with an optical microscope at 150× magnification to recognize the failure mode in each specimen. The technique of area measurement was conducted using the VHX-5000.

2.2.5. Scanning Electron Microscopy

Three resin-bonded beams, randomly selected from each subgroup (n = 3), were used for analysis of the composite-dentin interface morphology of specimens prepared as previously mentioned in the above test sessions. The specimen surfaces were etched with 37% H_3PO_4 gel for 10 s, rinsed with distilled water for another 10 s, air-dried, and then immersed in a 2.5% sodium hypochlorite solution for 3 min. The specimens were finally washed with distilled water and placed in ascending grades of 25%, 50%, 75%, and 100% ethanol for sequential dehydration [28]. Thereafter, all specimens were immediately transferred for desiccation in a critical point drying machine (Balzers 030, Shimadzu, Kyoto, Japan). Specimens were then mounted on aluminum SEM stubs with conductive tape (double-sided carbon tape) and subsequently sputter coated for 120 s with a (20/80) ratio of gold–palladium using a sputtering device (Hummer JR, Technics, CA, USA). After gold sputtering, a Quanta 250 FEG SEM (FEI Company, Eindhoven, The Netherlands) operated at an accelerating voltage of 10 kV at different magnifications was used to analyze the specimens.

2.2.6. Adhesive Contact Angle

The adhesive CA to the dentin was measured with an optical tensiometer (Biolin Scientific, Espoo, Finland) following a sessile drop method. For each adhesive group, three dentinal surfaces were prepared to reach a flat dentin surface with P320 SiC. Then, a 5 μL drop of the adhesive system was placed on the prepared dentin surfaces. For this test, only the AA and PA techniques for OBFL and CSE were evaluated. In addition, for OBU and PBU, adhesives were applied directly (PA). By doing so, OBFL groups were subjected to acid etching for 15 s, rinsing for 15–30 s, and drying to obtain a moist dentin. Next, the dentin surfaces were subjected to primer application according to the respective modalities tested (AA of the primer for 20 s, then air-drying for 5 s; PA of the primer for 20 s, then air-drying for 5 s). Specimens of the CSE groups were subjected to acidic-primer application according to the respective modalities tested (AA of the acidic-primer for 20 s, then air-drying for 5 s; PA of the acidic-primer for 20 s, then air-drying for 5 s). For OBU and PBU groups, since they were used in this study in a SE mode, the surfaces were not treated (only smear layer standardization by means of P320 SiC), and the adhesive system itself was placed on prepared dentin surfaces, besides the CA measurement was performed (PA of the adhesives, since an agitation could not be performed). An optical tensiometer (Biolin Scientific, Espoo, Finland) was used to evaluate the CA of the adhesive drop onto the material surface, which was measured after 10 s of contact by using a horizontal camera to track its profile. The experiment was repeated in triplicate (n = 3).

2.2.7. Statistical Analysis

SPSS (Version 29.0.1.0, IBM, Armonk, NY, USA) was used to perform statistical analysis. The data underwent analysis to examine the normal distribution and homogeneity of variance. The impact of the adhesive system and the application modalities on the μTBS to dentin was evaluated using a two-way analysis of variance (ANOVA). The BS was analyzed separately after 24 h and 6 months of aging. Data from the adhesive CA was subjected to a one-way ANOVA analysis including multiple comparisons (Bonferroni test), and a significance level of $\alpha = 0.05$ was applied to all analyses.

2.3. Results

2.3.1. Micro-Tensile Bond Strength Testing

Table 4 summarizes the values obtained for the μTBS after 24 h aging according to the material and the technique used.

Technique	CSE	OBFL	OBU	PBU
AA	^{A} 19.0 (3.2) ^{ab}	^{A} 29.7 (5.2) ^{a}	^{A} 28.3 (5.0) ^{a}	^{A} 26.2 (8.9) ^{a}
CV	^{A} 18.2 (6.1) ^{ab}	^{A} 24.1 (6.8) ^{a}	^{A} 25.1 (9.1) ^{a}	^{A} 18 (5.6) ^{ab}
CVM	^{A} 21.3 (3.9) ^{a}	^{A} 27.3 (4.1) ^{a}	^{A} 24.8 (2.8) ^{a}	^{A} 17.5 (9.4) ^{ab}
PA	^{B} 13.6 (3.8) ^{b}	^{A} 30.3 (5.9) ^{a}	^{A} 29.6 (5.2) ^{a}	^{B} 10.9 (3.4) ^{b}

Different uppercase letters indicate the presence of significant differences for each row ($p < 0.05$). Different lowercase letters indicate the presence of significant differences for each column ($p < 0.05$). Clearfil SE Bond (CSE); OptiBond FL (OBFL); OptiBond Universal (OBU); Prime&Bond Universal (PBU); Active application (AA); Compo-Vibes application (CV); Compo-Vibes modified application (CVM); and Passive application (PA).

Table 4: Mean and standard deviation of the micro-tensile bond strength test (MPa) of the different application modalities for the adhesive system tested after 24 h aging.

According to the ANOVA test, both factors and the interaction between them were significant ($p < 0.001$). The effect size for the factor adhesive was 0.5963, while the effect size for the factor technique was 0.2389; the effect size for the interaction between the factors was 0.3695. After 24 h, concerning the factor technique in the same adhesive group, PBU demonstrated significant differences between the techniques. Statistically higher BS was found for PBU in AA only when compared to the passive technique ($p < 0.05$), and PBU in PA showed statistically lower BS compared to the other techniques ($p < 0.05$). No significant difference was found between PBU in CV and PBU in CVM ($p > 0.05$).

For the CSE, significant differences between the techniques were found. Statistically higher BS was found for CSE in CVM compared to the PA technique ($p < 0.05$), and CSE in PA showed statistically lower BS compared to the other techniques ($p < 0.05$). No significant difference was found between CSE in AA and CSE in CV ($p > 0.05$).

Further, no significant differences were found between the used techniques among the other adhesive systems (OBU and OBFL) ($p > 0.05$).

In addition, concerning the factor material, only the PA demonstrated significant differences between the tested materials. Statistically higher BSs were found for OBU and OBFL in PA compared to the other adhesives (CSE and PBU) ($p < 0.05$), while no significant difference was found between PBU and CSE as well as OBU and OBFL in PA ($p > 0.05$). No significant differences were found between the adhesive systems used among the other techniques ($p > 0.05$).

Table 5 summarizes the values obtained for the μTBS after 6 months of aging according to the material and the technique used. According to the two-way ANOVA analysis, the factor material was not significant ($p = 0.153$). On the other hand, the factor technique and the interaction between the factors were significant ($p < 0.001$). The effect size for the factor adhesive was 0.2017, while the effect size for the factor technique was 0.5289; the effect size for the interaction between the factors was 0.4773.

Technique	**CSE**	**OBFL**	**OBU**	**PBU**
AA	^{A} 17.6 (3.8) ^{a}	^{A} 14.9 (2) ^{a}	^{A} 17.2 (6.6) ^{a}	^{A} 21.1 (2.9) ^{a}
CV	^{A} 9.5 (2.5) ^{b}	^{A} 11.3 (3.4) ^{a}	^{A} 7.9 (6.5) ^{b}	^{A} 13.4 (6.8) ^{b}
CVM	^{A} 18.3 (3.8) ^{a}	^{A} 15.5 (2.1) ^{a}	^{B} 7.9 (2.8) ^{b}	^{B} 9.8 (3.4) ^{b}
PA	^{A} 11.7 (6.3) ^{ab}	^{A} 12.5 (1.3) ^{a}	^{A} 12.4 (3.6) ^{a}	^{A} 7.7 (2.8) ^{b}

Different uppercase letters indicate the presence of significant differences for each row ($p < 0.05$). Different lowercase letters indicate the presence of significant differences for each column ($p < 0.05$). Clearfil SE Bond (CSE); OptiBond FL (OBFL); OptiBond Universal (OBU); Prime&Bond Universal (PBU); Active application (AA); Compo-Vibes application (CV); Compo-Vibes modified application (CVM); and Passive application (PA).

Table 5: Mean and standard deviation of the micro-tensile bond strength test (MPa) of the different application modalities for the adhesive system tested after 6 months of aging.

After 6 months of aging, concerning the factor technique in the same adhesive group, PBU, OBU, and CSE demonstrated significant differences between the techniques. Concerning PBU, statistically higher BS was found in AA compared to the other techniques ($p < 0.05$), while no significant difference was found between the BS values of the other techniques ($p > 0.05$).

AA and PA were significantly higher in the OBU adhesive ($p < 0.05$), compared to the lower values obtained in CV and CVM ($p < 0.05$). For the same adhesive, no significant difference was found between OBU in AA and PA, as well as between CV and CVM ($p > 0.05$).

Moreover, CSE in AA and CVM demonstrated statistically higher BS values compared to the other techniques ($p < 0.05$), while CSE in CV had statistically lower values compared to the other techniques ($p < 0.05$). No significant difference was found between CSE in AA and CVM ($p > 0.05$).

No significant differences were found between the techniques used for the OBFL adhesive ($p > 0.05$).

In addition, concerning the factor material, only when used with the CVM technique there were significant differences between the tested materials. A statistically higher BS was found for CSE and OBFL in CVM compared to the other adhesives (OBU and PBU) ($p < 0.05$), while no significant difference was found between OBFL and CSE, as well as OBU and PBU ($p > 0.05$). No significant differences were found between the adhesive systems used among the other techniques ($p > 0.05$).

Finally, Table 6 shows the means, SD, and statistical analysis of the BS of all the tested adhesives with each technique at 24 h and 6 months of aging in distilled water.

Technique/CSE	24 h	6 Months
AA	19.0 (3.2) ^{A}	17.6 (3.8) ^{A}
CV	18.2 (6.1) ^{A}	9.5 (2.5) ^{B}
CVM	21.3 (3.9) ^{A}	18.3 (3.8) ^{A}
PA	13.6 (3.8) ^{A}	11.7 (6.3) ^{A}
Technique/PBU	**24 h**	**6 months**
AA	26.2 (8.9) ^{A}	21.1 (2.9) ^{A}
CV	18 (5.6) ^{A}	13.4 (6.8) ^{A}
CVM	17.5 (9.4) ^{A}	9.8 (3.4) ^{B}
PA	10.9 (3.4) ^{A}	7.7 (2.8) ^{A}
Technique/OBU	**24 h**	**6 months**
AA	28.3 (5.0) ^{A}	17.2 (6.6) ^{B}
CV	25.1 (9.1) ^{A}	7.9 (6.5) ^{B}
CVM	24.8 (2.8) ^{A}	7.9 (2.8) ^{B}
PA	29.6 (5.2) ^{A}	12.4 (3.6) ^{B}
Technique/OBFL	**24 h**	**6 months**
AA	29.7 (5.2) ^{A}	14.9 (2) ^{B}
CV	24.1 (6.8) ^{A}	11.3 (3.4) ^{B}
CVM	27.3 (4.1) ^{A}	15.5 (2.1) ^{B}
PA	30.3 (5.9) ^{A}	12.5 (1.3) ^{B}

Different uppercase letters indicate the presence of significant differences for each row in each technique/bonding ($p < 0.05$). Clearfil SE Bond (CSE); OptiBond FL (OBFL); OptiBond Universal (OBU); Prime&Bond Universal (PBU); Active application (AA); Compo-Vibes application (CV); Compo-Vibes modified application (CVM); and Passive application (PA).

Table 6: Mean and standard deviation of the micro-tensile bond strength test (MPa) of the different application modalities as a function of the storing time for all the adhesive systems tested.

Concerning CSE, only CV at 6 months demonstrated significantly lower BS compared to 24 h ($p < 0.05$), whereas no statistical differences were found for the other techniques between 24 h and 6 months ($p > 0.05$).

Concerning PBU, only CVM at 6 months revealed significantly lower BS compared to 24 h ($p < 0.05$), while no statistical differences were found for the other techniques between 24 h and 6 months ($p > 0.05$).

Concerning OBU, all the techniques at 6 months demonstrated significant lower BS compared to 24 h ($p < 0.05$), and the same observations were found for the OBFL, where all the techniques at 6 months revealed significant lower BS compared to 24 h ($p < 0.05$).

2.3.2. Failure Mode Analysis

The number of adhesive, mixed, and cohesive failures is described in Table 7.

Technique/Material Fracture Mode (Adhesive/Mixed/Cohesive in Dentin or Resin)	CSE 24 h–6 Months	OBFL 24 h–6 Months	OBU 24 h–6 Months	PBU 24 h–6 Months
AA	16 adhesive/18 mixed/1 cohesive-18 adhesive/17 mixed/0 cohesive	11 adhesive/19 mixed/5 cohesive-17 adhesive/16 mixed/2 cohesive	11 adhesive/17 mixed/7 cohesive-17 adhesive/16 mixed/2 cohesive	11 adhesive/21 mixed/3 cohesive-16 adhesive/18 mixed/1 cohesive
CV	15 adhesive/17 mixed/3 cohesive-25 adhesive/10 mixed/0 cohesive	11 adhesive/22 mixed/2 cohesive-16 adhesive/17 mixed/2 cohesive	14 adhesive/19 mixed/2 cohesive-21 adhesive/10 mixed/4 cohesive	16 adhesive/17 mixed/2 cohesive-19 adhesive/15 mixed/1 cohesive
CVM	17 adhesive/15 mixed/3 cohesive-19 adhesive/16 mixed/0 cohesive	13 adhesive/22 mixed/0 cohesive-15 adhesive/15 mixed/5 cohesive	15 adhesive/18 mixed/2 cohesive-20 adhesive/14 mixed/1 cohesive	5 adhesive/28 mixed/2 cohesive-22 adhesive/12 mixed/1 cohesive
PA	20 adhesive/13 mixed/2 cohesive-21 adhesive/14 mixed/0 cohesive	14 adhesive/20 mixed/1 cohesive-17 adhesive/18 mixed/0 cohesive	13 adhesive/17 mixed/5 cohesive-15 adhesive/18 mixed/2 cohesive	23 adhesive/10 mixed/2 cohesive-27 adhesive/7 mixed/1 cohesive

Clearfil SE Bond (CSE); OptiBond FL (OBFL); OptiBond Universal (OBU); Prime&Bond Universal (PBU); Active application (AA); Compo-Vibes application (CV); Compo-Vibes modified application (CVM); and Passive application (PA).

Table 7: Failure pattern analysis of the bonding agents evaluated after the micro-tensile bond strength test.

For all the adhesive systems, most of the adhesive failures were adhesive or mixed fractures. On one hand, higher mixed failures were observed in samples that had higher BSs. On the other hand, higher adhesive failures in the samples revealed lower BSs among all the adhesive systems and application modes.

2.3.3. Scanning Electron Microscopy

SEM micrographs were taken in order to investigate the resin-dentin interface for the different adhesive systems with the different application modes (Fig. 31). All the adhesives showed marked resin infiltration into dentinal tubules in AA among all the modalities tested. Less marked infiltrations were observed for the other application modes, regardless of the adhesive system. Different lengths and diameters of the RTs were observed among all the techniques. According to the figures, dentin tubule orientation differs for each group.

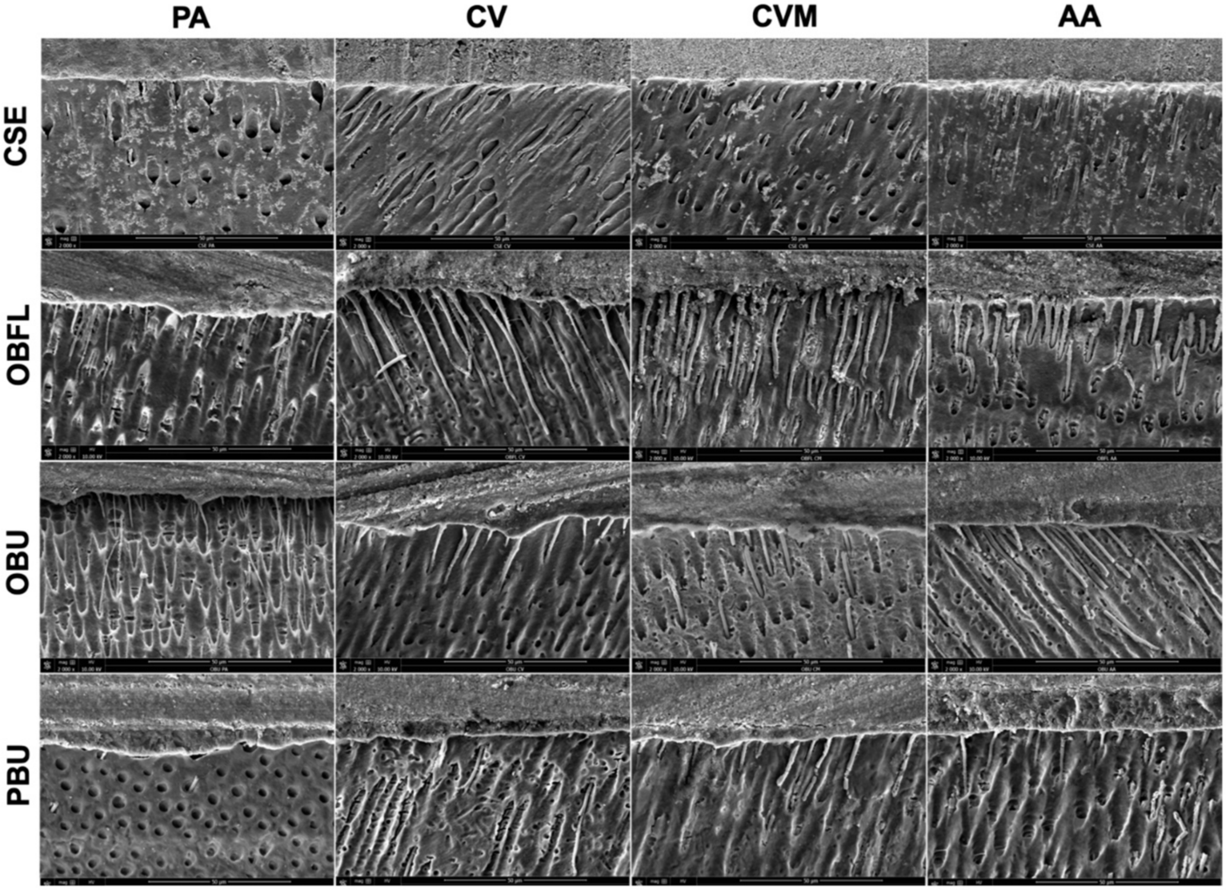


Figure 31: Representative scanning electron microscopy micrographs (×2000 magnifications) reveal the adhesive layer and tag penetration of the different adhesive systems tested with various application modalities. Clearfil SE Bond (CSE); OptiBond FL (OBFL); OptiBond Universal (OBU); Prime&Bond Universal (PBU); Active application (AA); Compo-Vibes application (CV); Compo-Vibes modified application (CVM); and Passive application (PA).

2.3.4. Adhesive Contact Angle

For this test, only the AA and PA techniques for OBFL and CSE were evaluated. Though OBU and PBU adhesives were applied directly (PA) to dentinal surfaces, an AA could not be performed.

For the PA mode, both UAs (OBU and PBU) demonstrated statistically lower CA compared to the other systems (CSE and OBFL) ($p < 0.05$). No significant differences were found between OBU and PBU as well as between CSE and OBFL ($p > 0.05$).

Concerning the AA mode, only CSE and OBFL were tested. In both groups, the AA demonstrated lower CA values compared to the same adhesives in PA ($p < 0.05$). No significant difference was found between OBFL and CSE in AA ($p > 0.05$) (Table 8 and Fig. 32).

	CSE	OBFL	OBU	PBU
PA (°)	^{B}37 (1.4) ^{a}	^{B}32.5 (5.1) ^{a}	^{A}16.3 (0.1)	^{A}12.9 (0.6)
AA (°)	^{A}25.3 (1.8) ^{b}	^{A}23.4 (5.7) ^{b}	X	X

Different uppercase letters indicate the presence of significant differences for each row ($p < 0.05$). Different lowercase letters indicate the presence of significant differences for each column ($p < 0.05$). Clearfil SE Bond (CSE); OptiBond FL (OBFL); OptiBond Universal (OBU); Prime&Bond Universal (PBU); Active application (AA); and Passive application (PA).

Table 8: Contact angle (°) of 5 μL of adhesive droplet on the dentinal surfaces following passive or active applications.

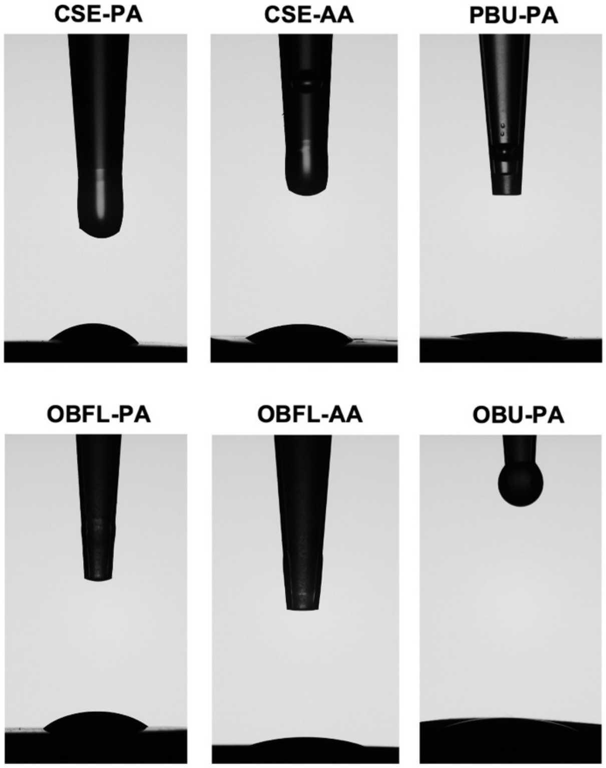


Figure 32: Representative images of the contact angles of different adhesives. All adhesives were measured after 10 s of dentinal contact by using an optical tensiometer to track their profiles. The placement of the adhesive quantifies the intrinsic aptitude of the adhesive liquid to spread on a flat and solid dentinal substrate. Clearfil SE Bond (CSE); OptiBond FL (OBFL); OptiBond Universal (OBU); Prime&Bond Universal (PBU); Active application (AA); and Passive application (PA).

2.4. Discussion

In the present study, different application modalities (AA, CV, CVM, and PA) were implemented to enhance the bond performance of four adhesive systems to dentin. "Compo-Vibes”, as a novel device, was used to evaluate its effect on the BS of the different tested adhesive systems by using a brush or a micro-brush. Moreover, active and passive applications were included in order to investigate the effect of both modes on the BS of the different adhesive systems to dentin at 24 h and 6 months of aging. As far as the available reviewed literature is concerned, there have been no studies that evaluated the efficacy of this new device, ‘’Compo-Vibes’’. Most of the previous studies only incorporated active/passive/ULA of adhesive systems into the dental substrate [13,22]. Furthermore, some application modalities were evaluated to determine their influence on the wetting ability of adhesive systems. The results of the present study demonstrated that the material factor (adhesive system) and the application factor (application modality) influenced the BS values at 24 h and 6 months of aging. Further, the dentin wettability was affected by some adhesives under some modalities. Therefore, both null hypotheses tested in this study must be rejected.

Concerning the technique factor, at 24 h, PBU and CSE presented a significant difference between their application modes ($p < 0.05$). AA and CVM demonstrated higher values for PBU and CSE, respectively, when compared to the other techniques, with a statistically higher BS found only when compared to the passive technique. All in all, the PA demonstrated lower values for both adhesives compared to the other techniques (Table 4).

According to precious research, the improvement in BS when an agitation (AA or CVM in this case) is used could be due to the deeper demineralization promoted by this technique, as fresh acidic resin monomers could be carried into the deeper areas [13,22]. Moreover, the agitation may increase solvent diffusion outward into the adhesive layer, allowing increased polymer cross-linking, degree of conversion, and other mechanical properties of the material [13,29]. The agitation action of adhesive systems (PBU and CSE) based on the hydrophobic nature of 10-MDP might have promoted deeper infiltration of MDP into the collagen network; therefore, their performance might differ when applied without agitation [6,12,30]. In this sense, as the mechanical properties of the adhesive layer increase with agitation, the quality of the adhesive interface increases, which could be translated into higher BS values and better conditioning of the substrate [13,30,31]. Passive-SE adhesives (CSE and PBU) application showed a noteworthy decrease in BS (Table 4). This could be elucidated by the higher amount of solvent inside the adhesive layer following the photopolymerization process. Accordingly, solvents presented after the light-curing increase the number of voids inside the HL and subsequently reduce the mechanical properties of the adhesive layer [29]. This might be the reason for the jeopardized immediate dentinal BS observed in this study for PBU and CSE in the PA modality.

Further, no significant differences were found between the used techniques among the other adhesive systems (OBU and OBFL) ($p > 0.05$). This proved the non-sensitivity of these adhesives (OBU and OBFL) to the modality applied (Table 4). The common feature between these adhesives relies on the fact that both materials are formulated with GPDM. Despite the fact that the literature regarding the effect of application modes on these adhesive systems is scarce, there are reports pointing out that the GPDM monomer can provide adequate micro-mechanical retention potential, BS, and durability similar to those of MDP-based materials [32,33]. It seems that the GPDM monomer after 24 h of BS to dentin is not sensitive to the application technique, and this feature could highlight the predictable results that this monomer provides and open the way for future research to be focused on this compound.

Regarding the factor material, at 24 h, only the PA demonstrated significant differences between the tested materials ($p < 0.05$). Higher BSs were found for OBU and OBFL in PA compared to the other adhesives (CSE and PBU). No significant difference was found between PBU and CSE, as well as OBU and OBFL in the PA (Table 4). Normally, the performance of an adhesive system is independent of the use of a single ingredient but rather of the overall balanced and optimal formulation, which contains a variety of components with different roles, including functional adhesive monomers [6,12,34]. PBU and CSE contain 10-MDP monomer, which was manufactured and patented by the Kuraray Noritake Dental Company [6,12]. Other manufacturers started implementing similar monomers, such as the GPDM monomer, which is found inside OBU and OBFL [12,35,36]. Technically, agitation action could have encouraged deeper penetration of the GPDM functional monomer into the collagen network, thus strengthening the adhesion of the resin composite to dentin [13,32], and no sensitivity to the passive or agitation modes was observed with this monomer [12,36], which was similar to the outcomes obtained in this study; hence, the performance of CSE and PBU immediately after 24 h might differ when applied without agitation (PA). Based on the information provided and the results of this study as well, passive applications should not be the application modality of choice for CSE and PBU. Worth is mentioning that the manufacturers of some specific materials (such as PBU in Table 3) claim to use their adhesive using an AA; therefore, clinicians must follow the right modality to ensure a proper bond [37]. Exclusively, the findings of this research propose that 10-MDP-based adhesive systems need to be applied with an agitation modality. However, 10-MDP-free adhesive systems could be applied in any tested modality (PA, AA, CV, and CVM). All in all, 10-MDP was sensitive to the PA modality, and GPDM was not sensitive to any modality applied.

With time, the HL is destroyed, and the strength of the dentin connection weakens due to the degradation of collagen fibrils and hydrophilic resin components. Specifically, this is due to the presence of collagen-degrading enzymes in dentin, such as MMPs and cysteine cathepsins [38]. The amplified awareness of the function of these enzymes in HL degradation has led to wide investigations targeting the prevention of collagenolytic activity at the resin-dentin interface [9,38,39]. In this manner, the samples tested were stored in distilled water at 37 °C in order to evaluate the effect of 6 months of aging on the dentinal BS of the different materials and techniques.

Furthermore, a significant difference in the BS after 6 months of water storage was observed for PBU, OBU, and CSE ($p < 0.05$). Concerning the technique factor, at 6 months, PBU had higher BS in AA compared to the other techniques ($p < 0.05$), while no significant difference was found between the BS values of the other techniques ($p > 0.05$) (Table 5). In order to elucidate the aforementioned outcome, one should keep in mind that PBU holds two functional monomers (10-MDP and PENTA) that deliver an elevated BS; however, the presence of hydrophilic characteristics deteriorates the adhesion after long periods of storage, causing the highest reduction in BS, especially when deviated from the AA that is recommended by the manufacturer (Table 3). All in all, the mixture inside PBU might not favor stability, which explains the results obtained in this study [40].

AA and PA were significantly higher in the OBU adhesive ($p < 0.05$), compared to the lower values obtained in CV and CVM ($p < 0.05$). For the same adhesive, no significant difference was found between OBU in AA and PA, as well as between CV and CVM ($p > 0.05$) (Table 5). A possible explanation of this result could be the negative effect of micro-vibration by means of CV and CVM over the long-term. The vibrational energy might negatively influence BS. Less difference in the depth of demineralization and resin infiltration might be estimated in SE adhesives [41,42], the penetration into the dentinal tubules is also lower than that of ER adhesives. Nonetheless, the restricted demineralization correlated to this type of adhesive system and the difficulty encountered by the adhesive in flowing through the smear layer may also contribute to the limited BSs when applied with CV and CVM. These data confirm the effects of Compo-vibes on the BSs of OBU used in SE mode with other agitation methods during their application, including continuous scrubbing, or PA.

Moreover, CSE in AA and CVM demonstrated statistically higher BS values compared to the other techniques ($p < 0.05$), while CSE in CV had statistically lower values compared to the other techniques ($p <$

0.05) (Table 5). CSE was the first SE adhesive system to incorporate 10-MDP monomer into both the bond and the primer [7,43]. Studies including CSE have established that MDP enables the formation of a stable chemical bond to the dentinal structure over time [44,45]. This could explain why this functional monomer is responsible for the higher BSs in AA and CVM. Moreover, it has been proven that the existence of HEMA inside the chemical composition of this adhesive system might compete with 10-MDP through bonding with the Ca of HAp, which might be harmful to the chemical bond of MDP to the dentinal substrate. This could explain why the non-stability of the bond between the different components inside the two bottles of this system is due to the sensitivity of this specific bonding (CSE) to Compo-Vibes (Smile Line, St-Imier, Switzerland) by means of CV modality and PA. Although the manufacturers do not provide a detailed percentage of each constituent inside the bonding agents, it might be that the presence of diverse percentages of the 10-MDP functional monomer influences the degree of vulnerability of the adhesive system to the degradation process [46].

No significant difference was found between the used techniques among the adhesive system OBFL ($p > 0.05$) (Table 5). Regarding this finding, this adhesive was based on GPDM [33,47], which was not sensitive to the technique after 6 months, explaining the results. In addition, OBFL was the only ER adhesive system tested in this study, with non-variance of the BS between modalities observed after 24 h and even after 6 months of water storage. This might be related to the characteristics of this product. Previously, this adhesive was considered the golden-standard material because of its good performance in immediate and long-term BS tests [47], which can be confirmed by this study. Despite the fact that the BS of OBFL after 6 months was not the highest when compared to the other adhesives, this was not significant. According to this data, the reason for its superior performance is related to the presence of GPDM, which can interact chemically with the HAp [5], and the highly filled bonding resin layer (48 wt%) over the primed dental surfaces [48]. Considering this, it seems that the ER approach ensured that this adhesive technique is still a good option.

Concerning the material factor, statistically higher BS was found for CSE and OBFL in CVM compared to the other adhesives (OBU and PBU) (Table 5). This is probably since these adhesives (OBU and PBU) were considered mild SE adhesives [6,12,49] compared to H_3PO_4 (pH = 0.5) applied with OBFL or with CSE with a mild SE feature (pH around 2) [50]. Therefore, demineralization induced by UAs tested in this study did not reach deeper regions of the dentin through the micro-vibration produced by the micro-brush inserted into the Compo-vibes (Smile Line, St-Imier, Switzerland) device. Thus, a hypothesis could be formulated that the micro-vibration was not adequate to support the flow of the UA system into the free dentinal spaces and facilitate tag formation when compared to SE II and ER III. All in all, for long-term performance, the modality applied by clinicians using the CVM could be specific for some adhesives such as CSE and OBFL, which had the highest values after 6 months of using this modality. However, this is not true for the UAs tested in this study, which had relatively low values with this modality and the highest values with the active modality. So, the application of these specific UAs should be conducted in coherence with the AA for a better result; otherwise, deterioration of the adhesive could occur [51].

No significant differences were found between the used adhesive systems among the other techniques (AA, PA, and CV). This study's results demonstrated that the AA mode is the most effective in increasing the BS throughout all the tested groups (Table 5). This shows that the active approach may be a more user-friendly alternative for the other application modalities in clinical practices. When a manual force is applied during the scrubbing of the adhesive systems on the dentin, the dentin surface acts as a sponge, and the collagen matrix is compressed [30]. The compressed collagen network enlarges when the pressure is eased, and the penetration of the adhesive system into the collagen network may be enhanced [52]. Scrubbing action speeds up the evaporation of the solvent and the dispersion of water inside the adhesive systems as well [53], leading to the incorporation of a higher monomer rate inside the smear layer and underlying dentin [54]. These residual solvents might negatively influence the adhesive performance by reducing the polymerization effectiveness and altering the mechanical properties [29]. All in all, the application with an agitation modality benefits all the adhesive systems ranging from ER to SE and UAs at the BS level, consequently enhancing the properties of the adhesive layer. This application modality does not necessitate any extra steps. In addition, a previous systematic review and meta-analysis conducted by Hardan et al., showed that the use of a scrubbing modality improves both the immediate and the aged dentin BS [13]. This indicates that the AA was efficient between each adhesive, even after a long time, and that aging could not negatively affect the bonding performance when this modality is chosen.

A novel adhesive application protocol based on the use of Compo-Vibes (Smile Line, St-Imier, Switzerland) by means of a brush (Smile Line, St-Imier, Switzerland) or micro-brush was incorporated in a study for the first time. Compo-Vibes (Smile Line, St-Imier, Switzerland) micro-vibrations by means of CV strengthened the bond to dentin for some adhesives, which can be justified by the enhanced monomer infiltration as well as prompting a better interaction with dentin. The release of the adhesive is triggered by the micro-vibration potential difference between the dentin surface and the adhesive. The CV modality provided similar performance as the AA but not the same BS values. A lower BS was observed for this modality. Moreover, this behavior shows that CV could not be recommended as an application technique for some adhesive systems.

For the PA, the values of BS demonstrated no significant differences for the used adhesives (Table 5). This could be explained by the fact that some adhesive systems (including PBU and CSE) do not support the passive modality after a long period of storage. The incomplete solvent evaporation and a lower rate of monomer penetration inside dentin were key factors to understand when using this modality. Therefore, an incomplete polymerization with hydrogel retained-water formation might reduce the resin-dentin BS. This supports the non-difference between adhesives [55].

After 6 months of storage, CSE and PBU in one of the Compo-Vibes (Smile Line, St-Imier, Switzerland) modality (CV for CSE and CVM for PBU) demonstrated lower values compared to their values at 24 h (Table 6). No previous study was conducted on a Compo-Vibes (Smile Line, St. Imier, Switzerland) device. These results might be related to the sensitivity of 10-MDP to CV and CVM, respectively, for CSE and PBU, resulting in lower performance with aging. Micro-vibration might prevent the stability of the monomers inside these adhesives. Additionally, companies that manufacture these adhesives are advocates of AA for the PBU product, but the same might not be said for CSE adhesives; consequently, their performance might vary when applied with other modalities. Outlook studies are needed to test this hypothesis.

OBU and OBFL demonstrated lower BS values after 6 months compared to the same bond at 24 h among all the application techniques due to the non-stability of the GPDM monomer with time (Table 6) [33]. It seemed that the GPDM monomer could go through hydrolysis at the highest rate in comparison with other monomers, such as the 10-MDP used in the formulation of the other adhesive systems. Its lower molecular weight and short-length spacer chains may compromise the chemical interaction with Ca and the dentin/enamel bonding performance [56]. In addition, dentin treated with GPDM appeared to be more hydrophilic than treated with 10-MDP [57], thus explaining the findings of this study.

Different failure modes were observed among all the groups after μTBS. Generally, the most observed failures were adhesive and mixed (Fig. 30 and Table 7). This is in accordance with a previous study [58]. The cohesive failure in this study was rarely observed, and this failure could be due to an error in the composite application or a fragility in the dentin, which could generate a cohesive fracture in the composite or dentin structure. Moreover, it could be linked to voids or air bubbles in the composite structure [59]. Higher BS values showed higher mixed values in the present study. These results are in accordance with a previous manuscript [60]. The μTBS test protocol utilized a load force capable of passing throughout the dentinal substrate and the resin composite before attaining the adhesive interface, with consequent stress concentration at these sites [61], causing a high percentage of mixed failures. Further, this statement might also denote the good hybridization reached between the adhesive systems and the dentinal substrate [60]. After 6 months of water storage, failure analysis was mostly adhesive. This is linked to the aging of an adhesive layer, yielding more adhesive fracture when compared to the baseline (24 h) mode of failure [30].

In this study, the resin-dentin interface of the specimens was analyzed. SEM observations demonstrated a high number of RTs among all the adhesive systems in AA compared to the other techniques (Fig. 31). This could be due to the higher monomer infiltration presented with this modality into the branches of dentinal tubules [62]. In addition, this was possibly due to the elimination of non-infiltrated resin plugs comprised inside the tags by means of acids and bases used to dissolve all of the dentin from the resin [63]. Moreover, this could be associated with the fact that this application technique has been demonstrated to improve the interaction between the adhesive and the substrate, altering positively the biochemical characteristics of dentin and facilitating the penetration of the material within the inter- and peritubular zones [62].

The evaluation of the tag density, length, and size, as well as the thickness of the HL, could be influenced by the position of the dentinal tubules. Tubule diameters and densities increase from the dentin-enamel junction to the central dentin area. Therefore, all the SEM observations could be related to the investigated anatomical zone [64].

In addition, the wettability analysis evaluates resin and dentin interactions [65]. Thus, for optimum adhesion, a proper adhesive system with adequate spreading capacity and a low CA is essential [66]. Generally, the CA can be altered by the viscosity of a solution, heterogeneity, and surface roughness [67]. An ideal wettability may be attained when the free surface energy of the dental substrate is maximized and the adhesive system displays a lower CA [68]. Substrates with high wettability levels have a greater surface energy than the liquid's surface tension [67]. The higher the viscosity of an adhesive system, the more difficult it is to wet a dental substrate [69]. In this study, CA values proved that both UAs demonstrated lower values compared to the other systems in the PA (Table 8 and Fig. 32). Dentin wetting was dramatically affected by acid etching. As it was pointed out in a previous work [70]. Since the acidity of UAs was lower than the other adhesives, lower CA was clearly observed. Thus, promoting higher spreading capacity.

Precisely, the AA mode could ameliorate the hydrophily of the dentinal surface among CSE and OBFL due to an increased spreading of the adhesive. This facilitated solvent evaporation and interaction with dentin [71]. Seemingly, to reduce the high viscosity of a monomer such as Bis-GMA included in both adhesives (CSE and OBFL) tested, diluent monomers such as HEMA are included in the formulation. This could lower the viscosity of the solution, facilitating co-monomer infiltration [69]. In addition, HEMA presented in these adhesives (CSE and OBFL) facilitates the wettability of AA because it is a hydrophilic humectant agent [72]. Presumably, both the dentin wetting by resin monomers and the spreading changed depending on the chemical characteristics of the adhesive. It could be hypothesized that the application modality might affect the surface wettability or directly influence the impregnation of adhesive monomers when using these systems [73].

However, one notable discovery presumed from this analysis was that there was no relation between the number of RTs evaluated by SEM (Fig. 31), the hydrophily of the different adhesive systems evaluated by CA (Fig. 32), and the BS values measured by μTBS (Table 4, Table 5 and Table 6). OBU demonstrated lower CA than OBFL and CSE and markedly observed tags; in contrast, after 6 months of storage, its BS values were almost lower than those of CSE, which had a higher CA. In addition, PBU demonstrated fewer RTs than OBFL; however, its BS values after 6 months were almost higher than OBFL values. These findings indicated that regardless of the adhesive layer and the length of the tags' penetration into the dentinal tubules, adhesives with different chemical compositions, type, and qualities of the functional monomer contained in the materials' composition may have an impact on the bonding performance in terms of degradation during prolonged storage in water [2]. Moreover, it was proven that there is no clear relationship between dentinal BS and surface wettability [74]. This can support the findings obtained in this study. In summary, BS, RTs penetration, and wettability were considered independent influencing factors when using each modality tested in this study with these dentinal bonding systems.

Each bonding agent should be accompanied by the right modality during the application process. A previous survey showed that approximately 25% of dentists interviewed did not recall the appropriate application procedure of their bonding agent [37]. Therefore, it is possible that in dental practices, bonding agents are not applied based on the manufacturer's instructions due to a lack of knowledge and time constraints in dentistry. A former study examined the effect of inaccurate use of six bonding agents on the BS [75] and found that the BS of resin composites to dentin was significantly weakened by deviations from the manufacturer's protocol. Hence, this study proved that there are specific modalities in place for each adhesive system.

Looking back at the advancements that adhesive systems have undergone throughout the previous 20 years, investigations into the actual improvements when it comes to technique sensitivity are crucial [6,62]. In this study, OBFL displayed the highest immediate and short-term values among all the tested adhesives. This shows that after 24 h, OBFL is not sensitive to any of the application modalities and supports previous studies' claims of this adhesive's noteworthy performance [12]. However, another study does not support the concept that this bonding agent is better than any other competitive products offered in the dental marketplace [76]. Having said that, practitioners and researchers alike should keep an eye on new literature findings. Some limitations could be addressed in this study. First of all, the number of materials tested was limited. Although representative brands of each of the types of materials available that are most currently used were included, it is well known that the *in vitro* performance of these adhesives is material-dependent, and more studies could be incorporated in future works. Moreover, for SEM observation, there were some samples that showed cracks and detached interfaces due to the high pressure of the SEM device. Additionally, the BS was only evaluated after 24 h and 6 months of aging in distilled water; more aging time or the use of other aging procedures such as thermocycling are desired in order to look for more signs of degradation of the adhesive interface.

2.5. Conclusions

Based on the findings of this study, it could be concluded that the BS could be influenced by both materials and application techniques. Following the right modality is considered an adhesive-dependent approach. It seems that the AA technique could be recommended as a gold-standard for the application of an adhesive system to dentin. Plus, for long-term performance, the modality applied by clinicians using the CVM could be specific for some adhesives such as CSE and OBFL, which had the highest values after

6 months of using this modality. Moreover, the CV technique resulted in stability for PBU; consequently, their performance might vary when applied to other modalities. Future studies are needed to test this hypothesis.

2.6. References

1. Bourgi, R.; Hardan, L.; Cuevas-Suárez, C.E.; Scavello, F.; Mancino, D.; Kharouf, N.; Haikel, Y. The Use of Warm Air for Solvent Evaporation in Adhesive Dentistry: A Meta-Analysis of In Vitro Studies. *J. Funct. Biomater*. **2023**, *14*, 285.
2. Kharouf, N.; Ashi, T.; Eid, A.; Maguina, L.; Zghal, J.; Sekayan, N.; Bourgi, R.; Hardan, L.; Sauro, S.; Haikel, Y. Does Adhesive Layer Thickness and Tag Length Influence Short/Long-Term Bond Strength of Universal Adhesive Systems? An in-Vitro Study. *Appl. Sci.* **2021**, *11*, 2635.
3. Paken, G.; Çömlekoğlu, M.E.; Sonugelen, M. Detection of the Hybrid Layer Biodegradation Initiation Factor with a Scanning Electron Microscope. *Microsc. Res. Tech.* **2021**, *84*, 2166–2175.
4. Pashley, D.H.; Tay, F.R.; Breschi, L.; Tjäderhane, L.; Carvalho, R.M.; Carrilho, M.; Tezvergil-Mutluay, A. State of the Art Etch-and-Rinse Adhesives. *Dent. Mater.* **2011**, *27*, 1–16.
5. Yoshihara, K.; Nagaoka, N.; Hayakawa, S.; Okihara, T.; Yoshida, Y.; Van Meerbeek, B. Chemical Interaction of Glycero-Phosphate Dimethacrylate (GPDM) with Hydroxyapatite and Dentin. *Dent. Mater.* **2018**, *34*, 1072–1081.
6. Sofan, E.; Sofan, A.; Palaia, G.; Tenore, G.; Romeo, U.; Migliau, G. Classification review of dental adhesive systems: From the IV generation to the universal type. *Ann. Stomatol.* (Roma) **2017**, *8*, 1-17. doi:10.11138/ads/2017.8.1.001.
7. Van Meerbeek, B.; Yoshihara, K.; Yoshida, Y.; Mine, A.; De Munck, J.; Van Landuyt, K. State of the Art of Self-Etch Adhesives. *Dent. Mater.* **2011**, *27*, 17–28.
8. Kharouf, N.; Eid, A.; Hardan, L.; Bourgi, R.; Arntz, Y.; Jmal, H.; Foschi, F.; Sauro, S.; Ball, V.; Haikel, Y.; et al. Antibacterial and Bonding Properties of Universal Adhesive Dental Polymers Doped with Pyrogallol. *Polymers* **2021**, *13*, 1538.
9. Bourgi, R.; Daood, U.; Bijle, M.N.; Fawzy, A.; Ghaleb, M.; Hardan, L. Reinforced Universal Adhesive by Ribose Crosslinker: A Novel Strategy in Adhesive Dentistry. *Polymers* **2021**, *13,* 704.
10. Hardan, L.; Bourgi, R.; Cuevas-Suárez, C.E.; Zarow, M.; Kharouf, N.; Mancino, D.; Villares, C.F.; Skaba, D.; Lukomska-Szymanska, M. The Bond Strength and Antibacterial Activity of the Universal Dentin Bonding System: A Systematic Review and Meta-Analysis. *Microorganisms* **2021**, *9*, 1230.
11. Triani, F.; Pereira da Silva, L.; Ferreira Lemos, B.; Domingues, J.; Teixeira, L.; Manarte-Monteiro, P. Universal Adhesives: Evaluation of the Relationship between Bond Strength and Application Strategies—A Systematic Review and Meta-Analyses. *Coatings* **2022**, *12*, 1501.
12. Meerbeek, B.V.; Yoshihara, K.; Van Landuyt, K.; Yoshida, Y.; Peumans, M. From Buonocore's Pioneering Acid-Etch Technique to Self-Adhering Restoratives. A Status Perspective of Rapidly Advancing Dental Adhesive Technology. *J. Adhes. Dent.* **2020**, *22*, 7–34.
13. Hardan, L.; Bourgi, R.; Kharouf, N.; Mancino, D.; Zarow, M.; Jakubowicz, N.; Haikel, Y.; Cuevas-Suárez, C.E. Bond Strength of Universal Adhesives to Dentin: A Systematic Review and Meta-Analysis. *Polymers* **2021**, *13*, 814.
14. Bourgi, R.; Hardan, L.; Rivera-Gonzaga, A.; Cuevas-Suárez, C.E. Effect of Warm-Air Stream for Solvent Evaporation on Bond Strength of Adhesive Systems: A Systematic Review and Meta-Analysis of in Vitro Studies. *Int. J. Adhes. Adhes.* **2021**, *105*, 102794.
15. Takamizawa, T.; Imai, A.; Hirokane, E.; Tsujimoto, A.; Barkmeier, W.W.; Erickson, R.L.; Latta, M.A.; Miyazaki, M. SEM Observation of Novel Characteristic of the Dentin Bond Interfaces of Universal Adhesives. *Dent. Mater.* **2019**, *35*, 1791–1804.
16. Ayres, A.P.; Bonvent, J.J.; Mogilevych, B.; Soares, L.E.S.; Martin, A.A.; Ambrosano, G.M.; Nascimento, F.D.; Van Meerbeek, B.; Giannini, M. Effect of Non-Thermal Atmospheric Plasma on the Dentin-Surface Topography and Composition and on the Bond Strength of a Universal Adhesive. *Eur. J. Oral Sci.* **2018**, *126*, 53–65. https://doi.org/10.1111/eos.12388.
17. Gutierrez, M.F.; Sutil, E.; Malaquias, P.; de Paris Matos, T.; de Souza, L.M.; Reis, A.; Perdigao, J.; Loguercio, A.D. Effect of Self-Curing Activators and Curing Protocols on Adhesive Properties of Universal Adhesives Bonded to Dual-Cured Composites. *Dent. Mater. Off. Publ. Acad. Dent. Mater.* **2017**, *33*, 775–787. https://doi.org/10.1016/j.dental.2017.04.005.
18. Sano, H.; Chowdhury, A.F.M.A.; Saikaew, P.; Matsumoto, M.; Hoshika, S.; Yamauti, M. The Microtensile Bond Strength Test: Its Historical Background and Application to Bond Testing. *JPN Dent. Sci. Rev.* **2020**, *56*, 24–31.

19. Beloica, M.; Goracci, C.; Carvalho, C.A.; Radovic, I.; Margvelashvili, M.; Vulicevic, Z.R.; Ferrari, M. Microtensile vs Microshear Bond Strength of All-in-One Adhesives to Unground Enamel. *J. Adhes. Dent* **2010**, *12*, 427–433.
20. Mokeem, L.S.; Garcia, I.M.; Balhaddad, A.A.; Cline, K.; Rakovsky, G.; Collares, F.M.; Melo, M.A.S. Dental Adhesives: State-of-the-Art, Current Perspectives, and Promising Applications. *Adhes. Biomed. Appl.* **2023**, 253–277.
21. Liber-Kneć, A.; Łagan, S. Surface Testing of Dental Biomaterials—Determination of Contact Angle and Surface Free Energy. *Materials* **2021**, *14*, 2716.
22. Jang, J.-H.; Jeon, B.-K.; Mo, S.Y.; Park, M.; Choi, D.; Choi, K.-K.; Kim, D.-S. Effect of Various Agitation Methods on Adhesive Layer Formation of HEMA-Free Universal Dentin Adhesive. *Dent. Mater. J.* **2018**, *38*, 101–106.
23. Santana, F.R.; Pereira, J.C.; Pereira, C.A.; Fernandes Neto, A.J.; Soares, C.J. Influence of Method and Period of Storage on the Microtensile Bond Strength of Indirect Composite Resin Restorations to Dentine. *Braz. Oral Res.* **2008**, *22*, 352–357.
24. Dikova, T.; Maximov, J.; Todorov, V.; Georgiev, G.; Panov, V. Optimization of Photopolymerization Process of Dental Composites. *Processes* **2021**, *9*, 779.
25. Elizalde-Hernández, A.; Hardan, L.; Bourgi, R.; Isolan, C.P.; Moreira, A.G.; Zamarripa-Calderón, J.E.; Piva, E.; Cuevas-Suárez, C.E.; Devoto, W.; Saad, A. Effect of Different Desensitizers on Shear Bond Strength of Self-Adhesive Resin Cements to Dentin. *Bioengineering* **2022**, *9*, 372.
26. Georgiev, G.; Dikova, T. Hardness Investigation of Conventional, Bulk Fill and Flowable Dental Composites. *J. Achiev. Mater. Manuf. Eng.* **2021**, *109*, 68–77.
27. Armstrong, S.; Breschi, L.; Özcan, M.; Pfefferkorn, F.; Ferrari, M.; Van Meerbeek, B. Academy of Dental Materials Guidance on in Vitro Testing of Dental Composite Bonding Effectiveness to Dentin/Enamel Using Micro-Tensile Bond Strength (MTBS) Approach. *Dent. Mater.* **2017**, *33*, 133–143.
28. Kharouf, N.; Arntz, Y.; Eid, A.; Zghal, J.; Sauro, S.; Haikel, Y.; Mancino, D. Physicochemical and Antibacterial Properties of Novel, Premixed Calcium Silicate-Based Sealer Compared to Powder–Liquid Bioceramic Sealer. *J. Clin. Med.* **2020**, *9*, 3096.
29. Ekambaram, M.; Yiu, C.K.Y.; Matinlinna, J.P. An Overview of Solvents in Resin–Dentin Bonding. *Int. J. Adhes. Adhes.* **2015**, *57*, 22–33.
30. Irmak, Ö.; Yaman, B.C.; Orhan, E.O.; Ozer, F.; Blatz, M.B. Effect of Rubbing Force Magnitude on Bond Strength of Universal Adhesives Applied in Self-Etch Mode. *Dent. Mater. J.* **2018**, *37*, 139–145.
31. Kameyama, A.; Haruyama, A.; Abo, H.; Kojima, M.; Nakazawa, Y.; Muramatsu, T. Influence of Solvent Evaporation on Ultimate Tensile Strength of Contemporary Dental Adhesives. *Appl. Adhes. Sci.* **2019**, *7*, 4. https://doi.org/10.1186/s40563-019-0120-0.
32. Koike, K.; Takamizawa, T.; Aoki, R.; Shibasaki, S.; Ishii, R.; Sai, K.; Kamimoto, A.; Miyazaki, M. Comparison of Dentin Bond Durability in Different Adhesive Systems Containing Glycerol-Phosphate Dimethacrylate (GPDM) Functional Monomers under Long-Term Water Storage. *Int. J. Adhes. Adhes.* **2023**, *124*, 103366.
33. Han, F.; Dai, S.; Yang, J.; Shen, J.; Liao, M.; Xie, H.; Chen, C. Glycerol Phosphate Dimethacrylate: An Alternative Functional Phosphate Ester Monomer to 10-Methacryloyloxydecyl Dihydrogen Phosphate for Enamel Bonding. *ACS Omega* **2020**, *5*, 24826–24837. https://doi.org/10.1021/acsomega.0c03523.
34. Thalacker, C. Dental Adhesion with Resin Composites: A Review and Clinical Tips for Best Practice. *Br. Dent. J.* **2022**, *232*, 615–619. https://doi.org/10.1038/s41415-022-4144-7.
35. Hoshika, S.; Kameyama, A.; Suyama, Y.; De Munck, J.; Sano, H.; Van Meerbeek, B. GPDM- and 10-MDP-Based Self-Etch Adhesives Bonded to Bur-Cut and Uncut Enamel—"Immediate" and "Aged" MTBS. *J. Adhes. Dent.* **2018**, *20*, 113–120. https://doi.org/10.3290/j.jad.a40307.
36. Tsujimoto, A.; Fischer, N.G.; Barkmeier, W.W.; Latta, M.A. Bond Durability of Two-Step HEMA-Free Universal Adhesive. *J. Funct. Biomater.* **2022**, *13*, 134.
37. Peutzfeldt, A.; Vigild, M. A Survey of the Use of Dentin-Bonding Systems in Denmark. *Dent. Mater.* **2001**, *17*, 211–216.
38. Tjäderhane, L.; Nascimento, F.D.; Breschi, L.; Mazzoni, A.; Tersariol, I.L.; Geraldeli, S.; Tezvergil-Mutluay, A.; Carrilho, M.R.; Carvalho, R.M.; Tay, F.R. Optimizing Dentin Bond Durability: Control of Collagen Degradation by Matrix Metalloproteinases and Cysteine Cathepsins. *Dent. Mater.* **2013**, *29*, 116–135.
39. Tjäderhane, L.; Nascimento, F.D.; Breschi, L.; Mazzoni, A.; Tersariol, I.L.S.; Geraldeli, S.; Tezvergil-Mutluay, A.; Carrilho, M.; Carvalho, R.M.; Tay, F.R.; Pashley, D.H. Strategies to Prevent Hydrolytic Degradation of the Hybrid Layer—A Review. *Dent. Mater.* **2013**, *29*, 999–1011. https://doi.org/10.1016/j.dental.2013.07.016.
40. Garcia, R.N.; de Araújo Neto, V.G.; Silva, C.R.; Miguel, L.C.M.; Giannini, M. Microshear Bond Strength of Universal Adhesives to Enamel and Dentin: An Eighteen-Month in Vitro Study. *Braz. Dent. Sci.* **2021**, *24*, 1–9.

41. Carvalho, R.M.; Chersoni, S.; Frankenberger, R.; Pashley, D.H.; Prati, C.; Tay, F.R. A Challenge to the Conventional Wisdom That Simultaneous Etching and Resin Infiltration Always Occurs in Self-Etch Adhesives. *Biomaterials* **2005**, *26*, 1035–1042.
42. Nakabayashi, N.; Pashley, D. Acid Conditioning and Hybridization of Substrates. In *Hybridization of Dental Hard Tissues*; Quintessence Publishing Company: Tokyo, Japan, **1998**; pp. 37–56.
43. Yoshida, Y.; Yoshihara, K.; Nagaoka, N.; Hayakawa, S.; Torii, Y.; Ogawa, T.; Osaka, A.; Meerbeek, B.V. Self-Assembled Nano-Layering at the Adhesive Interface. *J. Dent. Res.* **2012**, *91*, 376–381.
44. Carrilho, E.; Cardoso, M.; Marques Ferreira, M.; Marto, C.M.; Paula, A.; Coelho, A.S. 10-MDP Based Dental Adhesives: Adhesive Interface Characterization and Adhesive Stability—A Systematic Review. *Materials* **2019**, *12*, 790.
45. Perdigão, J.; Kose, C.; Mena-Serrano, A.P.; De Paula, E.A.; Tay, L.Y.; Reis, A.; Loguercio, A.D. A New Universal Simplified Adhesive: 18-Month Clinical Evaluation. *Oper. Dent.* **2014**, *39*, 113–127. https://doi.org/10.2341/13-045-C.
46. Yoshihara, K.; Nagaoka, N.; Okihara, T.; Kuroboshi, M.; Hayakawa, S.; Maruo, Y.; Nishigawa, G.; De Munck, J.; Yoshida, Y.; Van Meerbeek, B. Functional Monomer Impurity Affects Adhesive Performance. *Dent. Mater. Off. Publ. Acad. Dent. Mater.* **2015**, *31*, 1493–1501. https://doi.org/10.1016/j.dental.2015.09.019.
47. Loguercio, A.D.; Luque-Martinez, I.; Muñoz, M.A.; Szesz, A.L.; Cuadros-Sánchez, J.; Reis, A. A Comprehensive Laboratory Screening of Three-Step Etch-and-Rinse Adhesives. *Oper. Dent.* **2014**, *39*, 652–662.
48. Sanghvi, M.R.; Tambare, O.H.; More, A.P. Performance of Various Fillers in Adhesives Applications: A Review. *Polym. Bull.* **2022**, *79*, 10491–10553.
49. 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**, *107*, 2121–2131.
50. Kenshima, S.; Reis, A.; Uceda-Gomez, N.; Tancredo, L.D.L.F.; Filho, L.E.R.; Nogueira, F.N.; Loguercio, A.D. Effect of Smear Layer Thickness and PH of Self-Etching Adhesive Systems on the Bond Strength and Gap Formation to Dentin. *J. Adhes. Dent.* **2005**, *7*, 117–126.
51. Cuevas-Suárez, C.E.; Ramos, T.S.; Rodrigues, S.B.; Collares, F.M.; Zanchi, C.H.; Lund, R.G.; da Silva, A.F.; Piva, E. Impact of Shelf-Life Simulation on Bonding Performance of Universal Adhesive Systems. *Dent. Mater.* **2019**, *35*, e204–e219.
52. Reis, A.; Pellizzaro, A.; Dal-Bianco, K.; Gomes, O.; Patzlaff, R.; Loguercio, A.D. Impact of Adhesive Application to Wet and Dry Dentin on Long-Term Resin-Dentin Bond Strengths. *Oper. Dent.* **2007**, *32*, 380–387.
53. Reis, A.; Carrilho, M.; Breschi, L.; Loguercio, A. Overview of Clinical Alternatives to Minimize the Degradation of the Resin-Dentin Bonds. *Oper. Dent.* **2013**, *38*, E103–E127.
54. Amaral, R.; Stanislawczuk, R.; Zander-Grande, C.; Gagler, D.; Reis, A.; Loguercio, A.D. Bond Strength and Quality of the Hybrid Layer of One-Step Self-Etch Adhesives Applied with Agitation on Dentin. *Oper. Dent.* **2010**, *35*, 211–219.
55. do Amaral, R.C.; Stanislawczuk, R.; Zander-Grande, C.; Michel, M.D.; Reis, A.; Loguercio, A.D. Active Application Improves the Bonding Performance of Self-Etch Adhesives to Dentin. *J. Dent.* **2009**, *37*, 82–90.
56. Feitosa, V.P.; Sauro, S.; Ogliari, F.A.; Ogliari, A.O.; Yoshihara, K.; Zanchi, C.H.; Correr-Sobrinho, L.; Sinhoreti, M.A.; Correr, A.B.; Watson, T.F. Impact of Hydrophilicity and Length of Spacer Chains on the Bonding of Functional Monomers. *Dent. Mater.* **2014**, *30*, e317–e323.
57. Takamizawa, T.; Hirokane, E.; Sai, K.; Ishii, R.; Aoki, R.; Barkmeier, W.W.; Latta, M.A.; Miyazaki, M. Bond Durability of a Two-Step Adhesive with a Universal-Adhesive-Derived Primer in Different Etching Modes under Different Degradation Conditions. *Dent. Mater. J.* **2023**, *42*, 121–132.
58. Bagis, B.; Turkarslan, S.; Tezvergil-Mutluay, A.; Uctasli, S.; Vallittu, P.K.; Lassila, L.V. Effect of Ultrasonic Agitation on Bond Strength of Self-Etching Adhesives to Dentin. *J. Adhes. Dent.* **2008**, *10*, 441–445.
59. Dal-Bianco, K.; Pellizzaro, A.; Patzlaft, R.; de Oliveira Bauer, J.R.; Loguercio, A.D.; Reis, A. Effects of Moisture Degree and Rubbing Action on the Immediate Resin–Dentin Bond Strength. *Dent. Mater.* **2006**, *22*, 1150–1156.
60. Münchow, E.A.; Bossardi, M.; Priebe, T.C.; Valente, L.L.; Zanchi, C.H.; Ogliari, F.A.; Piva, E. Microtensile versus Microshear Bond Strength between Dental Adhesives and the Dentin Substrate. *Int. J. Adhes. Adhes.* **2013**, *46*. https://doi.org/10.1016/j.ijadhadh.2013.06.005.
61. El Zohairy, A.; De Gee, A.; De Jager, N.; Van Ruijven, L.; Feilzer, A. The Influence of Specimen Attachment and Dimension on Microtensile Strength. *J. Dent. Res.* **2004**, *83*, 420–424.
62. Hardan, L.; Bourgi, R.; Cuevas-Suárez, C.E.; Devoto, W.; Zarow, M.; Monteiro, P.; Jakubowicz, N.; Zoghbi, A.E.; Skaba, D.; Mancino, D. Effect of Different Application Modalities on the Bonding Performance of Adhesive Systems to Dentin: A Systematic Review and Meta-Analysis. *Cells* **2023**, *12*, 190.

63. Prati, C.; Chersoni, S.; Mongiorgi, R.; Pashley, D.H. Resin-Infiltrated Dentin Layer Formation of New Bonding Systems. *Oper. Dent.* **1998**, *23*, 185–194.
64. Sinhoreti, M.A.C.; Soares, E.F.; Abuna, G.F.; Correr, L.; Roulet, J.-F.; Geraldeli, S. Microtensile Bond Strength of Adhesive Systems in Different Dentin Regions on a Class II Cavity Configuration. *Braz. Dent. J.* **2017**, *28*, 474–481.
65. Sabatini, C.; Ortiz, P.A.; Pashley, D.H. Preservation of Resin–Dentin Interfaces Treated with Benzalkonium Chloride Adhesive Blends. *Eur. J. Oral Sci.* **2015**, *123*, 108–115.
66. Ruyter, I. The Chemistry of Adhesive Agents. *Oper. Dent.* **1992**, 5, 32–43.
67. Marshall, S.J.; Bayne, S.C.; Baier, R.; Tomsia, A.P.; Marshall, G.W. A Review of Adhesion Science. *Dent. Mater.* **2010**, *26*, e11–e16.
68. Tsujimoto, A.; Iwasa, M.; Shimamura, Y.; Murayama, R.; Takamizawa, T.; Miyazaki, M. Enamel Bonding of Single-Step Self-Etch Adhesives: Influence of Surface Energy Characteristics. *J. Dent.* **2010**, *38*, 123–130.
69. Pazinatto, F.B.; Marquezini Jr, L.; Atta, M.T. Influence of Temperature on the Spreading Velocity of Simplified-Step Adhesive Systems. *J. Esthet. Restor. Dent.* **2006**, *18*, 38–46.
70. Rosales, J.; Marshall, G.; Marshall, S.; Watanabe, L.; Toledano, M.; Cabrerizo, M.; Osorio, R. Acid-Etching and Hydration Influence on Dentin Roughness and Wettability. *J. Dent. Res.* **1999**, *78*, 1554–1559.
71. Rosales-Leal, J.I.; Osorio, R.; Holgado-Terriza, J.A.; Cabrerizo-Vı́lchez, M.A.; Toledano, M. Dentin Wetting by Four Adhesive Systems. *Dent. Mater.* **2001**, *17*, 526–532.
72. Nakabayashi, N.; Takarada, K. Effect of HEMA on Bonding to Dentin. *Dent. Mater.* **1992**, *8*, 125–130.
73. Toledano, M.; Mazzoni, A.; Monticelli, F.; Breschi, L.; Osorio, E.; Osorio, R. ElectroBond Application May Improve Wetting Characteristics of Etched Dentine. *J. Dent.* **2011**, *39*, 180–186.
74. Aguilar-Mendoza, J.A.; Rosales-Leal, J.I.; Rodríguez-Valverde, M.A.; González-López, S.; Cabrerizo-Vílchez, M.A. Wettability and Bonding of Self-Etching Dental Adhesives: Influence of the Smear Layer. *Dent. Mater.* **2008**, *24*, 994–1000.
75. Peutzfeldt, A.; Asmussen, E. Adhesive Systems: Effect on Bond Strength of Incorrect Use. *J. Adhes. Dent.* **2002**, *4*, 233–242.
76. Dreweck, F.; Burey, A.; de Oliveira Dreweck, M.; Fernandez, E.; Loguercio, A.D.; Reis, A. Challenging the Concept That OptiBond FL and Clearfil SE Bond in NCCLs Are Gold Standard Adhesives: A Systematic Review and Meta-Analysis. *Oper. Dent.* **2021**, *46*, E276–E295. https://doi.org/10.2341/20-059-LIT.

2.7. Publication of Chapter II

polymers

Article

Effectiveness of Different Application Modalities on the Bond Performance of Four Polymeric Adhesive Systems to Dentin

Rim Bourgi [1,2], Louis Hardan [1,†], Carlos Enrique Cuevas-Suárez [3], Walter Devoto [4], Cynthia Kassis [1], Khalil Kharma [1], Ryan Harouny [1,5], Tarek Ashi [2], Davide Mancino [2,6,7], Naji Kharouf [2,6,*] and Youssef Haikel [2,6,7,†]

[1] Department of Restorative Dentistry, School of Dentistry, Saint-Joseph University, Beirut 1107 2180, Lebanon; rim.bourgi@net.usj.edu.lb (R.B.); louis.hardan@usj.edu.lb (L.H.); cynthia.kassis@usj.edu.lb (C.K.); khalil.kharma@usj.edu.lb (K.K.); ryaneliott.harouny@net.usj.edu.lb (R.H.)
[2] Department of Biomaterials and Bioengineering, INSERM UMR_S 1121, University of Strasbourg, 67000 Strasbourg, France; tarekachi@live.com (T.A.); mancino@unistra.fr (D.M.); youssef.haikel@unistra.fr (Y.H.)
[3] Dental Materials Laboratory, Academic Area of Dentistry, Autonomous University of Hidalgo State, San Agustín Tlaxiaca 42160, Mexico; cecuevas@uaeh.edu.mx
[4] Independent Researcher, 16030 Sestri Levante, Italy; walter@walterdevoto.com
[5] Craniofacial Research Laboratory, Division of Biomaterials, School of Dentistry, Saint-Joseph University, Beirut 1107 2180, Lebanon
[6] Department of Endodontics and Conservative Dentistry, Faculty of Dental Medicine, University of Strasbourg, 67000 Strasbourg, France
[7] Pôle de Médecine et Chirurgie Bucco-Dentaire, Hôpital Civil, Hôpitaux Universitaire de Strasbourg, 67000 Strasbourg, France
* Correspondence: dentistenajikharouf@gmail.com; Tel.: +33-66752-2841
† These authors contributed equally to this work.

Abstract: One of the major goals of adhesive dentistry is to improve the interaction of the already-existing adhesives with different substrates by using different application techniques. Thus, the objective of the present in vitro study was to assess the bond performance of four adhesive systems, Prime&Bond Universal (PBU), Clearfil SE Bond (CSE), OptiBond Universal (OBU), and OptiBond FL (OBFL), to dentin using various application modes: passive application (PA), active application (AA), Compo-Vibes modified application (CVM), and Compo-Vibes application (CV). Eighty extracted human molars were allocated into four groups based on the application modalities tested. The micro-tensile bond strength as well as fracture mode were tested in accordance with ISO/TS 11.405 after 24 h and 6 months of aging. Adhesive contact angle (CA) and scanning electron microscope analysis were also performed ($n = 3$). Statistical tests were performed with $\alpha = 0.05$. After 24 h, a significant difference with a higher bond strength value was found for PBU in the AA modality and for CSE in the CVM modality ($p < 0.05$). However, no significant difference was shown between the techniques used among the other adhesives (OBFL and OBU). Moreover, at 24 h, only the PA demonstrated significant differences between the tested materials ($p < 0.05$). After 6 months, CSE, PBU, and OBU demonstrated significant differences between the techniques ($p < 0.05$), with a higher bond strength for CSE in AA and CVM modalities, for PBU in AA modality, and for OBU in AA and PA modalities. No significant differences were found between the techniques used among the OBFL ($p > 0.05$). In addition, only the CVM technique demonstrated significant differences between the tested materials after 6 months. CV and CVM showed a decreased value after aging for CSE and PBU, respectively. However, all the modalities decreased for OBU and OBFL after aging. All the adhesives showed marked resin infiltration into dentinal tubules in AA among all the modalities tested. Both universal adhesive systems (OBU and PBU) demonstrated statistically lower CA when compared to the other systems (CSE and OBFL) ($p < 0.05$) when applied in the PA mode. Concerning the AA mode, only CSE and OBFL were tested. The AA demonstrated lower CA values compared to the same adhesives in PA ($p < 0.05$). It could be concluded that the bond strength could be influenced by both materials and application techniques. It seems that the AA technique could be recommended as a gold standard for the application of an adhesive system to dentin. Plus, the CV and CVM modalities

Citation: Bourgi, R.; Hardan, L.; Cuevas-Suárez, C.E.; Devoto, W.; Kassis, C.; Kharma, K.; Harouny, R.; Ashi, T.; Mancino, D.; Kharouf, N.; et al. Effectiveness of Different Application Modalities on the Bond Performance of Four Polymeric Adhesive Systems to Dentin. *Polymers* **2023**, *15*, 3924. https://doi.org/10.3390/polym15193924

Academic Editors: Matej Par and Katarzyna Mańka-Malara

Received: 7 September 2023
Revised: 22 September 2023
Accepted: 25 September 2023
Published: 28 September 2023

Chapter III: Protocols for the Different Layer Application

3.1. Introduction

The intrinsic wet nature of dentin makes it a challenging substrate for resin composite bonding [1]. Moreover, most of the time in clinical settings, the dentin is still covered with smear layers, which prevent adhesive molecules from penetrating the dentin [2]. Consequently, removing or altering this layer by means of an acid etching stage preceding the application of the bonding agent is crucial for the formation of the HL [3]. Dental adhesives' ability to bond to dentin relies on the HL creation to warrant a strong bond between the resin monomers and dentin structure [4]. Lately, an additional alteration of these adhesive systems, the so-called UAs, has been familiarized into the dental market. Unlike their forerunners, these adhesives can be used in both SE and ER strategies [3–5].

Further improvements to dental adhesives involved initiating new molecules into the components of adhesive systems: 10-MDP, GPDM, 4-MET, and Phenyl-P. They were designated as functional monomers and were considered to chemically adhere to Ca in HAp [5]. Amongst these molecules, the 10-MDP monomer was stated to acquire the toughest chemical adhesion possible to HAp, creating constant and hydrolysis-resistant Ca salts because of the nano-layering process [6]. Therefore, an extra layer of adhesive application must be considered as a fundamental step in dental clinics. Furthermore, 10-MDP necessitates a suitable time of 20 s for its chemical interaction to take place; yet, employing a second layer of such a functional monomer without curing the first coat warrants the first layer to sufficiently interact with HAp and consequently encourages further bonding [7]. A double-layer application might be explained by the following theory: the first coat of the adhesive system demineralizes the dentinal substrate via etching using H_3PO_4 or acidic monomers and thus could be rapidly buffered by the HAp [2]; the additional layers of non-photopolymerized acidic monomers might successively increase etching by rising the concentration of acid components. The extra infiltration of resin monomers might concurrently appear due to the added amount of adhesive system [8].

The adhesives are usually able to create an HL with both immediate and medium-term high BS. However, losses of dentin-bonded interface integrity and BS are usually seen after aging [9]. There are many factors involved in this loss of bonding efficacy, including an unsatisfactory resin infiltration of the dentinal structure, phase separation, as well as a low level of adhesive polymerization, all of which might lessen the durability of a bonded interface [4]. All of these variables could be avoided by creating a gold-pattern application protocol designed to maximize the effectiveness of contemporary adhesive systems. Currently, there are not any standard adhesive application protocols to enhance the longevity of resin-dentin bonds created by adhesive systems.

Nevertheless, the hybridized dentin does not fully cover the depth of the demineralized dentin. The true HL is actually thinner than it appears in the SEM, since a demineralized dentin zone still exists, especially at the bottom [10]. However, this thinner HL and resulting inadequate stress-breaking action might be recompensed using a thicker adhesive coat at the top [11]. Former analyses with diverse adhesive systems stated that promising outcomes with the AA modality or an additional coat of the adhesive layer could be obtained to enhance their bond performance to dentin [12,13]. An active adhesive application can achieve a higher rate of monomer infiltration inside the collagen network, whereas an extra bonding layer might rise the thickness of the adhesive layer, therefore improving the distribution of stress when a load is applied and decreasing the degradation of the HL. The use of MLA increased the immediate BS, but this result could not be observed after aging [13]. Thus, it was deemed essential to know how many adhesive layers should be applied to the dentin structure in order to improve the bond performance. Previous papers proposed that double or triple adhesive coats enhance the BS by enabling monomer diffusion into the HL and increasing chemical interactions [8,14].

Another variation of the adhesive application can be found in the adhesive technique without polymerization, with favorable results [15,16]. Correspondingly, there are no previously published studies in the literature based on the adhesive layer application including triple adhesive layers in conjunction with the ABT, called MTLA. Appropriately, a description of this novel technique could be interesting for dentists aiming for a better adhesion to dentin. Hence, the aim of this article was to assess the effect of the MTLA of four adhesive systems on the dentin BS as well as the correlation between these parameters at 24 h and 6 months of aging. According to the null hypothesis, there is no effect of the ABT with MLA on the BS and morphological properties of adhesive systems to dentin substrates.

3.2. Materials and Methods

The study protocol was agreed upon by the ethical team of the dental faculty at the Saint-Joseph University of Beirut, Lebanon (FMD-221; reference number: #USJ-2022-140). A representation of the study groups is described in Fig. 33.

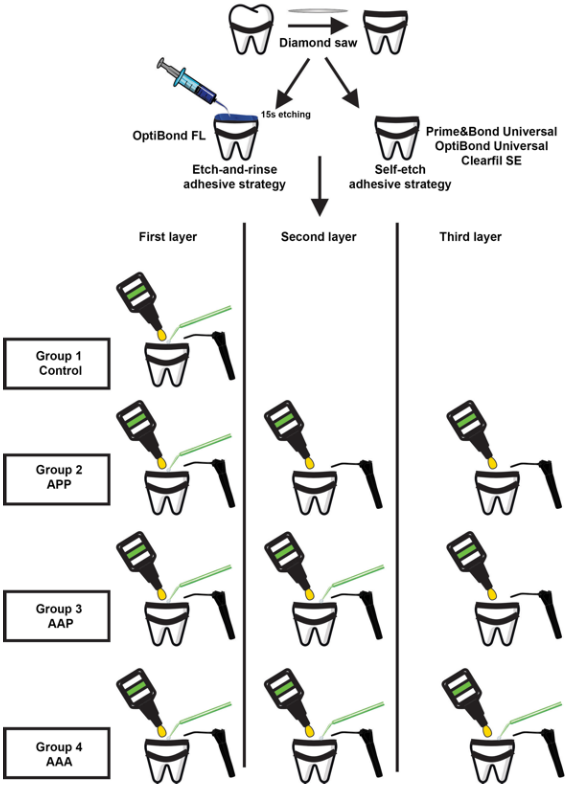


Figure 33: Representation of the four groups tested in this research. Single active application (A); triple application, Active–Passive–Passive (APP); triple application, Active–Active–Passive (AAP); triple application, Active–Active–Active (AAA).

3.2.1. Tooth Specimen Preparation

Eighty (n = 80) sound human molars without any signs of cracking in the enamel or caries were extracted for orthodontic reasons and examined for μTBS. These molars were collected, freed of soft tissue, and kept at 4 °C for a month in a solution of 0.2% sodium azide to prevent microbial growth. Then, roots were segmented, and their crowns were fixed in gypsum to reveal the buccal enamel. Later, enamel substrate was abraded using an orthodontic grinder (Essencedental, Araraquara, SP, Brazil) until exposing and covering a flat medium dentin surface that conserved 4 mm of dentin in thickness. A regular and standardized smear layer was produced on the dentin by means of P320 SiC during one-minute, under water irrigation, with a grinder–polisher (Buehler Ltd., Lake Bluff, IL, USA) at a motor speed of 70 rpm.

3.2.2. Bonding Procedure

Following dentinal surface exposure, four groups, based on the adhesive layer application including the triple adhesive layers and ABT, were randomly formed. One coat (control) and three coats of adhesives were applied without photopolymerization after each application. ABT of adhesives to dentinal substrate was performed for 20 s manually by a single operator using a micro-brush applicator (Kerr, Orange, CA, USA). Additionally, the magnitude of force to be applied during rubbing action was standardized by one investigator who performed the adhesion process.

Two UAs (PBU, Dentsply DeTrey GmbH, Konstanz, Germany; OBU, Kerr Co, Orange, CA, USA), one ER III adhesive system (OBFL, Kerr Co, Orange, CA, USA), and one SE II adhesive system (CSE, Kuraray Noritake Dental Inc., Tokyo, Japan) were assessed. The compositions of the adhesive systems tested in the current research are shown in Table 9.

Material	Classification	Composition *	Manufacturer	Recommendation by the Manufacturer for Adhesive Application
PBU	**Mild Universal** pH = 2.5	10-MDP, PENTA, isopropanol, water, photo-initiator, bi- and multifunctional acrylate	Dentsply DeTrey GmbH, Konstanz, Germany	Apply PBU to all cavity surfaces. Avoid pooling. Keep PBU slightly agitated for 20 s. Evaporate solvent with air for at least 5 s. Light cure.
OBU	**Universal** pH = 2.5–3.0	Acetone, HEMA, GDMA, ethanol, GPDM	Kerr Co, Orange, CA, USA	Using the disposable applicator brush, apply a generous amount of OBU adhesive to the enamel/dentin surface. Scrub the surface with a

				brushing motion for 20 s. Dry the adhesive with gentle air first and then medium air for at least 5 s with oil-free air. The surface should have a glossy uniform appearance. If not, repeat the bonding and drying steps. Light cure.
OBFL	**Three-step etch-and-rinse** pH primer: 1.9; pH bonding: 6.9	Etchant: 37.5% H_3PO_4 Primer: HEMA, GPDM, MMEP, water, ethanol, CQ, and BHT Adhesive: Bis-GMA, HEMA, GDMA, CQ, and filler (fumed SiO_2, barium aluminoborosilicat, Na_2SiF_6), coupling factor A174	Kerr Co, Orange, CA, USA	Apply OBFL primer using an applicator brush over enamel and dentin surfaces with a light scrubbing motion for 15 s. Gently air-dry for approximately 5 s. At this point, the dentin surface should have a slightly shiny appearance. Using a new applicator brush, apply OBFL adhesive to the prepared enamel and dentin surfaces with a light scrubbing motion for 15 s, creating a thin coating. Gently air-dry for approximately 5 s. Light cure.
CSE	**Two-step self-etch** pH primer = 1.76 pH bond = 2	Primer: 10-MDP, HEMA, hydrophilic dimethacrylate, CQ, DEPT, water Bond: MDP, HEMA, Bis-GMA, hydrophobic dimethacrylate, CQ,	Kuraray Noritake Dental Inc., Tokyo, Japan	Apply primer for 20 s. Dry with mild air-flow. Apply bond.

	DEPT, silanized colloidal silica	Apply air-flow gently. Light cure.

* Based on companies' MSDS. 10-MDP = 10-methacryloyloxydecyl dihydrogen phosphate; PENTA = dipentaerythritol pentaacrylate phosphate; HEMA = 2-hydroxy ethyl methacrylate; GDMA = glycerol-dimethacrylate; GPDM = glycerophosphate dimethacrylate; MMEP = methacrylo-yloxy-ethyl-dihydrogen phosphate; CQ = camphorquinone; SiO_2 = silicon dioxide; Na_2SiF_6 = sodium hexafluorosilicate; BHT = butyl hydroxy toluene; Bis-GMA = bisphenol A-glycidyl methacrylate; DEPT = N,N-diethyl-p-toluidine; Clearfil SE Bond (CSE); OptiBond FL (OBFL); OptiBond Universal (OBU); Prime&Bond Universal (PBU).

Table 9: Manufacturers and compositions of the adhesives used.

The number of teeth per group (n = 5) was expected based on a preceding analysis [17] that assessed the effect of MLA on the dentinal BS in a comparative study design with four independent groups; there was a 5.87 minimum detectable difference in means, a 1.54 SD, a power of 0.8, and $\alpha = 0.05$. For the first group (control), one coat of all the tested adhesives was applied for 20 s with the ABT: A. For the second group, MTLA was applied as follows: application of the first layer with the ABT, application of the second layer without the ABT, and application of the third layer without the ABT (group 2 of triple application: APP). For the third group, MTLA was applied as follows: application of the first layer with the ABT, application of the second layer with the ABT, and application of the third layer without the ABT (group 3 of triple application: AAP). Further, for group four, the first, second, and third layers were used with the ABT (group 4 of triple application: AAA).

Solvent evaporation after each layer of primer or adhesive was performed for 5 s to 10 s by means of an air-drying syringe until there was no visible movement of the material. Next, bonding agents were polymerized for 20 s at room temperature using a LED multiwave light-curing unit, CuringPen-E (Eighteeth, Changzhou, China), calibrated at 1000 mW/cm^2. After bonding to the flat dentinal surfaces, three increments of resin composites (Reflectys, Itena Clinical, Paris, France) were created with a maximum thickness of 2 mm each. Each coat was photopolymerized for 20 s with the same light-curing unit.

3.2.3. Micro-Tensile Bond Strength Testing

Following adhesion procedure, specimens were stored in distilled water at 37 °C for 24 h. Then, by means of a low-speed precision cutting machine (EXAKT Vertriebs GmbH, Norderstedt, Germany), each tooth was longitudinally segmented across the bonded interfaces in the bucco-lingual and mesio-distal orientations to create resin-dentinal beams with a cross-sectional area of almost 1.0 mm × 1.0 mm (Fig. 34).

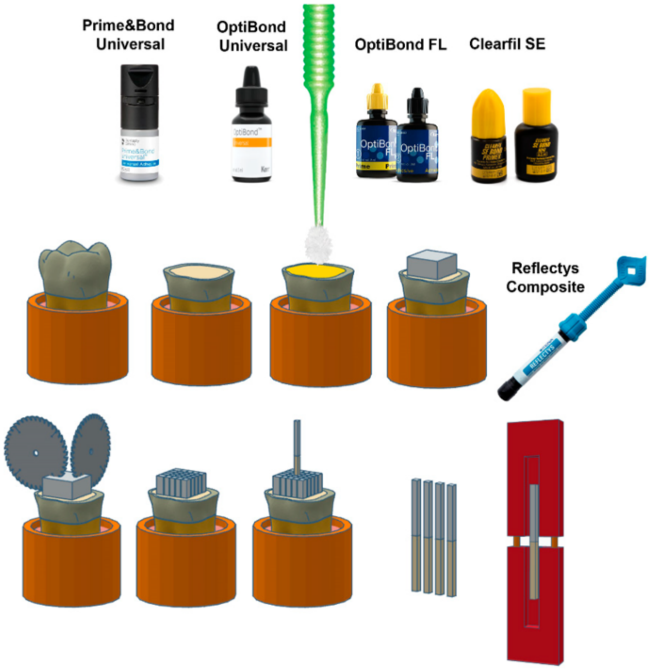


Figure 34: Representation of the tooth preparation, bonding procedure, and resin-dentin beams tested in the current manuscript.

According to ISO/TS 11405, a determined number of resin-dentin beams (n = 12) from each tooth was assigned to be calculated immediately (24 h) or following storage in distilled water at 37 °C for a period of 6 months.

The beams were then secured to a Geraldeli’s jig for μTBS testing by means of cyanoacrylate resin (Zapit Dental Ventures of North America, Corona, CA, USA), and they were put over a tensile force by means of a universal testing machine (YLE GmbH Waldstraße, Bad König, Germany) at a crosshead speed of 1.0 mm/min with a load cell of 500 N until failure [18]. Each failed sample was measured with a digital caliper using a precision of 0.01 mm (Model CD-6BS Mitutoyo, Tokyo, Japan). The failure load of each individual specimen (N) was divided by the mean cross-sectional area (mm^2), and the results were defined in MPa. The mean BS of the examined resin-dentinal beams from each tooth was considered as the value for that tooth.

3.2.4. Failure Mode Analysis

Following the μTBS assessment, the mode of failure for each specimen was examined by means of an optical numeric microscope (Keyence, Osaka, Japan). In order to express the type of fracture, the use of a VHX-5000 software is required for the evaluation of the percentage of each area at 150× magnification. The failures were categorized into adhesive, cohesive (failure in the composite or dentin), and mixed (as one area showed cohesive fracture, though other areas revealed an adhesive failure) failure modes [3].

3.2.5. Scanning Electron Microscopy

After storage period in distilled water for 24 h, three resin-dentin beams were used to analyze the composite-dentin interface morphology of specimens of each group. Afterwards, the interface between resin composite and dentinal structure was etched by means of 37% H_3PO_4 for a period of 10 s, and then washed with distilled water for 10 s, and submerged in a 2.5% sodium hypochlorite solution for 3 min [19]. Later, the tested samples were washed with distilled water and dehydrated in a succession of ethanol solutions (25%, 50%, 75%, and 100%). Thereafter, all samples were directly moved to a critical point drying machine (Balzers 030, Shimadzu, Kyoto, Japan) for desiccation. These specimens were subsequently attached on aluminum SEM stubs and sputter-coated with a ration of (20/80) gold–palladium alloys by means of a sputtering device (Hummer JR, Technics, CA, USA). Finally, the prepared specimens were examined using the Quanta 250 FEG SEM (FEI Company, Eindhoven, The Netherlands) functioning at an accelerating voltage (10 kV) of the electrons and at different magnifications.

3.2.6. Statistical Analysis

The Sigma Plot (Version 12, Systat, San Jose, CA, USA) was employed for the statistical analyses. The data experienced analysis to assess the normal distribution and homogeneity of variance. To evaluate the influence of the bonding agent and the application modalities (MTLA with ABT) on the μTBS to dentinal substrate, a two-way ANOVA was conducted. The BS was separately examined after 24 h and 6 months of storage. Multiple comparisons were performed using Tukey's post hoc test. A significance level of $\alpha = 0.05$ was used for all the analyses.

3.3. Results

3.3.1. Micro-Tensile Bond Strength Testing

Table 10 recapitulates the values attained for the μTBS following aging for 24 h, conferring to the material and the technique applied. According to the two-way ANOVA, both factors tested were significant (adhesive, $p = 0.005$; technique, $p < 0.001$, with an interaction between the factors, $p = 0.005$).

Technique	**CSE**	**OBFL**	**OBU**	**PBU**
A	^{X}19.02 (3.19) ^{a}	^{X}29.66 (5.25) ^{a}	^{X}28.3 (5.02) ^{a}	^{X}26.16 (8.9) ^{a}
APP	^{X}16.86 (2.74) ^{a}	^{XY}11.87 (4.66) ^{b}	^{XY}13.6 (2.25) ^{b}	^{Y}7.34 (2.2) ^{b}
AAP	^{X}17.12 (5.20) ^{a}	^{X}15.25 (2.79) ^{b}	^{X}12.5 (3.73) ^{b}	^{X}10.17 (3.1) ^{b}
AAA	^{X}19.77 (2.98) ^{a}	^{XY}17.16 (6.39) ^{b}	^{X}20.6 (8.73) ^{ab}	^{Y}11.49 (2.8) ^{b}

Different uppercase letters indicate the presence of statistically significant differences for each row ($p < 0.05$). Different lowercase letters indicate the presence of statistically significant differences for each column ($p < 0.05$). Clearfil SE Bond (CSE); OptiBond FL (OBFL); OptiBond Universal (OBU); Prime&Bond Universal (PBU); Single active application (A); triple application, Active–Passive–Passive (APP); triple application, Active–Active–Passive (AAP); triple application, Active–Active–Active (AAA).

Table 10: Mean and standard deviation of the micro-tensile bond strength test to dentin of the different application modalities for the dental adhesive systems at 24 h of aging.

For CSE, there were no significant differences in the dentinal BS within the different techniques used ($p > 0.05$). For OBFL, OBU, and PBU, statistically significant higher values were perceived for the A technique ($p < 0.05$) when compared to the other techniques. Plus, there were no significant differences between the APP, AAP, and AAA techniques ($p > 0.05$) for OBFL and PBU. For OBU, there were no significant differences between the A and AAA techniques ($p > 0.05$).

Regarding the effect of the adhesive system within each technique, for the A and the AAP techniques, there were no significant variations between the different adhesive systems tested ($p > 0.05$). PBU had statistically lower values in comparison to the other adhesive systems when used with the APP and AAA techniques ($p < 0.05$).

Table 11 shows the values acquired for the μTBS to dentin following a period of 6 months of aging according to the material and the technique applied in this study. The results from the two-way ANOVA showed that the factor adhesive was not significant ($p = 0.282$); on the other hand, the factor technique and the interaction between the factors were significant ($p < 0.001$ and $p = 0.005$, respectively).

Technique	CSE	OBFL	OBU	PBU
A	^{X}17.60 (3.75) ^{a}	^{X}13.73 (3.12) ^{a}	^{X}16.71 (6.13) ^{a}	^{X}20.11 (2.95) ^{a}
APP	^{X}7 (3.98) ^{b}	^{X}10.26 (5.8) ^{b}	^{X}6.75 (3.26) ^{b}	^{X}7.51 (3.75) ^{b}
AAP	^{X}10.31 (4.22) ^{b}	^{X}8.38 (1.47) ^{b}	^{X}8.57 (2.46) ^{b}	^{X}6.7 (2.74) ^{b}
AAA	^{Y}10.43 (2.77) ^{b}	^{X}18.03 (5.26) ^{a}	^{Y}9.24 (1.76) ^{b}	^{Y}9.06 (4.24) ^{b}

Different uppercase letters indicate the presence of statistically significant differences for each row ($p < 0.05$). Different lowercase letters indicate the presence of statistically significant differences for each column ($p < 0.05$). Clearfil SE Bond (CSE); OptiBond FL (OBFL); OptiBond Universal (OBU); Prime&Bond Universal (PBU); Single active application (A); triple application, Active–Passive–Passive (APP); triple application, Active–Active–Passive (AAP); triple application, Active–Active–Active (AAA).

Table 11: Mean and standard deviation of the micro-tensile bond strength test to dentin of the different application modalities for the dental adhesive systems at 6 months of aging.

For CSE, OBU, and PBU, the A technique showed significant higher values than the other techniques ($p < 0.01$). For the same adhesives, the differences in the BS values for AAA, AAP, and APP were not significant ($p > 0.05$). For OBFL, the highest values were observed for the A and the AAA techniques, which were statistically higher than AAP and APP ($p < 0.001$).

Tukey’s post hoc test displayed significant differences within the AAA technique, where OBFL achieved statistically higher values than the other adhesives ($p < 0.001$). On the other hand, for the rest of the techniques tested, there were no significant differences between the BS values ($p > 0.05$).

Table 12 shows the comparison of the BS values following 24 h and 6 months of aging for each adhesive system and technique tested. CSE showed BS stability only when applied with the A technique ($p = 0.537$). For OBFL, no significant changes in the BS were observed for APP and AAA ($p > 0.05$). For OBU, this behavior (BS stability) was observed only in the AAP technique ($p = 0.08$). Finally, for PBU, all the techniques used resulted in BS stability over time ($p > 0.05$).

Technique/Adhesive	Aging	
CSE	24 h	6 months
A	19.02 (3.19) ^{X}	17.60 (3.75) ^{X}
APP	16.86 (2.74) ^{X}	7 (3.98) ^{Y}
AAP	17.12 (5.20) ^{X}	10.31 (4.22) ^{Y}
AAA	19.77 (2.98) ^{X}	10.43 (2.77) ^{Y}
OBFL	24 h	6 months

A	29.66 (5.25) ^{X}	13.73 (3.12) ^{Y}
APP	11.87 (4.66) ^{X}	10.26 (5.8) ^{X}
AAP	15.25 (2.79) ^{X}	8.38 (1.47) ^{Y}
AAA	17.16 (6.39) ^{X}	18.03 (5.26) ^{X}
OBU	24 h	6 months
A	28.3 (5.02) ^{X}	16.71 (6.13) ^{Y}
APP	13.6 (2.25) ^{X}	6.75 (3.26) ^{Y}
AAP	12.5 (3.73) ^{X}	8.57 (2.46) ^{X}
AAA	20.6 (8.73) ^{X}	9.24 (1.76) ^{Y}
PBU	24 h	6 months
A	26.16 (8.9) ^{X}	20.11 (2.95) ^{X}
APP	7.34 (2.2) ^{X}	7.51 (3.75) ^{X}
AAP	10.17 (3.1) ^{X}	6.7 (2.74) ^{X}
AAA	11.49 (2.8) ^{X}	9.06 (4.24) ^{X}

Different uppercase letters indicate the presence of statistically significant differences between 24 h and 6 months. Clearfil SE Bond (CSE); OptiBond FL (OBFL); OptiBond Universal (OBU); Prime&Bond Universal (PBU); Single active application (A); triple application, Active–Passive–Passive (APP); triple application, Active–Active–Passive (AAP); triple application, Active–Active–Active (AAA).

Table 12: Comparison of the mean and standard deviation of the micro-tensile bond strength test to dentin of the different application modalities for the dental adhesive systems examined at 24 h and 6 months of aging.

3.3.2. Failure Mode Analysis

The numbers of fracture modes are shown in Tables 13–16.

Technique	Material	Aging	Failure Types			
			Adhesive	Mixed	Cohesive Resin	Cohesive Dentin
A	CSE	24 h	14	16	0	0
		6 months	13	15	1	1
APP	CSE	24 h	10	14	3	3
		6 months	17	9	2	2
AAP	CSE	24 h	13	16	1	0
		6 months	17	11	2	0
AAA	CSE	24 h	11	15	2	2
		6 months	16	10	2	2

Clearfil SE Bond (CSE); Single active application (A); triple application, Active–Passive–Passive (APP); triple application, Active–Active–Passive (AAP); triple application, Active–Active–Active (AAA).

Table 13: Failure mode analysis of the Clearfil SE Bond adhesive system tested following the bond strength test.

Technique	Material	Aging	Failure Types			
			Adhesive	Mixed	Cohesive Resin	Cohesive Dentin
A	OBFL	24 h	11	19	0	0
		6 months	16	12	1	1
APP	OBFL	24 h	15	15	0	0
		6 months	16	14	0	0
AAP	OBFL	24 h	13	15	2	0
		6 months	18	12	0	0
		24 h	11	16	2	1

AAA	OBFL	6 months	14	16	0	0

OptiBond FL (OBFL); Single active application (A); triple application, Active–Passive–Passive (APP); triple application, Active–Active–Passive (AAP); triple application, Active–Active–Active (AAA).

Table 14: Failure mode analysis of the OptiBond FL adhesive system tested following the bond strength test.

Technique	Material	Aging	Failure Types			
			Adhesive	Mixed	Cohesive Resin	Cohesive Dentin
A	OBU	24 h	11	17	1	1
		6 months	18	12	0	0
APP	OBU	24 h	14	16	0	0
		6 months	20	10	0	0
AAP	OBU	24 h	15	15	0	0
		6 months	21	9	0	0
AAA	OBU	24 h	11	13	3	3
		6 months	18	12	0	0

OptiBond Universal (OBU); Single active application (A); triple application, Active–Passive–Passive (APP); triple application, Active–Active–Passive (AAP); triple application, Active–Active–Active (AAA).

Table 15: Failure mode analysis of the OptiBond Universal adhesive system tested following the bond strength test.

Technique	Material	Aging	Failure Types			
			Adhesive	Mixed	Cohesive Resin	Cohesive Dentin
A	PBU	24 h	10	20	0	0
		6 months	12	18	0	0
APP	PBU	24 h	15	15	0	0
		6 months	14	15	0	1
AAP	PBU	24 h	14	16	0	0
		6 months	20	9	1	0
AAA	PBU	24 h	14	16	0	0
		6 months	15	14	1	0

Prime&Bond Universal (PBU); Single active application (A); triple application, Active–Passive–Passive (APP); triple application, Active–Active–Passive (AAP); triple application, Active–Active–Active (AAA).

Table 16: Failure mode analysis of the Prime&Bond Universal adhesive system tested following the bond strength test.

The failures were mainly adhesive or mixed fractures in all of the bonding systems evaluated. Higher mixed failures were reported in the specimens with higher BSs when compared to higher adhesive failure in the samples with lower BSs across all adhesive systems and MTLA specimens.

3.3.3. Scanning Electron Microscopy

Representative SEM micrographs of the dentinal-resin interface of the different adhesive systems tested are presented in Fig. 35. Differences in the thickness of the adhesive layer and RTs formation can be observed among the different techniques tested. Thicker adhesive layers were witnessed in the APP, AAP, and AAA groups compared to the A group. A higher number of RTs was observed in the AAA groups. Only the OBFL adhesive showed the formation of RTs in all modalities tested.

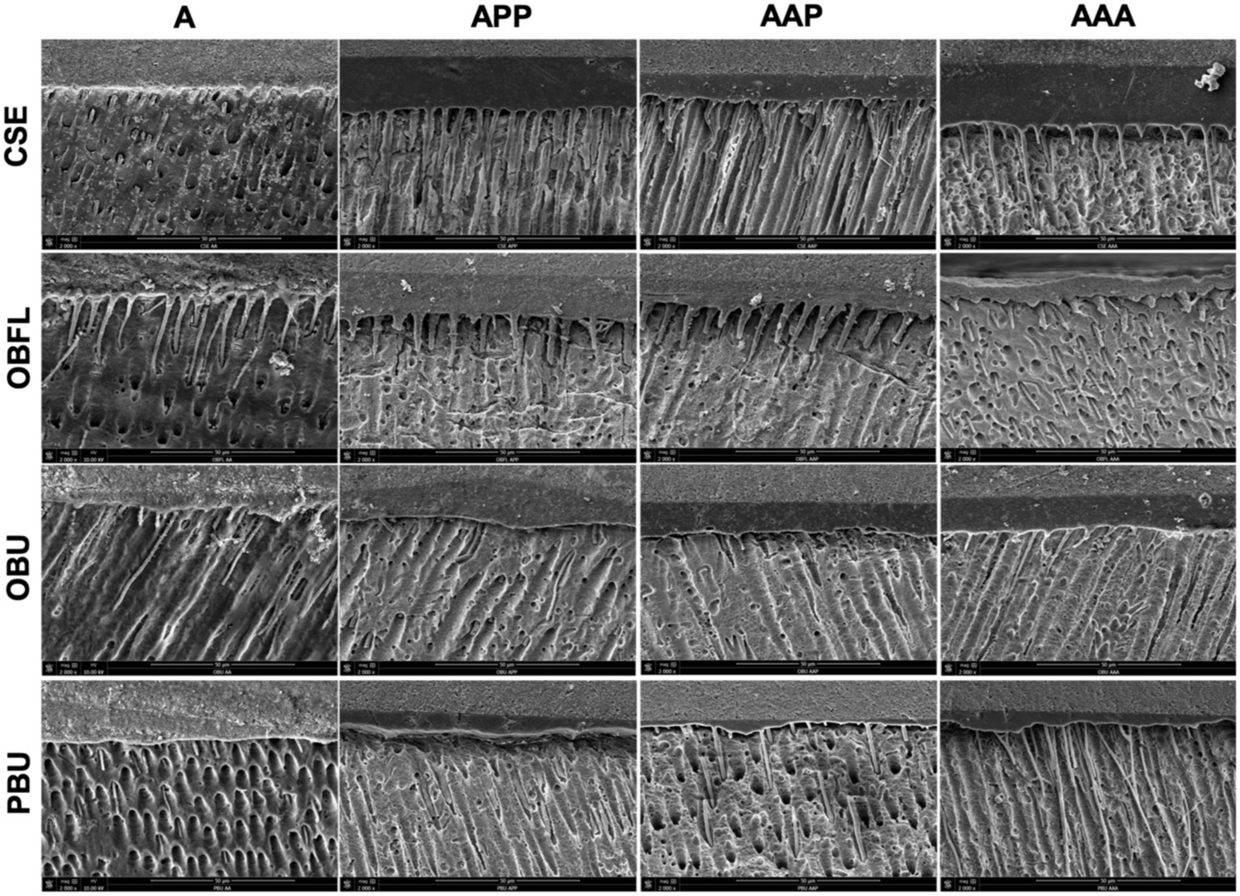


Figure 35: Scanning electron microscopy images (×2000 magnifications) determine the adhesive layer and resin tag infiltration of the distinctive dental adhesive systems examined with the modified triple-layer application and the control group. Clearfil SE Bond (CSE); OptiBond FL (OBFL); OptiBond Universal (OBU); Prime&Bond Universal (PBU); Single active application (A); triple application, Active–Passive–Passive (APP); triple application, Active–Active–Passive (AAP); triple application, Active–Active–Active (AAA).

3.4. Discussion

Adhesive dentistry became a trend decades ago, and with this rise in popularity, multiple techniques were developed in an attempt to reduce the sensitivity of adhesives [12]. In particular, MLA was proposed to enhance the monomer infiltration of adhesives to dentin [13]. Yet, the variation of the application of each layer, either in an active or a passive manner, was not previously assessed in the literature for triple-layer applications. The result of the present investigation led to the partial rejection of the null hypothesis since the dentinal bonding properties of some contemporary adhesives tested were affected by the effect of MTLA.

Among all tested adhesives, at 24 h, only CSE did not display any significant variances in the BS within the different techniques used ($p > 0.05$). CSE is an SE adhesive, which has a high concentration of acidic monomers inside an aqueous solution. These monomers release H+ ions and etch the dental substrate in synchronization with their diffusion into the substrate [20]. Since a variation in the BS was not observed, the claim that CSE can withstand one coat of application as well as MTLA can be made.

Starting with the second layer, additional benefits for the BS will be negligible, and the outcome will resemble that of the one-layer application. To clarify, when a second coat of adhesive was applied to the dentin, a large number of H+ ions were liberated to permit the etching agent to operate for a longer duration [21]. However, previous reports [22,23] found that an increased SE system action time through a surge in H+ ions did not develop an observable effect on the BS, which supports the outcomes of this study. Thus, no difference was discovered between the tested groups (A, APP, AAP, and AAA), although there was a slight decline in the BS only when the PA was incorporated between layers (APP and AAP). So, in theory, the amount of H+ ions does not have an effect on the immediate BS of the CSE bond regardless of the number of layers applied.

For OBFL, OBU, and PBU, the values observed for the A technique were higher in a significant manner ($p < 0.05$). On the other hand, there were no significant differences between the APP, AAP, and AAA techniques ($p > 0.05$) for OBFL and PBU. For OBU, there were not any statistically differences between the A and AAA techniques ($p > 0.05$). With that said, one coat of each of these adhesives (OBFL, OBU, and PBU) is enough to effectively produce an HL enclosed by an adhesive coat that will offer appropriate pairing to successively applied resin composite, although a drop in the dentin BS can occur when two or more coatings are used. Also, increasing the number of layers could result in deficiencies in the application technique; for example, the clinician might not provide sufficient drying time for the primers or the adhesives. Further, hydrophilic components inside the adhesives may accumulate between layers and lead to adhesive degradation [16].

Regarding the effect of the adhesive system within each technique, there were no significant differences amongst the different adhesive systems ($p > 0.05$) for the A and AAP techniques. PBU had statistically significant lower values in comparison with the other adhesive systems when used with the APP and AAA techniques ($p < 0.05$). All things considered, the PBU application was affected when the second layer and third layer were similar, for example, when AA is used twice after the first ABT, with the same being said for true passive applications in a row at the second and third layer. With APP, the BS was at its lowest values. This could be clearly related to the adhesive itself, which might not be able to withstand MTLA. UAs raise the capability for demineralization with the substrates by taking up their water content, and whenever the water level increases in the adhesive, the polymerization of the adhesive coat applied to the substrate becomes less sufficient. This means that each time a layer of PBU is added, the amount of water surges [3]. Plus, in this study, photopolymerization was performed only at the end of the MTLA, which can be attributed to the high sensitivity of PBU to these techniques after 24 h. The recommended application time for PBU is 20 s with a slight agitation [3]. This improves monomer infiltration into the dentinal substrate as well as solvent evaporation. This could justify the reduced benefit of further layers (MTLA in this case). Another factor for the results of PBU is an insufficient air-drying time, which is recommended to be around 15 s to 30 s for some UAs. Strong air-drying enhances the mechanical characteristics and solvent evaporation, which leads to a stronger adhesive layer at the dentinal interface [13]. Clinicians are recommended to eliminate any remaining solvent to reach the optimal bond performance of the cured adhesive, as well as to carefully choose the material and solvent types. Seemingly, for PBU, the clinician should apply only one coat in an active mode.

After 6 months, for CSE, OBU, and PBU, the A technique showed statistically higher values than the other techniques ($p < 0.01$). For the same adhesives, the differences in the BS values for AAA, AAP, and APP were not significant ($p > 0.05$). These adhesive systems were applied in SE mode in this study, thus explaining that this strategy did not support the MTLA, which has lower values when compared to a single coat application. SE adhesive systems contain water or hydrophilic resin to enhance monomer penetration into the dentin [24,25], but this hydrophilicity can induce water sorption and an eventual instability of the HL with time [26]. For CSE, the MTLA may not have added benefits on the dentinal BS due to this adhesive having a thicker adhesive layer when applied in only one coat. The relatively thick adhesive layer could scatter the stress distribution at the interface among dentin and resin composites during testing, successively raising the BS of the adhesive and justifying the choice of not adding a second layer [27,28].

Further, the UAs tested in this research were applied in an SE mode, and if some solvents remain after evaporation (OBU = 30-60% acetone, ~5-10% ethanol; PBU = 5-24.5% water, 10-24.5% isopropanol) [16,29], the hydrolysis of resin polymers and the enzymatic degradation of collagen may occur over time [3,30]. The accumulation of solvents between layers in the MTLA is detrimental to these UAs. Another explanation might be that the thick smear layer prevents the active functional monomers from penetrating and interacting with the dentin to create a suitable HL [31]. Accordingly, the poorly dissolved smear layer weakens the adhesive layer. All in all, the bonding agents used in the SE mode in this manuscript (CSE, OBU, and PBU) benefits from a one-layer application after 6 months of water storage.

For OBFL, the highest values were observed for the A and AAA techniques after aging (6 months), which were statistically higher than AAP and APP ($p < 0.001$). OBFL is an ER adhesive with an ability to strongly bond to dentin over long storage times [32]. A previous study stated that the BS was improved through ER adhesives with MLA [33]. This was in agreement with the findings of this study only with AAA for MTLA. The solvent content inside the adhesive and the co-monomer infiltration into dentin are the key players in enhancing the BS if applied properly to the dentin. Plus, incomplete evaporation of the water and ethanol solvents in OBFL can significantly reduce the BS. This can explain why A and AAA resulted in superior BS values compared to the other techniques due to sufficient solvent removal [34]. In addition, this is due to the inclusion of filler in the composition of OBFL and the close attention to the application technique [3,35]. This high filler load inside OBFL strengthens the HL and may serve as a shock absorber [36], which might also clarify its high dentin BSs for both the A and AAA techniques. For OBFL specifically, the manufacturer quotes the following for the primer component: "apply with a light brushing motion for 15 s" [3]. Based on what was established, the inclusion of PA even in one layer of MTLA (APP and AAP) led to a drop in the BS.

The factor adhesive was only significant for the AAA technique, where OBFL achieved statistically higher values than the other adhesives ($p < 0.001$) following 6 months of distilled water storage. On the other hand, for the rest of the techniques tested, there were no significant differences between the BS values ($p > 0.05$). In the general run of things, OBFL was the only adhesive affected by one of the techniques tested in this research. Specifically, the AAA favored OBFL. This is attributable to the fact that ER adhesives offer superior BSs when compared to SE following multiple adhesive coats [37]. A prior examination by Hashimoto et al., [38] noted that four succeeding layers of ER adhesives without the polymerization of each layer strengthen the BS. This was in agreement with the discovery of this research when AAA was used.

After 6 months, all adhesives were unfavorably influenced by a PA. This can be related to the enhanced BS and the value of the adhesion, which is only attainable by the continuous rubbing of OBFL. The agitation of an adhesive maintains the fresh acidic solution in conjunction with the dental substrate, leads to a high rate of monomer infiltration, and promotes solvent evaporation, thereby reinforcing the adhesion to dentin [3,12,39,40]. This perhaps explains the higher adhesion with the A technique for some adhesives. For that reason, no difference was found for the tested adhesive (OBFL) with this technique. Further, repeating the A technique by means of three layers (AAA) could accumulate the benefits of the agitation application only for OBFL. Hardan et al., [12] claimed that ER adhesives were improved by the MLA technique immediately and after long-term storage. Adding to these clarifications, the presence of fillers in OBFL [3,36] with three layers of applications (AAA) might be the reason for this acceptable BS. High filler loads will affect bonding, as they might form clusters and hinder infiltration within the collagen matrix [41]. However, the combination of active agitation with MLA was a good choice for the highly filled OBFL. This explains that this specific technique will perform as a layer reinforced (LR)-MTLA.

So, the combination of ER adhesive, the AAA with continuous rubbing, and the presence of fillers inside the adhesive (OBFL), ameliorates the long-term bond performance to dentin when choosing the MTLA as the application modality.

For the comparison of the BS values at 24 h and 6 months of aging, CSE showed BS stability only when applied with the A technique ($p = 0.537$). A decline in the BS was observed for all of the tested MTLAs. This can be interpreted by the fact that this adhesive system is based on 10-MDP and HEMA [3]. In the case of using the MTLA, the functional monomers inside CSE, which are considered as adhesion promoters, will affect the stability of the bond with time. The hydrophilic characteristic of these monomers, like HEMA, raises the dentinal BS of the adhesives, and some functional monomers such as 10-MDP could bond chemically to Ca [42], while as advocated in the scientific literature, 10-MDP-containing SE adhesives have better bond durability [43]. This was only observed in the current study when the A technique was used. Hence, 10-MDP alone was not the reason for the stability or the decline of the BS. It appears that the impact of HEMA on bond weakening and water sorption is tremendous in a way that negates the positive influence of 10-MDP on the dental substrate when used with MTLA. This confirms the benefit of one-layer application by means of agitation for CSE (A technique), and shows the variation of bond stability between the tested techniques in this study. When multiplying the applied layers, the activity and concentration of these monomers increase, negatively affecting the aged BS outcome. Generally speaking, and according to previous investigations, nano-layering could be affected by agitation, 10-MDP concentration, and the construction of the functional monomers presented in the adhesive [3,7,13].

For OBFL, when comparing the value between 24 h and 6 months, no significant changes in the BS were observed for APP and AAA ($p > 0.05$). Regarding APP, the BS was immediately lower and maintained its low value over time. However, for AAA, the BS was preserved, saving the higher long-term bond performance among all of the tested MTLAs with OBFL. This sheds light on a novel technique for the OBFL with long-term stability. This technique combines the advantages of both MLA and ABT, making it effective for this specific bonding application. Suitably, it can be called the LR-MTLA. Referring to a previous report [44], bonding agents presenting dental etchants, primers, and hydrophobic adhesives in individual bottles with no solvent content in the adhesives are better in respect to adhesion stability, as long as the effect of the hydrophilic mixtures on the level of polymer conversion is absent, with OBFL being an example of this [45]. This could justify why the BS of OBFL did not decrease between 24 h and 6 months in APP and AAA. The decrease in the BS for the A and AAP techniques affirmed that OBFL supports MLA [12], but the condition should be the agitation of all of the layers applied. Additionally, the deterioration of the dentin BS of OBFL is linked to different monomers presented in the formulation of primers like GPDM and HEMA that can influence the features of the polymers obtained, the bonding potential, and the degradation over time [46,47].

For OBU, the stability of the BS was observed only for the AAP technique ($p = 0.08$), which already had low values after 24 h and after 6 months as well. This could be linked to the functional monomer, GPDM, which seems to be sensitive to the technique used in this study. Although GPDM was reported to be adhered to HAp, it was unable to form a monomer-Ca salt that can remain stable with time [48]. Likewise, the bond between GPDM and HAp was shown to be weak, and this was documented in several articles [48,49,50]. HEMA, which is found in OBU, is compatible with the dentinal structure, and its hydrophilicity contributes to the ease of its infiltration into the demineralized substrate, but also makes it vulnerable to water sorption and hydrolysis [51]. Moreover, OBU contains acetone, which can reduce the BS if not sufficiently evaporated [3]. This can explain the low BS values obtained after 6 months.

Finally, for PBU, all of the techniques used resulted in BS stability over time ($p > 0.05$). So, this adhesive can only support one coat (A), since MTLA already had a low BS and stayed that way after 6 months. The stable BS was linked to PENTA [52,53], 10-MDP [54], and methacrylamide [55] monomers inside the composition of this specific bonding. PENTA was proven to be more stable than MDP, where the BS was maintained at the end of the adhesive's shelf-life [53]. It could be theorized that, contrary to 10-MDP monomers, the existence of five vinyl groups inside the chemical structure of PENTA might enhance its resistance to water degradation. Therefore, four vinyl groups will still be present for connection maintenance with the P group following hydrolysis, which enables copolymerization and adhesion to the dentin simultaneously [52,56]. In this respect, PBU maintained its stability. PBU is an adhesive that does not contain HEMA in its formulation, and this particular composition can aid in effectively eliminating water during the air-drying process [3,54]. Additionally, methacrylamide monomers were produced to substitute HEMA in PBU in order to avoid phase separation and reduce water sorption inside the adhesive [30,55].

Following the μTBS analysis, the failure mode was assessed in all of the groups tested in this study. Mostly, the adhesive failures were predominantly adhesive or mixed in all the bonding systems evaluated. The BS test used a load force qualified to pass through the dentin and the resin composite before reaching the adhesive interface, with resulting stress intensity at these locations [57], initiating a relatively higher ratio of mixed failures. Additionally, this declaration may also designate a suitable dentinal hybridization [58]. After aging in distilled water for a period of 6 months, the failure analysis was commonly adhesive. This is related to the aging of an adhesive layer, developing further adhesive fracture compared to the baseline mode of failure (after 24 h) across all adhesive systems and MTLA specimens [59].

The SEM observations denoted, after 24 h, an elevated number of RTs amongst the AAA groups compared to the other techniques where passive applications were applied. When passing from A to AAA, the resin penetration increased, except for OBFL, where the infiltration was higher in all the techniques tested. This could be due to the fact that ABT allows for a superior monomer penetration inside the branches of dentinal tubules [3,12]. Further, this was perhaps because of the removal of the non-penetrated resin plugs inside the tags via the acids and bases used to dissolve the dentin from the resin [60]. Moreover, this might be linked to the statement that the ABT has been proven to increase the interaction among adhesive systems and dentinal substrates, varying the biochemical characteristics of dentin in a positive way, and simplifying the infiltration of the material inside the inter and peritubular region [3,12]. The OBFL adhesive exhibited a unique characteristic in the tests—it consistently generated RTs across all the modalities examined. This behavior can be attributed to the specific etching step that this adhesive necessitates for the bonding process [44]. Previous data supports the notion that this etching step plays a critical role in promoting a deeper penetration of the adhesive into the dentin substrate [61]. This deeper penetration results in longer RTs and the formation of thicker HL [62]. Considering this, regardless of the application modality employed, the use of H_3PO_4 for removing the smear layer and smear plugs led to enhanced adhesive infiltration. This step also facilitated the adhesive's penetration into the dentin tubules, thereby improving both the length and morphology of the RTs [63].

While the adhesive layer's thickness could be perceived as a possible factor influencing the BS, particularly in terms of enhancing stress distribution within the body assembly, there remains an ongoing debate regarding the correlation between the thickness of the adhesive layer and the BS [64]. It was previously stated that the increase in the adhesive layer thickness would efficiently distribute stress at the interface between the composite material and the tooth [11]. Despite this, differences in the composition (solvent agents and fillers) can lead to differences in the results expected, as observed in the present study. Considering this, the exact application of an adhesive system is material-dependent.

Some limitations could be drawn from this research. First of all, only a reduced number of adhesive systems were tested, and it is worth mentioning that a representative from the ER II or SE I adhesive systems is missing. Also, more UAs should be included in future works. In addition to these, a variation in the methodology, in terms of the photopolymerization of each layer, should be tested in the future. Further studies might be accomplished with an accurate, safe, and non-destructive method like micro-computed tomography (micro-CT) instead of SEM. The assessments of the tag density, length, and size, in addition to the thickness of the HL, might be affected by the location of the dentin tubules. Tubule diameters and densities rise from the dentin/enamel junction to the central dentinal area. So, all of the SEM interpretations might be interrelated to the examined anatomical region. Assessments like cytotoxicity tests must be explored in future studies. BS analyses with more aging procedures could be conducted, such as thermocycling, in an attempt to look for extra signs of adhesive degradation at the interface. It should be highlighted that the main cause for the failure of dental restorations is NL formed by a reduced dentin BS. Therefore, additional research should be performed to validate the present preliminary outcomes.

3.5. Conclusions

Based on the findings of this study, the subsequent conclusions can be addressed:

1. The laboratory adhesive properties were mostly material-dependent.
2. For better BS performance, CSE, OBU, and PBU were benefited from the A technique; for OBFL, the use of the AAA technique could be recommended to achieve stability in the adhesive layer.
3. The combination of ABT with an MLA was a good choice for the highly filled OBFL. This explains that the LR-MTLA was considered a novel approach in the field of adhesive dentistry with an acceptable bond stability after 6 months.
4. Clinicians must consider the chemistry and the physical features of each adhesive system in an attempt to determine its ideal performance before applying the MTLA.

3.6. References

1. Reis, A.; Loguercio, A.; Favoreto, M.; Chibinski, A. Some Myths in Dentin Bonding: An Evidence-Based Perspective. *J. Dent. Res.* **2023**, *102*, 376–382.

2. Saikaew, P.; Sattabanasuk, V.; Harnirattisai, C.; Chowdhury, A.F.M.A.; Carvalho, R.; Sano, H. Role of the Smear Layer in Adhesive Dentistry and the Clinical Applications to Improve Bonding Performance. *Jpn. Dent. Sci. Rev.* **2022**, *58*, 59–66.
3. Bourgi, R.; Hardan, L.; Cuevas-Suárez, C.E.; Devoto, W.; Kassis, C.; Kharma, K.; Harouny, R.; Ashi, T.; Mancino, D.; Kharouf, N.; et al. Effectiveness of Different Application Modalities on the Bond Performance of Four Polymeric Adhesive Systems to Dentin. *Polymers* **2023**, *15*, 3924.
4. Hardan, L.; Bourgi, R.; Cuevas-Suárez, C.E.; Zarow, M.; Kharouf, N.; Mancino, D.; Villares, C.F.; Skaba, D.; Lukomska-Szymanska, M. The Bond Strength and Antibacterial Activity of the Universal Dentin Bonding System: A Systematic Review and Meta-Analysis. *Microorganisms* **2021**, *9*, 1230.
5. Cadenaro, M.; Josic, U.; Maravić, T.; Mazzitelli, C.; Marchesi, G.; Mancuso, E.; Breschi, L.; Mazzoni, A. Progress in Dental Adhesive Materials. *J. Dent. Res.* **2023**, *102*, 254–262.
6. Hardan, L.; Daood, U.; Bourgi, R.; Cuevas-Suárez, C.E.; Devoto, W.; Zarow, M.; Jakubowicz, N.; Zamarripa-Calderón, J.E.; Radwanski, M.; Orsini, G.; et al. Effect of Collagen Crosslinkers on Dentin Bond Strength of Adhesive Systems: A Systematic Review and Meta-Analysis. *Cells* **2022**, *11*, 2417.
7. Yoshihara, K.; Yoshida, Y.; Hayakawa, S.; Nagaoka, N.; Irie, M.; Ogawa, T.; Van Landuyt, K.L.; Osaka, A.; Suzuki, K.; Minagi, S. Nanolayering of Phosphoric Acid Ester Monomer on Enamel and Dentin. *Acta Biomater.* **2011**, *7*, 3187–3195.
8. Ito, S.; Tay, F.R.; Hashimoto, M.; Yoshiyama, M.; Saito, T.; Brackett, W.W.; Waller, J.L.; Pashley, D.H. Effects of Multiple Coatings of Two All-in-One Adhesives on Dentin Bonding. *J. Adhes. Dent.* **2005**, *7*, 133–141.
9. Cardoso, M.; de Almeida Neves, A.; Mine, A.; Coutinho, E.; Van Landuyt, K.; De Munck, J.; Van Meerbeek, B. Current Aspects on Bonding Effectiveness and Stability in Adhesive Dentistry. *Aust. Dent. J.* **2011**, *56*, 31–44.
10. Aljifan, M.K.; Alshehri, A.M.; Alharbi, R.M.; Al Alhareth, M.S.; Alharbi, Z.A.; Alamri, S.M.; Alshahrani, N.S.; Alyamani, A.E.; Alzahrani, A.A.; Alqarni, A.A. An Overview of Dentin Conditioning and Its Effect on Bond Strength. *Int. J. Community Med. Public Health* **2023**, *10*, 1.
11. Zheng, L.; Pereira, P.N.; Nakajima, M.; Sano, H.; Tagami, J. Relationship between Adhesive Thickness and Microtensile Bond Strength. *Oper. Dent.* **2001**, *26*, 97–104.
12. Hardan, L.; Bourgi, R.; Cuevas-Suárez, C.E.; Devoto, W.; Zarow, M.; Monteiro, P.; Jakubowicz, N.; Zoghbi, A.E.; Skaba, D.; Mancino, D. Effect of Different Application Modalities on the Bonding Performance of Adhesive Systems to Dentin: A Systematic Review and Meta-Analysis. *Cells* **2023**, *12*, 190.
13. Hardan, L.; Bourgi, R.; Kharouf, N.; Mancino, D.; Zarow, M.; Jakubowicz, N.; Haikel, Y.; Cuevas-Suárez, C.E. Bond Strength of Universal Adhesives to Dentin: A Systematic Review and Meta-Analysis. *Polymers* **2021**, *13*, 814.
14. Chowdhury, A.; Saikaew, P.; Alam, A.; Sun, J.; Carvalho, R.M.; Sano, H. Effects of Double Application of Contemporary Self-Etch Adhesives on Their Bonding Performance to Dentin with Clinically Relevant Smear Layers. *J. Adhes. Dent.* **2019**, *21*, 59–66.
15. Pinto, M.V.; Pires, S.; Marto, C.M.; Amaro, I.; Coelho, A.; Sousa, J.; Ferreira, M.M.; Botelho, M.F.; Carrilho, E.; Abrantes, A.M. Microleakage Study of a Bulk Fill over an Uncured Adhesive System. *J. Compos. Sci.* **2023**, *7*, 40.
16. Al-Nabulsi, M.; Daud, A.; Yiu, C.; Omar, H.; Sauro, S.; Fawzy, A.; Daood, U. Co-Blend Application Mode of Bulk Fill Composite Resin. *Materials* **2019**, *12*, 2504. https://doi.org/10.3390/ma12162504.
17. Zecin-Deren, A.; Sokolowski, J.; Szczesio-Wlodarczyk, A.; Piwonski, I.; Lukomska-Szymanska, M.; Lapinska, B. Multi-Layer Application of Self-Etch and Universal Adhesives and the Effect on Dentin Bond Strength. *Molecules* **2019**, *24*, 345.
18. Armstrong, S.; Breschi, L.; Özcan, M.; Pfefferkorn, F.; Ferrari, M.; Van Meerbeek, B. Academy of Dental Materials Guidance on in Vitro Testing of Dental Composite Bonding Effectiveness to Dentin/Enamel Using Micro-Tensile Bond Strength (μTBS) Approach. *Dent. Mater.* **2017**, *33*, 133–143.
19. Kharouf, N.; Arntz, Y.; Eid, A.; Zghal, J.; Sauro, S.; Haikel, Y.; Mancino, D. Physicochemical and Antibacterial Properties of Novel, Premixed Calcium Silicate-Based Sealer Compared to Powder–Liquid Bioceramic Sealer. *J. Clin. Med.* **2020**, *9*, 3096.
20. Al-Abd Al, M.A.F.; Al-Badr, R.J.; Abbas, M.S. Modern Adhesive Dentistry: A Review of Literatures. *Med. J. Ahl Al-Bayt Univ.* **2023**, *2*, 6–13.
21. Rocha Gomes Torres, C.; Barcellos, D.C.; Pucci, C.R.; de Morais Gouvêa Lima, G.; Rodrigues, C.M.; Siviero, M. Influence of Methods of Application of Self-Etching Adhesive Systems on Adhesive Bond Strength to Enamel. *J. Adhes. Dent.* **2009**, *11*, 279–286.
22. Kumagai, R.Y.; Takagaki, T.; Sato, T.; Nikaido, T.; Giannini, M.; Reis, A.; Tagami, J. Resin Cement/Enamel Interface: A Morphological Evaluation of the Acid-Base Resistant Zone, Enamel Etching Pattern, and Effect of Thermocycling on the Microshear Bond Strength. *J. Adhes. Dent.* **2023**, *25*, 71–78.

23. Itou, K.; Torii, Y.; Takimura, T.; Chikami, K.; Ishikawa, K.; Suzuki, K. Effect of Priming Time on Tensile Bond Strength to Bovine Teeth and Morphologic Structure of Interfaces Created by Self-Etching Primers. *Int. J. Prosthodont.* **2001**, *14*, 225–230.
24. Van Meerbeek, B.; Yoshihara, K.; Yoshida, Y.; Mine, A.J.; De Munck, J.; Van Landuyt, K.L. State of the art of self-etch adhesives. *Dent. Mater*. **2011**, *27*, 17-28.
25. Maciel, K.; Carvalho, R.; Ringle, R.; Preston, C.; Russell, C.; Pashley, D.H. The Effects of Acetone, Ethanol, HEMA, and Air on the Stiffness of Human Decalcified Dentin Matrix. *J. Dent. Res.* **1996**, *75*, 1851–1858.
26. Frankenberger, R.; Pashley, D.H.; Reich, S.M.; Lohbauer, U.; Petschelt, A.; Tay, F.R. Characterisation of Resin–Dentine Interfaces by Compressive Cyclic Loading. *Biomaterials* **2005**, *26*, 2043–2052.
27. Erhardt, M.C.; Osorio, R.; Pisani-Proenca, J.; Aguilera, F.S.; Osorio, E.; Breschi, L.; Toledano, M. Effect of Double Layering and Prolonged Application Time on MTBS of Water/Ethanol-Based Self-Etch Adhesives to Dentin. *Oper. Dent.* **2009**, *34*, 571–577.
28. Fujiwara, S.; Takamizawa, T.; Barkmeier, W.W.; Tsujimoto, A.; Imai, A.; Watanabe, H.; Erickson, R.L.; Latta, M.A.; Nakatsuka, T.; Miyazaki, M. Effect of Double-Layer Application on Bond Quality of Adhesive Systems. *J. Mech. Behav. Biomed. Mater.* **2018**, *77*, 501–509.
29. Lapinska, B.; Konieczka, M.; Zarzycka, B.; Sokolowski, K.; Grzegorczyk, J.; Lukomska-Szymanska, M. Flow Cytometry Analysis of Antibacterial Effects of Universal Dentin Bonding Agents on Streptococcus Mutans. *Molecules* **2019**, *24*, 532–532. https://doi.org/10.3390/molecules24030532.
30. Hardan, L.; Orsini, G.; Bourgi, R.; Cuevas-Suárez, C.E.; Nicastro, M.; Lazarescu, F.; Filtchev, D.; Cornejo-Ríos, E.; Zamarripa-Calderón, J.E.; Sokolowski, K. Effect of Active Bonding Application after Selective Dentin Etching on the Immediate and Long-Term Bond Strength of Two Universal Adhesives to Dentin. *Polymers* **2022**, *14*, 1129.
31. Belli, R.; Sartori, N.; Dalmagro Peruchi, L.; Coutinho Guimarães, J.; Cardoso Vieira, L.C.; Narciso Baratieri, L.; Monteiro, S., Jr. Effect of Multiple Coats of Ultra-Mild All-in-One Adhesives on Bond Strength to Dentin Covered with Two Different Smear Layer Thicknesses. *J. Adhes. Dent.* **2011**, *13*, 507.
32. Fontes, S.T.; Cubas, G.B.; Flores, J.B.; Montemezzo, M.L.; Pinto, M.B.; Piva, E. Resin-dentin bond strength of 10 contemporary etch-and-rinse adhesive systems after one year of water storage. *General Dentistry* **2010**, *58*, 257-261.
33. Chowdhury, A.F.M.A.; Islam, R.; Alam, A.; Matsumoto, M.; Yamauti, M.; Carvalho, R.M.; Sano, H. Variable Smear Layer and Adhesive Application: The Pursuit of Clinical Relevance in Bond Strength Testing. *Int. J. Mol. Sci.* **2019**, *20*, 5381. https://doi.org/10.3390/ijms20215381.
34. Schärer, B.M.; Peutzfeldt, A. Impact of Adhesive Application Errors on Dentin Bond Strength of Resin Composite. *Biomater. Investig. Dent.* **2022**, *9*, 101–109.
35. Kasraei, S.; Atai, M.; Khamverdi, Z.; Nejad, S.K. The Effect of Nanofiller Addition to an Experimental Dentin Adhesive on Microtensile Bond Strength to Human Dentin. *Front. Dent.* **2009**, *6*, 36–41.
36. Peumans, M.; De Munck, J.; Van Landuyt, K.L.; Poitevin, A.; Lambrechts, P.; Van Meerbeek, B. A 13-Year Clinical Evaluation of Two Three-Step Etch-and-Rinse Adhesives in Non-Carious Class-V Lesions. *Clin. Oral Investig.* **2012**, *16*, 129–137.
37. Mandava, D.; Ajitha, P.; Narayanan, L.L. Comparative Evaluation of Tensile Bond Strengths of Total-Etch Adhesives and Self-Etch Adhesives with Single and Multiple Consecutive Applications: An in Vitro Study. *J. Conserv. Dent. JCD* **2009**, *12*, 55.
38. Hashimoto, M.; Sano, H.; Yoshida, E.; Hori, M.; Kaga, M.; Oguchi, H.; Pashley, D.H. Effects of Multiple Adhesive Coatings on Dentin Bonding. *Oper. Dent.* **2004**, *29*, 416–423.
39. Dal-Bianco, K.; Pellizzaro, A.; Patzlaft, R.; de Oliveira Bauer, J.R.; Loguercio, A.D.; Reis, A. Effects of Moisture Degree and Rubbing Action on the Immediate Resin–Dentin Bond Strength. *Dent. Mater.* **2006**, *22*, 1150–1156.
40. Bowen, R.L. Adhesive bonding of various materials to hard tooth tissues. III. Bonding to dentin improved by pretreatment and the use of surface-active comonomer. *J. Dent. Res*. **1965**, *44*, 903-905.
41. Sofan, E.; Sofan, A.; Palaia, G.; Tenore, G.; Romeo, U.; Migliau, G. Classification review of dental adhesive systems: From the IV generation to the universal type. *Ann. Stomatol.* (Roma) **2017**, *8*, 1-17. doi:10.11138/ads/2017.8.1.001.
42. Pimentel de Oliveira, R.; de Paula, B.L.; Ribeiro, M.E.; Alves, E.; Costi, H.T.; Silva, C. Evaluation of the Bond Strength of Self-Etching Adhesive Systems Containing HEMA and 10-MDP Monomers: Bond Strength of Adhesives Containing HEMA and 10-MDP. *Int. J. Dent.* **2022**, *2022*, 5756649.
43. Fukegawa, D.; Hayakawa, S.; Yoshida, Y.; Suzuki, K.; Osaka, A.; Van Meerbeek, B. Chemical Interaction of Phosphoric Acid Ester with Hydroxyapatite. *J. Dent. Res.* **2006**, *85*, 941–944.
44. Pashley, D.H.; Tay, F.R.; Breschi, L.; Tjäderhane, L.; Carvalho, R.M.; Carrilho, M.; Tezvergil-Mutluay, A. State of the Art Etch-and-Rinse Adhesives. *Dent. Mater.* **2011**, *27*, 1–16.
45. Moura, S.K.; Lemos, L.V.F.M.; Myszkovisk, S.; Provenzano, M.G.A.; Balducci, I.; Myaki, S.I. Bonding Durability of Dental Sealants to Deciduous and Permanent Teeth. *Braz. J. Oral Sci.* **2014**, *13*, 198–202.

46. Azad, E.; Atai, M.; Zandi, M.; Shokrollahi, P.; Solhi, L. Structure–Properties Relationships in Dental Adhesives: Effect of Initiator, Matrix Monomer Structure, and Nano-Filler Incorporation. *Dent. Mater.* **2018**, *34*, 1263–1270. https://doi.org/10.1016/j.dental.2018.05.013.
47. Silva E Souza Junior, M.H.; Carneiro, K.G.K.; Lobato, M.F.; Rodrigues Silva E Souza, P.d.A.; de Goes, M.F.; Silva e Souza, M.H.J.; Carneiro, K.G.K.; Lobato, M.F.; Silva e Souza, P.d.A.R.; de Goes, M.F. Adhesive Systems: Important Aspects Related to Their Composition and Clinical Use. *J. Appl. Oral Sci.* **2010**, *18*, 207–214.
48. Yoshihara, K.; Nagaoka, N.; Hayakawa, S.; Okihara, T.; Yoshida, Y.; Van Meerbeek, B. Chemical Interaction of Glycero-Phosphate Dimethacrylate (GPDM) with Hydroxyapatite and Dentin. *Dent. Mater.* **2018**, *34*, 1072–1081.
49. Ahmed, M.H.; Yao, C.; Van Landuyt, K.; Peumans, M.; Van Meerbeek, B. Extra Bonding Layer Compensates Universal Adhesive's Thin Film Thickness. *J. Adhes. Dent.* **2020**, *22*, 483–501.
50. Wang, R.; Shi, Y.; Li, T.; Pan, Y.; Cui, Y.; Xia, W. Adhesive Interfacial Characteristics and the Related Bonding Performance of Four Self-Etching Adhesives with Different Functional Monomers Applied to Dentin. *J. Dent.* **2017**, *62*, 72–80.
51. Ahmed, M.; Yoshihara, K.; Yao, C.; Okazaki, Y.; Van Landuyt, K.; Peumans, M.; Van Meerbeek, B. Multiparameter Evaluation of Acrylamide HEMA Alternative Monomers in 2-Step Adhesives. *Dent. Mater.* **2021**, *37*, 30–47.
52. Cuevas-Suárez, C.E.; Ramos, T.S.; Rodrigues, S.B.; Collares, F.M.; Zanchi, C.H.; Lund, R.G.; da Silva, A.F.; Piva, E. Impact of Shelf-Life Simulation on Bonding Performance of Universal Adhesive Systems. *Dent. Mater.* **2019**, *35*, e204–e219.
53. Iliev, G.; Hardan, L.; Kassis, C.; Bourgi, R.; Cuevas-Suárez, C.E.; Lukomska-Szymanska, M.; Mancino, D.; Haikel, Y.; Kharouf, N. Shelf Life and Storage Conditions of Universal Adhesives: A Literature Review. *Polymers* **2021**, *13*, 2708.
54. Bourgi, R.; Daood, U.; Bijle, M.N.; Fawzy, A.; Ghaleb, M.; Hardan, L. Reinforced Universal Adhesive by Ribose Crosslinker: A Novel Strategy in Adhesive Dentistry. *Polymers* **2021**, *13*, 704.
55. Saeed, N.A.; Tichy, A.; Kuno, Y.; Hosaka, K.; Tagami, J.; Nakajima, M. Effect of Surface Moisture on Bur-Cut Dentin on Bonding of HEMA-Free and HEMA-Containing Universal Adhesives with or without Methacrylamide Monomer. *J. Adhes. Dent.* **2021**, *23*, 327–334.
56. Teshima, I. Degradation of 10-Methacryloyloxydecyl Dihydrogen Phosphate. *J. Dent. Res.* **2010**, *89*, 1281–1286. https://doi.org/10.1177/0022034510379018.
57. El Zohairy, A.; De Gee, A.; De Jager, N.; Van Ruijven, L.; Feilzer, A. The Influence of Specimen Attachment and Dimension on Microtensile Strength. *J. Dent. Res.* **2004**, *83*, 420–424.
58. Münchow, E.A.; Bossardi, M.; Priebe, T.C.; Valente, L.L.; Zanchi, C.H.; Ogliari, F.A.; Piva, E. Microtensile versus Microshear Bond Strength between Dental Adhesives and the Dentin Substrate. *Int. J. Adhes. Adhes.* **2013**, *46*, 95–99. https://doi.org/10.1016/j.ijadhadh.2013.06.005.
59. Irmak, Ö.; Yaman, B.C.; Orhan, E.O.; Ozer, F.; Blatz, M.B. Effect of Rubbing Force Magnitude on Bond Strength of Universal Adhesives Applied in Self-Etch Mode. *Dent. Mater. J.* **2018**, *37*, 139–145.
60. Maciel Pires, P.; Dávila-Sánchez, A.; Faus-Matoses, V.; Nuñez Martí, J.M.; Lo Muzio, L.; Sauro, S. Bonding Performance and Ultramorphology of the Resin-Dentine Interface of Contemporary Universal Adhesives. *Clin. Oral Investig.* **2022**, *26*, 4391–4405.
61. Langer, A.; Ilie, N. Dentin Infiltration Ability of Different Classes of Adhesive Systems. *Clin. Oral Investig.* **2013**, *17*, 205–216.
62. Oliveira, S.S.; Pugach, M.K.; Hilton, J.F.; Watanabe, L.G.; Marshall, S.J.; Marshall Jr, G.W. The Influence of the Dentin Smear Layer on Adhesion: A Self-Etching Primer vs. a Total-Etch System. *Dent. Mater.* **2003**, *19*, 758–767.
63. Shinchi, M.; Soma, K.; Nakabayashi, N. The Effect of Phosphoric Acid Concentration on Resin Tag Length and Bond Strength of a Photo-Cured Resin to Acid-Etched Enamel. *Dent. Mater.* **2000**, *16*, 324–329.
64. Kharouf, N.; Ashi, T.; Eid, A.; Maguina, L.; Zghal, J.; Sekayan, N.; Bourgi, R.; Hardan, L.; Sauro, S.; Haikel, Y. Does Adhesive Layer Thickness and Tag Length Influence Short/Long-Term Bond Strength of Universal Adhesive Systems? An in-Vitro Study. *Appl. Sci.* **2021**, *11*, 2635.

3.7. Publication of Chapter III

Journal of
Functional
Biomaterials

MDPI

Article

Effect of Modified Triple-Layer Application on the Bond Strength of Different Dental Adhesive Systems to Dentin

Rim Bourgi [1,2,*], Naji Kharouf [2,3,*], Carlos Enrique Cuevas-Suárez [4], Monika Lukomska-Szymańska [5], Walter Devoto [6], Cynthia Kassis [1], Omar Hasbini [7], Davide Mancino [2,3,8], Youssef Haikel [2,3,8,†] and Louis Hardan [1,†]

[1] Department of Restorative Dentistry, School of Dentistry, Saint-Joseph University, Beirut 1107 2180, Lebanon; cynthia.kassis@usj.edu.lb (C.K.); louis.hardan@usj.edu.lb (L.H.)
[2] Department of Biomaterials and Bioengineering, INSERM UMR_S 1121, University of Strasbourg, 67000 Strasbourg, France; mancino@unistra.fr (D.M.); youssef.haikel@unistra.fr (Y.H.)
[3] Department of Endodontics and Conservative Dentistry, Faculty of Dental Medicine, University of Strasbourg, 67000 Strasbourg, France
[4] Dental Materials Laboratory, Academic Area of Dentistry, Autonomous University of Hidalgo State, San Agustín Tlaxiaca 42160, Mexico; cecuevas@uaeh.edu.mx
[5] Department of General Dentistry, Medical University of Lodz, 92-213 Lodz, Poland; monika.lukomska-szymanska@umed.lodz.pl
[6] Independent Researcher, 16030 Sestri Levante, Italy; walter@walterdevoto.com
[7] Department of Prosthetic Dentistry, School of Dentistry, Saint-Joseph University, Beirut 1107 2180, Lebanon; omar.hasbini@net.usj.edu.lb
[8] Pôle de Médecine et Chirurgie Bucco-Dentaire, Hôpital Civil, Hôpitaux Universitaire de Strasbourg, 67000 Strasbourg, France
* Correspondence: rim.bourgi@net.usj.edu.lb (R.B.); dentistenajikharouf@gmail.com (N.K.); Tel.: +33-66752-2841 (N.K.); +961-71455529 (R.B.)
† These authors contributed equally to this work.

Abstract: The goal of this article was to assess the effect of modified triple-layer application (MTLA) in conjunction with the active bonding technique on the bond strength of four adhesive systems to dentinal substrate. The adhesives tested were Prime&Bond Universal (PBU), OptiBond Universal (OBU), OptiBond FL (OBFL), and Clearfil SE (CSE). The adhesives were applied according to the following strategies: single active application (A) and triple adhesive layer application including Active–Passive–Passive (APP); AAP; and AAA. The micro-tensile bond strength test was evaluated following 24 h or 6 months of storage. The composite–dentin interface morphology was investigated using scanning electron microscopy. The data were statistically analyzed with a significance level of $\alpha = 0.05$. At 24 h of aging, all of the factors tested were not significant ($p > 0.05$) for CSE. For OBFL, OBU, and PBU, statistically higher values were observed for the A technique ($p < 0.05$). Plus, there were no significant variances between the APP, AAP, and AAA techniques ($p > 0.05$) for OBFL and PBU. However, for OBU, there were no significant differences between the A and AAA techniques ($p > 0.05$). After 6 months of aging, the A technique showed statistically higher values when compared to the other techniques ($p < 0.01$), except for OBFL, where the A and AAA techniques showed promising outcomes. When comparing the bond strength values of 24 h and 6 months, only for PBU, all of the techniques used resulted in bond strength stability over time ($p > 0.05$). Thicker adhesive layers were observed when MTLA was applied. Only the OBFL adhesive showed the formation of resin tags in all of the modalities tested. The bonding performances of the different application techniques used were material-dependent.

Keywords: active application; aging; bond strength; etch-and-rinse adhesives; self-etch adhesives; universal adhesives

check for updates

Citation: Bourgi, R.; Kharouf, N.; Cuevas-Suárez, C.E.; Lukomska-Szymańska, M.; Devoto, W.; Kassis, C.; Hasbini, O.; Mancino, D.; Haikel, Y.; Hardan, L. Effect of Modified Triple-Layer Application on the Bond Strength of Different Dental Adhesive Systems to Dentin. *J. Funct. Biomater.* **2023**, *14*, 522. https://doi.org/10.3390/jfb14100522

Academic Editor: Conrado Aparicio

Received: 20 September 2023
Revised: 10 October 2023
Accepted: 12 October 2023
Published: 17 October 2023

Chapter IV: Protocols for the Air-dry Temperature

4.1. Introduction

The backstory of adhesive systems has resulted in a significant improvement in the bonding procedure, allowing for simultaneous demineralization and resin penetration into the hard-dental tissues [1]. Presently, contemporary dental adhesives are primarily categorized into two main groups, providing clinicians with the option to choose between ER or SE adhesives [2]. The acidic monomers in the SE dental adhesives demineralize dentin in the same way that an etchant/conditioner used in the ER dental adhesives does [3]. As perhaps the most recent generation of bonding agents, UAs have been developed with the goal of minimizing operational difficulties. In addition, these systems optimize BS and are capable of connecting to a variety of substances [4].

The term "adhesive system" refers to a material that contains the key components agents (etchant, primer, and bond) in different combinations [5]. Irrespective of their classification, dental adhesives consist of hydrophobic and hydrophilic methacrylate monomers, along with photo-initiators, co-initiator systems, and volatile solvents. Co-polymers including polyacrylic acid, fillers, and silane molecules are also used in the most modern UAs. Solvents, being a crucial component of adhesive systems, play a vital role in achieving optimal bonding to dental substrates [2]. Ethanol, acetone, and water are the frequently used solvents inside adhesives, and up to 80% of solvents in weight were included inside the composition of commercial dental adhesives [6]. Some adhesive systems (particularly SE adhesives) contain more than one solvent (for example, ethanol and water). Tert-butanol is a solvent that has been lately incorporated into commercial dental adhesives. While previous studies have shown promising results with alternative solvents like tetrahydrofuran and dimethyl sulfoxide [7,8], they have not yet been utilized in commercial resin adhesives.

Solvents serve as a route for transporting co-monomer blends and initiators to the dental substrate. They dilute the monomers with a relative viscosity, aiding in their penetration and spreading into the dentin structure [9]. Consequently, an adequate ratio of solvents and monomer must be considered necessary for obtaining a high dentinal BS. Any extra solvent within the bonded interface should be evaporated by air-drying [10]. Otherwise, several detrimental consequences could be seen, such as the obstruction of the polymerization of resin monomers, facilitating the degradation of resin-dentin-bonded interfaces, as well as preventing the penetration of resin into the demineralized dentin [11]. All in all, voids within the interface of an adhesive are created, thus decreasing the BS [12]. Increasing solvent content not only dilutes the co-monomer mix but also reduces the concentration of the photo-initiator. This leads to a decreased conversion of resin monomers [11].

The evaporation of solvents from resin blends can be attained either by permitting an evaporation period between adhesive application and photopolymerization or by air-drying by means of a triple syringe. By doing so, several factors influence solvent evaporation, including the type of solvent and co-monomer, operator skill, syringe-to-tooth distance, and air temperature [9,11]. Various methods have been proposed to improve solvent evaporation from dental adhesives, including prolonging adhesive application time, applying multiple adhesive layers, extending adhesive polymerization, and employing active adhesive application techniques. Additionally, some efforts have made in using a warm air stream to facilitate solvent evaporation [13].

High air temperatures might activate molecules for better monomer and adhesive polymerization, which might reduce the dentin collagen matrix degradation [9]. Previously, it was demonstrated that a longer time of warm air evaporation with 38 °C helps in solvent evaporation with an increase in dentin BS [14]. Particularly, when using an air temperature of 60 °C, an increase of around 20% in the resin-dentin bonds could be detected [12]. This might be attributed to the heat from the warm air, which raises the kinetic energy of solvent molecules, facilitating the vaporization of the residual solvent and water [13]. Prior investigations have explored warm air temperatures ranging from 37 °C to 80 °C, indicating the need for determining the ideal temperature for warm air blowing [9,10,12,13]. Warm air temperatures between 40 °C and 60 °C were found to be effective for enhancing solvent evaporation. Nonetheless, the 60 °C temperature was better for stable BS and minimized bond breakdown [13].

To the best of the authors' knowledge, specific devices for delivering warm air for dental use are scarce, so a prototype of therapeutically relevant warm air blowing was built and tested in this work. The aim of this current research was to test whether the use of different air temperatures (20 °C, 40 °C, and 60 °C) for solvent evaporation improves the performance of four adhesive systems to dentin. For this purpose, a prototype device for warm air delivery was developed. Based on the null hypothesis, variations in air temperatures for solvent evaporation were presumed to have no impact on the BS or morphological properties of various adhesive systems to dentin.

4.2. Materials and Methods

4.2.1. Tooth Selection

After receiving approval from the ethical committee of the dental faculty at the Saint-Joseph University of Beirut, Lebanon (FMD-221; file number: #USJ-2022-140), this study was conducted in accordance with the guidelines outlined in the approved protocol.

In addition, the simple randomization procedure utilized a computer-generated random sequence from www.randomizer.org (1 March 2023) to ensure an unbiased and equitable allocation of teeth, thus improving internal validity and mitigating selection bias.

In this respect, sixty (n = 60) non-carious human molar teeth were collected and randomly used. All teeth were cleaned by means of an ultrasonic scaler and polished in a rubber cup attached to a low-speed motor (MotorTurbo & E-ASP1, Eighteeth, Changzhou, China). Then, the teeth were stored in a solution of 0.2% sodium azide at 4 °C after they had been cleaned and polished [15]. The teeth selected for the current study were recently extracted for orthodontic or periodontal reasons and were free of caries, abrasion facets, cracks, damage due to extraction, and fluorosis.

4.2.2. Dentin Specimen Preparation

After mounting the teeth in gypsum blocks, the occlusal third of the crowns was removed using an orthodontic grinder (Essencedental, Araraquara, SP, Brazil). Subsequently, a consistent smear layer was created on all mid-coronal dentin specimens by sanding with a P320 SiC for 1 min under running water. The surfaces were then rinsed with distilled water for 30 s before the application of the adhesive and resin composite. Plus, by using a stereomicroscope (Stereo-zoom S8, Leica, Heidelberg, Germany), the exposed dentinal surfaces were assessed for the absence of enamel.

4.2.3. Bonding Procedures

Three groups based on the air-drying temperature were used: solvent evaporation was achieved with either of warm (40 °C), (60 °C), and cold air as control group (20 °C) for 10 s at a distance of 5 cm. A digital thermostat was used to verify the temperature degree and its consistency throughout the blowing time. In all three cases, the air stream was generated by means of a device for delivering warm or cold air. The air stream had a speed of 5.50 m/s, with an air flow rate of 0.0138 m^3/s. The device is a prototype that was manufactured and tested according to ISO standards. This prototype employs pressure to propel dry air through a tube. The swirling system's pressure causes air molecules to agitate, generating heat that warms the air gently as it flows out from the tip orifice.

The number of teeth per group (n = 5/air temperature) was estimated based on a previous study that evaluated the effect of warm air application for solvent evaporation on the BS to dentin in a comparative study design [16], an 8.8 minimum detectable difference in means, a 2.9 SD, a power of 0.8, and $\alpha = 0.05$. The specimen preparation protocol is schematically described in Fig. 36.

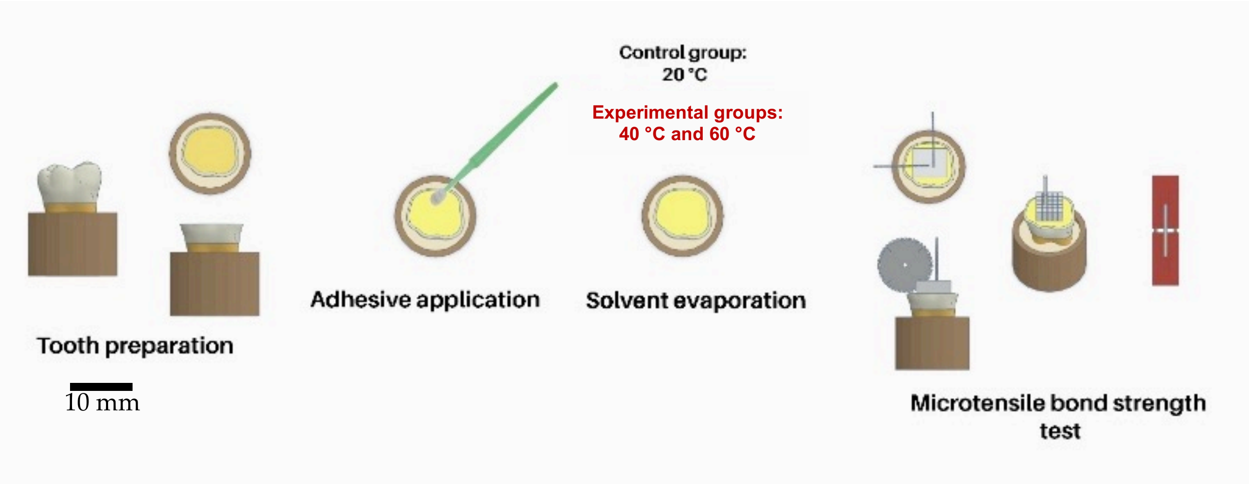


Figure 36: Specimen preparation protocol.

Four different adhesive systems based on different solvents were used in this research as follows: two UAs (Water-isopropanol-based adhesive, the PBU (Dentsply DeTrey GmbH, Konstanz, Germany); Acetone-ethanol-based adhesive, the OBU (Kerr Co, Orange, CA, USA)); one ER III adhesive system based on water-ethanol, the OBFL (Kerr Co, Orange, CA, USA); and one SE II adhesive system based on water, the CSE (Kuraray Noritake Dental Inc., Tokyo, Japan). Blinding was not applicable. The chemical compositions of the adhesive systems tested in the current study are presented in Table 17.

Adhesive and Manufacturer	Classification of the Material	Main Composition *	Adhesive Application Protocol

PBU (Dentsply DeTrey GmbH, Konstanz, Germany)	**Mild Universal** pH = 2.5	10-MDP, PENTA, isopropanol, water, photo-initiator, bi- and multifunctional acrylate	Using a micro-brush applicator, dispense one drop of PBU to all dentinal surfaces. Avoid pooling. Keep PBU slightly agitated for 20 s. Evaporate solvent with air delivered from the device (cold or warm) for at least 10 s. Light irradiate for 20 s.
OBU (Kerr Co, Orange, CA, USA)	**Universal** pH = 2.5–3.0	Acetone, HEMA, GDMA, ethanol, GPDM	Using a micro-brush applicator, a generous amount of OBU adhesive was applied to the dentinal surfaces. Scrub the surface with a brushing motion for 20 s. Dry the adhesive with air delivered from the device (cold or warm) for at least 10 s. Light irradiate for 20 s.
OBFL (Kerr Co, Orange, CA, USA)	**Three-step etch-and-rinse** pH primer: 1.9; pH bonding: 6.9	Etchant: 37.5% H_3PO_4 Primer: HEMA, GPDM, MMEP, water, ethanol, CQ, and BHT Adhesive: Bis-GMA, HEMA, GDMA, CQ, and filler (fumed SiO_2, barium aluminoborosilicat, Na_2SiF_6), coupling factor A174	Using a micro-brush applicator, apply OBFL primer over dentin surfaces with a light scrubbing motion for 20 s. Dry the primer with air delivered from the device (cold or warm) for at least 10 s. At this point, the dentin surface should have a slightly shiny appearance. Using a new micro-brush applicator, apply OBFL adhesive to the prepared dentin surfaces with a light scrubbing motion for 20 s, creating a thin coating.

			Gently air-dry for approximately 5 s from the device (cold-air). Light irradiate for 20 s.
CSE (Kuraray Noritake Dental Inc., Tokyo, Japan)	**Two-step self-etch** pH primer = 1.76 pH bond = 2	Primer: 10-MDP, HEMA, hydrophilic dimethacrylate, CQ, DEPT, water Bond: MDP, HEMA, Bis-GMA, hydrophobic dimethacrylate, CQ, DEPT, silanized colloidal silica	Using a micro-brush applicator, apply primer for 20 s. Dry with air delivered from the device (cold or warm) for at least 10 s. Using a new microbrush applicator, apply bond. Apply air-flow gently from the device (cold-air). Light irradiate for 20 s.

* Based on companies' MSDS. 10-MDP = 10-methacryloyloxydecyl dihydrogen phosphate; PENTA = dipentaerythritol pentaacrylate phosphate; HEMA = 2-hydroxy ethyl methacrylate; GDMA = glycerol-dimethacrylate; GPDM = glycerophosphate dimethacrylate; MMEP = methacryloyloxy-ethyl-dihydrogen phosphate; CQ = camphorquinone; SiO_2 = silicon dioxide; Na_2SiF_6 = sodium hexafluorosilicate; BHT = butyl hydroxy toluene; Bis-GMA = bisphenol A-glycidyl methacrylate; DEPT = N,N-diethyl-p-toluidine; Clearfil SE Bond (CSE); OptiBond FL (OBFL); OptiBond Universal (OBU); Prime&Bond Universal (PBU).

Table 17: Manufacturers and compositions of the adhesives tested in the current research.

After applying one coat of each adhesive system (Table 17) for 20 s using a micro-brush applicator (Kerr, Orange, CA, USA), air-blowing (based on different air-drying temperature) of the adhesive layers were photopolymerized for 20 s at room temperature (1000 mW/cm^2, CuringPen-E (Eighteeth, Changzhou, China). Moreover, a single operator (RB) who completed the adhesion method standardized the level of force to be delivered during the rubbing action. All bonded surfaces were built up in three layers with resin composites (Reflectys, Itena Clinical, Paris, France) of 2 mm thickness for each time. Each layer was photopolymerized for 20 s at a vertical distance of 1 mm to the dentinal surface using the same light-curing unit. The resin-dentin samples were kept in distilled water at 37 °C for 24 h and 6 months, respectively, before μTBS testing [17].

4.2.4. Micro-Tensile Bond Strength Testing

After various distilled water storage periods (24 h and 6 months), the restored teeth were sectioned occluso-gingivally using a low-speed precision cutting machine (EXAKT Vertriebs GmbH, Norderstedt, Germany) to produce resin-dentin slabs with a cross-sectional area of approximately 1.0 mm^2. The μTBS was performed in agreement with ISO/TS 11405. The upper half of the slab consisted of the resin composite, while the lower half was formed by the underlying dentinal part. Each tooth yielded approximately twelve slabs, which were kept moist until testing. These slabs were then randomly divided into two subgroups, with μTBS testing conducted after 24 h (six slabs/tooth = thirty slabs for five teeth) and 6 months (six slabs/tooth = thirty slabs for five teeth) in each subgroup. The results obtained from the six slabs tested for each tooth were averaged, and the resulting mean was used for statistical analysis [17]. Specimens stored for 6 months were kept in distilled water at 37 °C with weekly replacement. Each slab was stuck to a Geraldeli's jig by means of a glue (Zapit, Dental Ventures of North America, Corona, CA, USA) and exposed to a tensile load test using a universal testing machine (YLE GmbH Waldstraße, Bad König, Germany) with a crosshead speed of 1 mm/min and a load cell of 500 N. The measurements of each failed specimen were recorded using a digital caliper (Model CD-6BS Mitutoyo, Tokyo, Japan) with 0.01 mm of exactness. Accordingly, the μTBS was determined by dividing the fracture force in newtons (N) by the bonded area in square millimeters (mm^2) and expressed as megapascals (MPa).

4.2.5. Failure Mode Analysis

Each fractured portion's failure mode was fixed to aluminum stubs and examined using an optical numeric microscope (Keyence, Osaka, Japan) with a magnification of 150×. To calculate the percentage of each fractured area and to designate the type of failure, VHX-5000 software was used. If the bonded interface failed between the resin composite and dentin, the failure was classified as adhesive; if the bonded interface failed in the resin composite or dentin, the failure was classified as cohesive; and if a combination of both adhesive and cohesive failures was recorded, the failure was considered as mixed (Fig. 37).

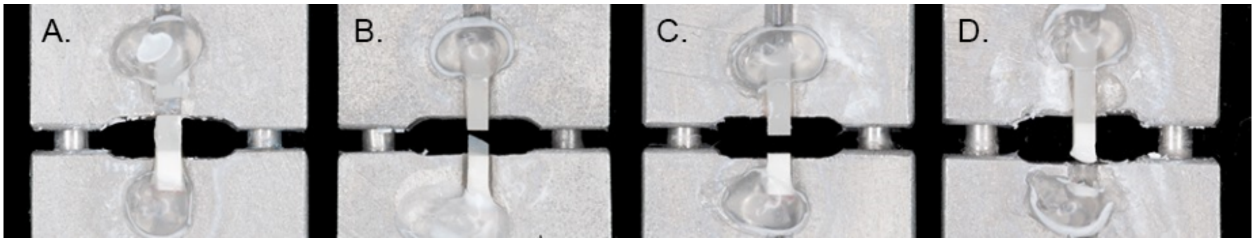


Figure 37: Representative images of the failure mode after the bond strength test. A. cohesive in resin, B. mixed, C. adhesive, and D. cohesive in dentin.

4.2.6. Scanning Electron Microscopy

The ultrastructural observation of the restorative-dentin interface (three slabs from each subgroup were kept in hermetic boxes and stored in dry states) was accomplished using SEM. Specimens were prepared as previously stated in the above test session. Following that, the sample surface underwent polishing using SiC abrasive discs with grit sizes of 1200, 2400, and 4000. Subsequently, 37% H_3PO_4 was applied to the polished surfaces for 10 s, followed by a rinse with distilled water for 10 s and drying. The samples were then immersed in a 2.5% sodium hypochlorite solution for 3 min to address the smear layer and observe dentinal infiltrations. After rinsing, the specimens underwent dehydration using a graded series of ethanol solutions (25%, 50%, 75%, and 100%). They were then sputter-coated with a gold–palladium alloy (20/80 weight % ratio) for 120 s using a sputtering device (Hummer JR, Technics, CA, USA). Finally, the samples were analyzed with a Quanta 250 FEG SEM (FEI Company, Eindhoven, The Netherlands, 10 kV) at a magnification of 1500×, with a working length of 10 mm to observe the resin-dentin bonded interface.

4.2.7. Solvent Evaporation Rate

Around 10 μL of each adhesive system, equivalent to about one coat using a saturated micro-brush, was aspirated with a micropipette (Pipetman, Gilson, NY, USA) from the original flat container and transferred to small light-proof glass containers of known weight. Subsequently, they were promptly placed on an analytical balance (Mettler, type H6; Columbus, OH, USA; capacity up to 160 g), and the baseline mass was recorded to the nearest 0.0001 mg. Different air-drying temperatures (20 °C, 40 °C, and 60 °C) were then applied with the device for every 10 s before placing the adhesive into the analytical balance, at a distance of 5 cm from the container, and the residual mass of all the adhesive systems tested was recorded until the container stopped losing weight to measure the maximal amount of evaporable mixtures. To eliminate the influence of light radiation, an electronic balance was covered with suitable light filters. Five samples (n = 5) of each adhesive under each air-drying condition were analyzed. The percentage of mass loss, relative to the mean baseline recording, was calculated for each tested specimen.

4.2.8. Statistical Analysis

Data from BS was analyzed using the Sigma Plot (Version 14, Systat, San Jose, CA, USA) software. Previously, the data were subjected to analysis to assess the normal distribution and homogeneity of variance. To evaluate the influence of the adhesive system and the temperature used for solvent evaporation on the μTBS to dentin, a two-way ANOVA was conducted. The BS was evaluated after 24 h and 6 months of storage, with multiple comparisons conducted using Tukey's post hoc test. A significance level of $\alpha = 0.05$ was employed for all analyses.

4.3. Results

4.3.1. Micro-Tensile Bond Strength Testing

Table 18 shows the values obtained for the μTBS after 24 h aging according to the adhesive and the temperature for solvent evaporation used. The results showed that the factor adhesive was not statistically significant ($p = 0.052$), while the temperature has a statistically significant effect ($p < 0.001$). The interaction between the factors was not statistically significant ($p = 0.880$). The temperature for solvent evaporation was only statistically significant for the adhesive PBU, where the differences between 20 °C and 60 °C were significant ($p = 0.025$). The rest of comparisons were not statistically significant ($p > 0.05$).

Temperature for solvent evaporation	Prime&Bond Universal	OptiBond Universal	OptiBond FL	Clearfil SE
20 °C	^{A} 13.3 (3.4) ^{a}	^{A} 20.9 (3.1) ^{a}	^{A} 20.5 (5.5) ^{a}	^{A} 20.5 (5.5) ^{a}
40 °C	^{A} 22.1 (9.9) ^{ab}	^{A} 26.8 (7.6) ^{a}	^{A} 29.3 (4.5) ^{a}	^{A} 26.2 (8.2) ^{a}
60 °C	^{A} 24.6 (4.1) ^{b}	^{A} 24.2 (3.8) ^{a}	^{A} 29.9 (6.3) ^{a}	^{A} 28.6 (10.4) ^{a}

Different lowers script letters indicate the presence of statistically significant differences between temperatures for solvent evaporation within each adhesive system (p<0.05). Different upper script letters indicate the presence of statistically significant differences between adhesive systems within each temperature for solvent evaporation ($p < 0.05$).

Table 18: Mean and standard deviation of the micro-tensile bond strength test (MPa) of the different temperatures used for solvent evaporation for each adhesive system tested after 24 h aging.

Table 19 shows the values obtained for the μTBS after 6 months of aging according to the adhesive and the temperature for solvent evaporation used. The statistical analysis revealed that only the factor temperature for solvent evaporation was statistically significant ($p < 0.001$), while the factor adhesive ($p = 0.369$), and the interaction between the factors ($p = 0.821$) were not statistically significant. The post hoc analyses showed that only for CSE adhesive, there were statistically significant differences between 20 °C and 60 °C air temperature ($p = 0.008$). The rest of the comparison were not statistically significant ($p > 0.05$).

Temperature for solvent evaporation	Prime&Bond Universal	OptiBond Universal	OptiBond FL	Clearfil SE
20 °C	^{A} 12.69 (6.6) ^{a}	^{A} 16.08 (7.3) ^{a}	^{A} 16.0 (7.4) ^{a}	^{A} 12.7 (5.0) ^{a}
40 °C	^{A} 19.24 (6.1) ^{a}	^{A} 24.3 (5.99) ^{a}	^{A} 22.1 (11.4) ^{a}	^{A} 22.5 (6.1) ^{ab}
60 °C	^{A} 19.61 (8.6) ^{a}	^{A} 21.47 (6.6) ^{a}	^{A} 26.2 (6.6) ^{a}	^{A} 26.7 (4.5) ^{b}

Different lowers script letters indicate the presence of statistically significant differences between temperatures for solvent evaporation within each adhesive system (p<0.05). Different upper script letters indicate the presence of statistically significant differences between adhesive systems within each temperature for solvent evaporation ($p < 0.05$).

Table 19: Mean and standard deviation of the micro-tensile bond strength test (MPa) of the different temperatures used for solvent evaporation for each adhesive system tested after 6 months aging.

The mean and SD for the μTBS of PBU according to the different temperatures of air used for solvent evaporation and storing time is presented in the Table 20. According to the statistical analysis, only the factor temperature was statistically significant ($p = 0.015$). On the other hand, the factor aging ($p = 0.269$) and the interaction between the factors ($p = 0.781$) were not statistically significant. For all air temperatures, there were not statistically significant differences between the 24 h and 6 months aging ($p > 0.05$). After 24 h aging, the post hoc analysis exposed that statistically significant differences only for the comparison between 20 °C ad 60 °C ($p = 0.004$). On the other hand, after 6 months there were no statistically significant differences among the temperatures used ($p = 0.278$).

Group	24 hours	6 months
20 °C	^{A} 13.3 (3.4) ^{a}	^{A} 12.69 (6.6) ^{a}
40 °C	^{A} 22.1 (9.9) ^{ab}	^{A} 19.24 (6.1) ^{a}
60 °C	^{A} 24.6 (4.1) ^{b}	^{A} 19.61 (8.6) ^{a}

Different superscript letters indicate the presence of statistically significant differences between storing times within each air temperature (p<0.05). Different lower script letters indicate the presence of statistically significant differences between air temperature within each storing time ($p < 0.05$).

Table 20: Mean and standard deviation of the micro-tensile bond strength test (MPa) of the different temperatures of air used for solvent evaporation for Prime&Bond Universal.

The mean and SD for the μTBS of OBU according to the different temperatures of air used for solvent evaporation and storing time is presented in the Table 21. According to the statistical analysis, the factor temperature was statistically significant ($p = 0.045$). On the other hand, the factor aging ($p = 0.143$) and the interaction between the factors were not statistically significant ($p = 0.892$). Both at 24 h and 6 months, there were no statistically significant differences ($p \geq 0.282$; $p \geq 0.096$). For the comparison of the BS values between 24 h and 6 months aging, the differences were not statistically significant ($p \geq 0.218$).

Group	24 hours	6 months
20 °C	20.9 (3.1)	16.08 (7.3)
40 °C	26.8 (7.6)	24.3 (5.99)
60 °C	24.2 (3.8)	21.47 (6.6)

There were not statistically significant differences in any comparison in rows or columns ($p > 0.05$).

Table 21: Mean and standard deviation of the micro-tensile bond strength test (MPa) of the different temperatures of air used for solvent evaporation for OptiBond Universal.

The mean and SD for the μTBS of CSE bond according to the different temperatures of air used for solvent evaporation and storing time is presented in the Table 22. According to the statistical analysis, only the factor temperature was statistically significant ($p = 0.005$). On the other hand, the factor adhesive ($p = 0.090$) and the interaction between the factors were not statistically significant ($p = 0.633$). At 24 h aging, there were no statistically significant differences between the different temperatures of air used ($p \leq 0.175$). At 6 months aging, the only comparison that resulted significant was between 20 °C and 60 °C (0.011). For the comparison of the BS values between 24 h and 6 months aging, the differences were not statistically significant for all temperature tested ($p \leq 0.090$).

Group	24 hours	6 months
20 °C	^{A} 20.5 (5.5) ^{a}	^{A} 12.7 (5.0) ^{a}
40 °C	^{A} 26.2 (8.2) ^{a}	^{A} 22.5 (6.1) ^{ab}
60 °C	^{A} 28.6 (10.4) ^{a}	^{A} 26.7 (4.5) ^{b}

Different superscript letters indicate the presence of statistically significant differences between storing times within each air temperature ($p<0.05$). Different lower script letters indicate the presence of statistically significant differences between air temperature within each storing time ($p<0.05$).

Table 22: Mean and standard deviation of the micro-tensile bond strength test (MPa) of the different temperatures of air used for solvent evaporation for Clearfil SE bond.

The mean and SD for the μTBS of OBFL according to the different temperatures of air used for solvent evaporation and storing time is presented in the Table 23. According to the statistical analysis, the factor temperature was statistically significant ($p = 0.017$). On the other hand, the factor aging ($p = 0.068$) and the interaction between the factors were not statistically significant ($p = 0.866$). According to the post hoc analyses, there were no statistically significant differences between the different temperatures of air for solvent evaporation at 24 h ($p \geq 0.127$) or 6 months ($p \geq 0.095$). For the comparison of the BS values between 24 h and 6 months aging, the differences were not statistically significant for all temperature tested ($p < 0.139$).

Group	24 hours	6 months
20 °C	20.5 (5.5)	16.0 (7.4)
40 °C	29.3 (4.5)	22.1 (11.4)
60 °C	29.9 (6.3)	26.2 (6.6)

There were not statistically significant differences in any comparison in rows or columns ($p > 0.05$).

Table 23: Mean and standard deviation of the micro-tensile bond strength test (MPa) of the different temperatures of air used for solvent evaporation for OptiBond FL.

4.3.2. Failure Mode Analysis

The results of the failure mode analysis for all the tested groups are exhibited in Fig. 38. The evaluation of the failure modes indicated a predominantly adhesive or mixed failure across all temperature variations of air used for solvent evaporation with each adhesive system. A low prevalence of cohesive failure in resin or dentin was observed.

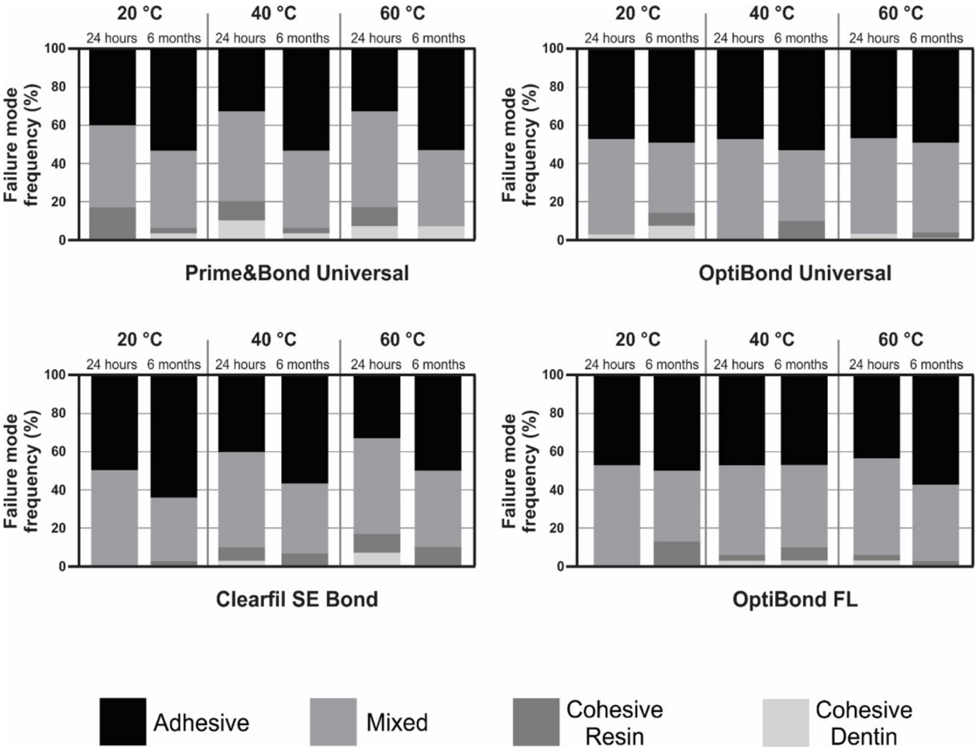


Figure 38: Failure mode distribution of the adhesives systems evaluated after bond strength test.

4.3.3. Scanning Electron Microscopy

An ultrastructural observation of the restorative-dentin interface was performed for the four adhesive systems when using different air temperatures (20 °C, 40 °C, and 60 °C) for solvent evaporation (Fig. 39).

The thickness of the adhesive layer and the creation of RTs qualitatively varied amongst the temperatures evaluated. For OBFL, an elevated number of RTs was observed between all the cold and warm air groups when compared to the others adhesive systems (PBU, OBU, and CSE). When passing from 20 °C to 60 °C, the thickness of the adhesive layer had a tendency to decrease, except for OBFL, where the adhesive layer was compact in all the temperatures employed. Besides, the resin penetration increased for the ER III (OBFL), where remarkable infiltrations were seen in all the tested temperature.

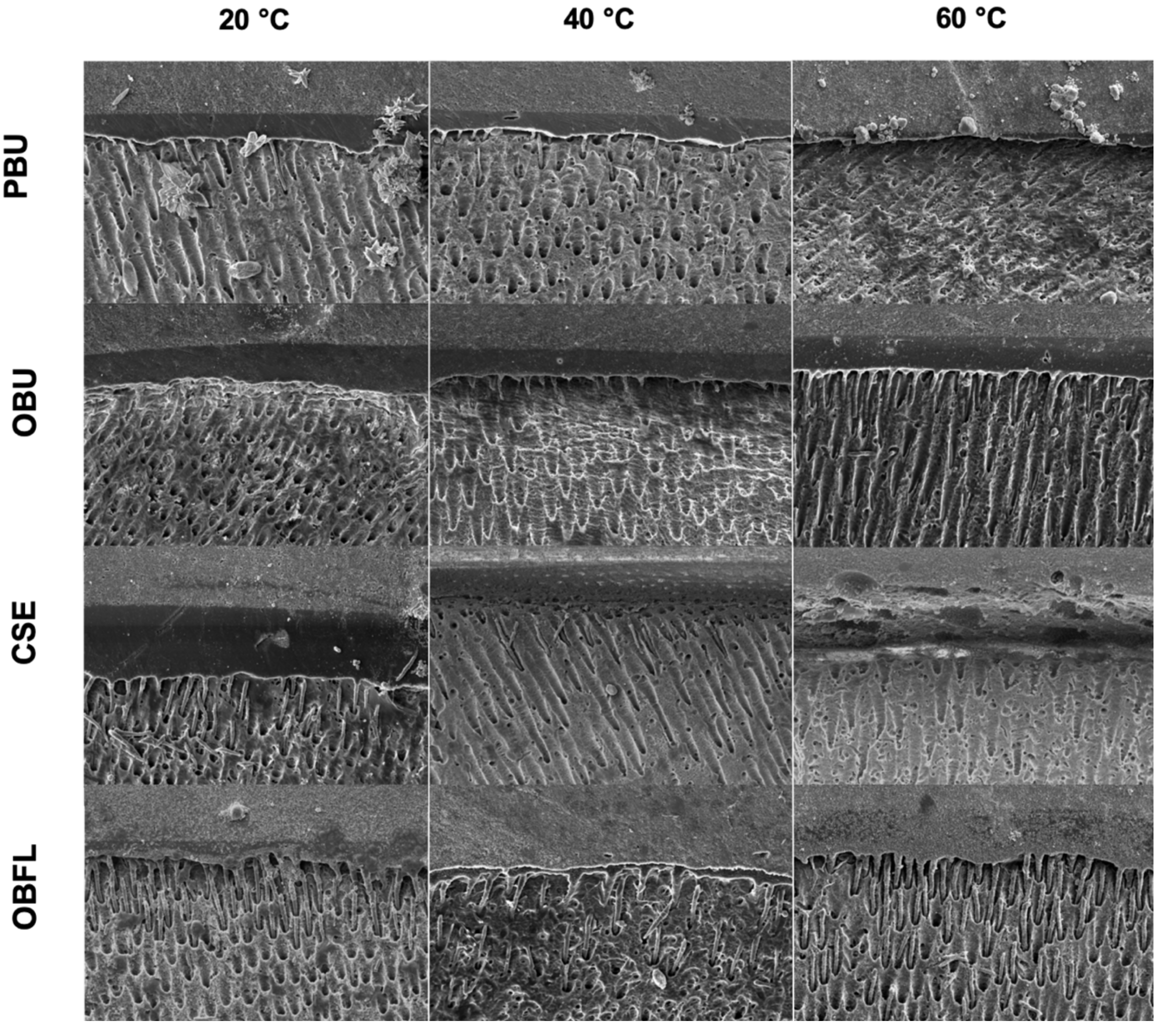


Figure 39: Scanning electron microscopy images of the restorative-dentin interface (x 1500 magnification) displayed the tag formation and resin penetration for the four adhesive systems when using different air temperatures (20 °C, 40 °C, and 60 °C) for solvent evaporation. Prime&Bond Universal (PBU); OptiBond Universal (OBU); Clearfil SE Bond (CSE); and OptiBond FL (OBFL).

4.3.4. Solvent Evaporation Rate

Results from the solvent evaporation rate test are presented in Fig. 40. For all adhesive systems tested, the use of 40 °C or 60 °C air for solvent evaporation led to an increased mass loss. At this temperature the mass loss for PBU, OBFL, and CSE reached around 90 wt%. On the other hand, when a temperature of 20 °C for air streaming was used, in all adhesives systems, the mass loss was around 50 wt%.

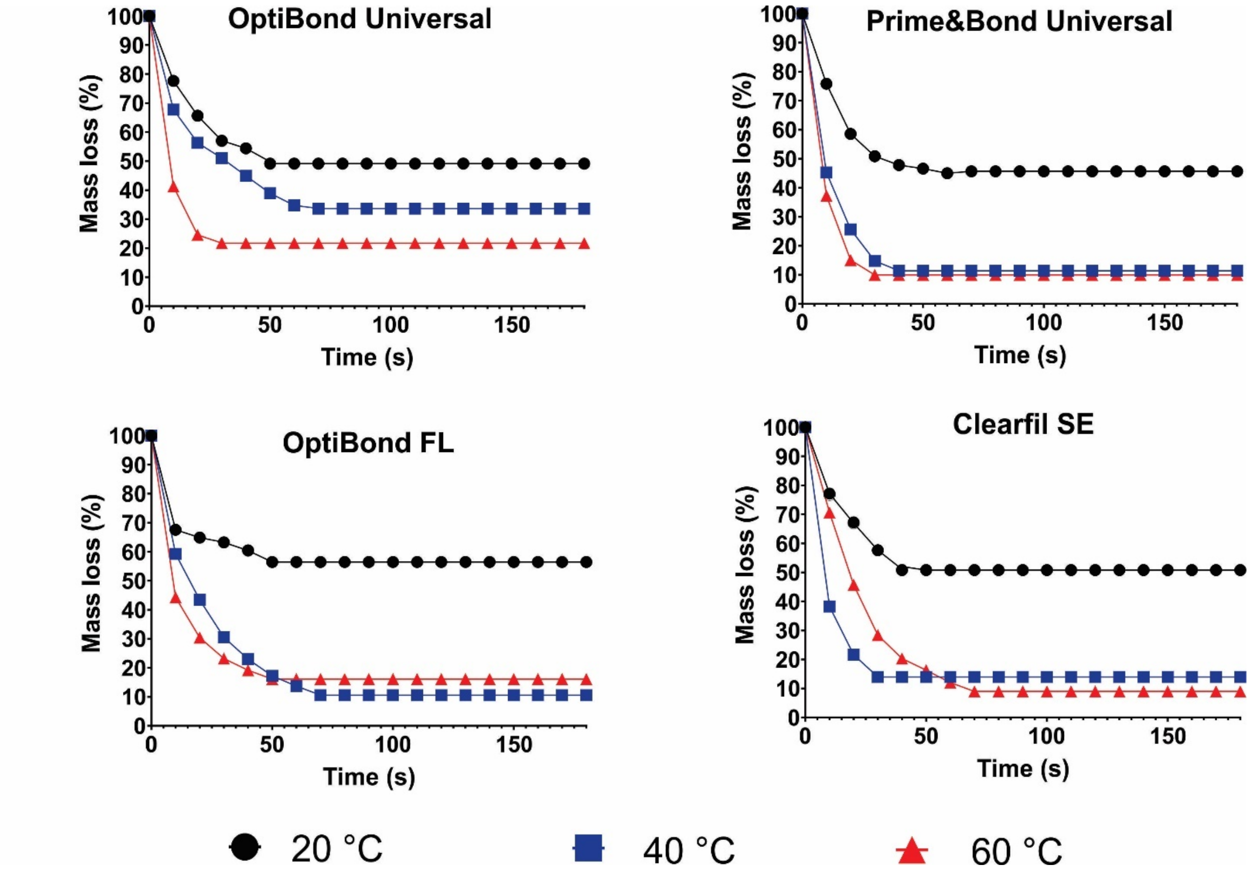


Figure 40: Solvent evaporation rate of the different adhesive systems tested according to the temperature of air stream.

4.4. Discussion

For a successful dental restoration, it is essential to establish a robust chemical bond between the acidic functional monomer present in adhesives and the HAp within the dental substrate [1]. In light of the highly volatile nature of solvents, an adhesive can properly eliminate leftover water and regulate the solvent combined in an adhesive layer by means of air-blowing application for the attainment of a target adhesive performance [9]. Previous studies focused on air temperatures ranging from 37 °C to 80 °C as one of the most crucial factors of the air-blowing application [13,14,18]. Furthermore, as previously discussed, the gold-standard temperature of a warm air stream when applied to dentin should be between 50 °C and 60 °C [13]. Consequently, the 40 °C and the 60 °C were selected as the middle-level air temperatures in this present study. Therefore, this research aimed to study the influence of different air-drying temperatures (20 °C, 40 °C, and 60 °C) on the solvent evaporation of four adhesive systems to dentin. For this purpose, a prototype for a warm air stream was introduced. The results showed that the air temperatures affected the dentin BS of some of the adhesives used. Thus, this necessitates the rejection of the anticipated null hypothesis.

With all examined adhesives, at 24 h, only PBU displayed a significant variance in BS within the different temperatures used for solvent evaporation ($p < 0.05$). This difference was noticed between the 20 °C and 60 °C temperatures. Particularly, PBU is a (HEMA)-free adhesive, and given the intricacy of its chemical composition, the *in vitro* presentation of UAs has been reported to be material-dependent [19]. In this current investigation, the absence of HEMA led to adverse effects on phase separation, primarily due to lingering water within the adhesive layer. Consequently, this condition resulted in a subpar bonding performance of PBU in the group exposed to a temperature of 20 °C. This was in line with a previous study where an HEMA-free adhesive showed a lower BS when compared to HEMA-based adhesives in 23 ± 2 °C groups [1]. In contrast, according to the previous research, solvent removal inside the adhesive layer of HEMA-free adhesives is considered to be an optimal option with higher temperatures up to 60 °C. Additionally, water (etching aid) and isopropanol (polarity adjustment) were considered in PBU as solvents [20]. It is likely that the isopropanol (a type of alcohol fully soluble in water) present in this adhesive (PBU) would ease adhesive spreading in between collagen fibers [21] at a higher temperature. Employing a warm air stream for solvent evaporation significantly improved the adhesive solutions' ability to bind to dentin. The observed effect was likely due to the temperature increase within the substance, which facilitated solvent evaporation. The impact was especially obvious in adhesives based on alcohol/water [10]. This is in agreement with the discoveries of this present study. All in all, high temperatures (40 and to 60 °C) for the air delivery of solvent evaporation ameliorate the immediate BS performance of PBU to a dentin substrate.

For OBU, CSE, and OBFL, the rest of the comparisons were not statistically significant between all the temperatures tested after 24 h of aging ($p > 0.05$). Understanding that HEMA is used in the composition of almost all adhesives [4,5], it is essential to recognize the benefits and disadvantages of HEMA. This monomer, characterized by its low molecular weight and hydrophilic nature, demonstrates exceptional capability in penetrating and "wetting" dentinal substrates. Its hydrophilicity designates it as a significant adhesion-promoting agent, as it has been shown to enhance the initial BSs of adhesive systems. This enhancement occurs through an increased monomer penetration into dentin and the facilitation of a HL formation [4]. This is in harmony with the finding achieved in this study, as the OBU, CSE, and OBFL adhesives contain HEMA in their formulations. The co-solvents present in the formulation may also have an influence on the evaporation technique, since almost all HEMA-based adhesives were solvated with ethanol, which has a superior hydrogen bonding capacity (19.4 (J/cm^3)1/2) than isopropanol (16.4 (J/cm^3)1/2) within PBU [22]. So, undoubtedly, the adhesive layer of the HEMA-containing adhesives may have retained the ethanol hydrogen (OBU and OBFL) and the hydrogen (CSE) bound to water, correspondingly to OBU, OBFL, and CSE employed in this research at any temperature, and reduced their degree of polymerization to dentin. Seemingly, the consistent BSs observed across the tested temperatures after 24 h could be attributed to the presence of water within the adhesive layer. This water may have been transferred to the surface and effectively removed by the air-blowing application, regardless of the temperature used (20 °C, 40 °C, and 60 °C). Considering this, it seems that the HEMA-contained adhesives were not sensitive to any temperatures employed in this research after 24 h.

Adhesives are often capable of producing HL with a strong instant and medium-term BS. Aging is frequently associated with the deterioration of dentin-bonded interface integrity and BS [23,24]. In this study, a 6-month storage in distilled water was performed. Following this aging, only CSE presented a significant difference between 20 °C and 60 °C air temperatures ($p < 0.05$). Starting with 40 °C, additional benefits were remarkable until achieving the highest BS at 60 °C. To clarify, CSE is an SE II adhesive system [25]. Indeed, water (CSE) and solvents deliver the ionization medium of the SE activity, and solvents lower their viscosity to facilitate resin infiltration into the porosities of the prepared tooth surface, as well as promote polymer chain mobility [16]. However, the remaining solvents inside the polymerized adhesive and HL might impede polymer network development [13,26]. This was not the case in the warm air groups (40 and 60 °C) tested for CSE after 6 months, so the clinician should emphasize the importance of an optimal strategy for enhancing the solvent evaporation and protecting the HL from any degradations. Solvents should be removed from adhesive systems as much as feasible prior to photopolymerization [16]. This is a key point because when the mixture of water and a solvent (water in the case of CSE) from the adhesive evaporates, the monomer density rises and becomes concentrated on the adhesive layer, reducing additional solvent vaporization [13]. However, when a warm air stream at roughly 60 °C was used, a considerable increase of around 20% in the resin-dentinal bond was noticed [12], and it was higher with the values of the present research. On a positive note, the use of warm air allowed for an increase in dentin's BS of more than 50% than the cold air (an increase from 12.7 (5.0) to 26.7 (4.5) MPa with a warm air stream). The increase in the resin-dentin bonding is probably due to the improvement in the mechanical properties of the adhesive layer, which can be attributed to the higher rates of solvent evaporation [9]. This, perhaps, could be linked to the fact that energy is released when heat is applied to the dentin. In the conditions of this study, the heat supplied by the warm air stream might have disrupted the molecular arrangement of the adhesive molecules. Correspondingly, the solvent evaporation rate increased from the bonding surface, permitting a higher resin-dentin bond to be achieved after 6 months of aging, as seen from the study results (for 40 and 60 °C).

CSE with a mild SE feature (pH of around 2) was used in this study for a partial demineralization of dentin [25], leaving a significant number of HAp crystals around the collagen fibrils [27]. Regarding the warm air groups, it is likely that 10-MDP and HAp may have interacted more chemically, and the BS increased accordingly. Further, it has been shown that removing HEMA from SE adhesives would reduce water sorption [28], but another research found that a 10% HEMA concentration would improve the adhesive system's performance [29]. Considering that 20-40% of HEMA was present in the composition of the SE II "CSE" as described in their safety data sheet, the presence of extra %HEMA would have led to the formation of an aqueous and unstable gel that requires warm air application on the adhesive in order to achieve the optimal dentinal BS and stability with time. All things considered, CSE benefits from the warm air temperatures (definitely the 60 °C temperature) used in this study after 6 months of water storage.

Another notable discovery presumed from this analysis was that differences in BS between PBU, OBU, and OBFL for the different temperatures were not significant ($p > 0.05$) after 6 months of aging. While it is commonly observed that resin-dentin bonding reaches adequacy immediately, a decline in bonding effectiveness over time has also been documented [30]. However, these findings are not consistent with the results of this research, since despite the slight discrepancies in the mean values of BS, the maximum values were emphasized with warm air temperatures. Summarily, the adhesive BS remained consistent after 6 months of water storage with no changes. The chemical composition of the adhesive explains this plainly.

Because PBU is a HEMA-free adhesive, water contamination during the bonding process may initially lead to a decrease in dentin BS and the development of flaws within the adhesive layer and resin composite. This phenomenon occurs due to a phase separation between water and the hydrophobic components of the adhesive [20]. After 6 months of water storage, these flaws would result in less lasting bonding to dentin [31]. This was only applicable for the cold air group. As BS remained constant, this result confirms the study's findings. For PBU, the results showed lower values when cold air was used, and these values remained lower after 6 months. For the warm air groups, especially the 60 °C temperature, higher BS values were shown after 6 months, associated with the same values at 24 h. This confirms the sensitivity of PBU to cold air and the resistance to the weakening of the BS with time when using warm air. Consequently, when employing the cold air temperature, it is advisable not to prioritize the use of the tested HEMA-free adhesive as the treatment of choice, and clinicians should opt for the warm air strategy with a 60 °C temperature. Moreover, the water content of the UAs varies [32]. The reduced water content may result in a hydrophobic adhesive surface with superior resistance to hydrolytic breakdown. Previous research found that adhesives with more than 25% water suffered phase separation [33], and that low water contents in adhesive systems led to a superior pH and less chemical interaction with substrates [34]. That being so, adjusting the water content of adhesives prior to application to tooth surfaces might be critical. Even within the identical adhesive category, the ideas underlying the creation of UAs vary depending on the manufacturer. A water content of 10-15%, along with the presence of constituents considered to limit the impact of surface moisture, would be optimal for UAs [35]. As PBU contains 5-24.5% water [25], this could explain the non-significant discrepancy in BS between groups after 6 months.

For OBU, as acetone (highly volatile solvent) was present as 30-60% inside the bottle (with ~5-10% ethanol) [25], no significant difference in dentin BS was observed between the 6-month temperatures. Given that acetone has a relatively high vapor pressure, evaporation happens considerably faster in acetone-based adhesives than in ethanol-based adhesives, having less direct influence on BS [10]. Likewise, a prior study discovered that the solvent evaporation of experimental adhesives formulated with acetone remained similar when subjected to either room-temperature air stream or a 40 °C air stream [11]. These variables might explain why using a warm air stream for solvent volatilization did not increase the binding strength of acetone-based adhesives extensively [10].

There were no statistically significant differences in the BS values for the OBFL adhesive system ($p > 0.05$). This adhesive was based on GPDM [25,36], which was not sensitive to any warm air stream used after 6 months, which rationalizes the results. Moreover, OBFL was the sole ER adhesive system evaluated in this investigation, demonstrating consistent BSs after 24 h and even after 6 months of water storage. This finding could be attributed to the unique characteristics of this product. OBFL has been previously recognized as the gold-standard material due to its exceptional efficacy in both immediate and long-term BS tests [3], a finding corroborated by the current study. The presence of GPDM, which may engage in chemical interactions with HAp, and the densely filled bonding resin layer (48 wt%) applied over the primed dental surfaces, likely contribute to its superior performance, as indicated by this research [37].

Having this in mind, it appears that the ER strategy assured that this adhesive method remains a viable alternative with a correct air stream (60 °C air stream was the optimal choice when using this adhesive after the CSE). Another explanation of the values obtained for OBFL (ethanol-based and water-based adhesive) is that there is no direct link between the solvent content in the adhesive and the degree of cure [38]. This might hypothesize that OBFL contains a balanced mixture of solvents able to favor the warm air technique since a stable and high value was obtained with warmer temperatures.

Considering the effect of the adhesive system within each temperature (after 24 h and 6 months aging), there were no noteworthy variances among all the distinctive adhesive systems ($p > 0.05$). A possible explanation of the acquired results is that additional compositional variations, like initiators, percentage of water content, presence or absence of other functional monomers, such as 10-MDP, GPDM, among others, might be implicated in the bonding performance of such adhesives to dentinal substrates. These findings reveal that, while the solvent is an important determinant, other components in the adhesive formulation also influence the evaporation rate. The type of solvent and the mixing of components, counting HEMA (OBU, CSE, and OBFL), have been shown to impact the rate of solvent evaporation for commercial and experimental adhesives [39]. In spite of everything, regardless of the variation in components used in the adhesives tested in this study, the 60 °C temperature with almost the highest BS could be the reason for the formation of suitable adhesive layers.

To compare the BS values at 24 h and 6 months of aging, all of the air-drying temperatures (20 °C, 40 °C, and 60 °C) resulted in BS stability over time ($p > 0.05$). For the sub-optimal presentation of OBFL and CSE adhesive systems, it is theorized that BS results would be standardized following an extended period of aging. There is much documented success of these bonding agents, and it continues to be a gold-standard in the category of SE and ER strategies [40-42]. Plus, the HL of UAs using the SE approach (like PBU and OBU used in this study) appears to last longer, as this bonding agent comprises functional monomers that can interact chemically with HAp and protect the collagen fibrils over time [24].

For PBU, all of the temperatures used resulted in BS stability. Regarding the cold temperature, the BS was directly lower and kept its low value with time. However, for warm temperatures, the dentinal BS was conserved, saving the higher dentinal long-term bond presentation. This unchanging value was due to the presence of PENTA [43], 10-MDP [20,25], and methacrylamide monomers within the bonding arrangement [25,44]. In other investigations, adhesives including 10-MDP and PENTA demonstrated effectiveness in long-term clinical trials [45,46]. This was confirmed in this *in vitro* study. PENTA has been shown to be more stable than MDP in terms of BS retention at the end of the adhesive's shelf life [43,47]. PBU maintained its stability in this regard. PBU is an HEMA-free adhesive and can help to efficiently eliminate water throughout the air-drying procedure [20]. Furthermore, methacrylamide monomers were synthesized as substitutes for HEMA in PBU to prevent phase separation and reduce water sorption within the adhesive [25,43,44,48]. The conclusion of this analysis is that PBU performed well at a high temperature of 60 °C immediately and after aging.

For OBU, the stability of the BS was observed in all the temperatures used with acceptable values in all the groups. Because of the presence of acetone in the composition of OBU, the BS could be reduced if not adequately evaporated [10,13,25,49]. It was shown in a previous investigation that an adhesive with a higher concentration of acetone (47% to 67%) reduced the values of resin-dentinal BS [50]. Knowing that OBU contains approximately the same percentage of acetone, the BS remained stable. In addition, the presence of HEMA in OBU might make it vulnerable to degradation and water uptake [51]. However, this is not in agreement with this study as the BS remained stable; thus, solvent evaporation was made easy with the device presented in this research. Bearing that in mind, an adhesive containing a high concentration of acetone should be evaporated well and preferably with 40 °C warm air.

For CSE, all the 24 h values exhibited acceptable values. Yet, the stability of the BS was shown with time in all the temperatures employed, with a lower value for the cold air group after 6 months when compared to the higher value of 60 °C than 40 °C. The 10-MDP-based SE adhesive have better bond durability with aging [52]. This phenomenon was observed in the current study across all temperature variations. Plus, fillers present in the CSE increase BS and enhance the mechanical assets of an adhesive system [53]. Normally, appropriate resin-dentin bonding is usually directly reached as shown in the CSE groups, and minimized bonding effectiveness develops with time [30]. The drop in bonding was only seen in the 20 °C after 6 months and not significantly important to the 24 h value, but it was crucial when compared with the same adhesive with aging. This sheds light on the importance of aging on the BS of the adhesive to dentin. When choosing the CSE, a clinician can select the 60 °C warm air.

For OBFL, notwithstanding the small divergences in the mean values of BS, it can be concluded that solvent evaporation at elevated temperatures was higher, although not significantly so. According to a previous study [54], adhesive systems offering dental etchant, dental primer, and hydrophobic adhesive in each bottle without a solvent content in the adhesive are superior with regard to the adhesion stability, as long as the hydrophilic combinations have no influence on the degree of polymer conversion, with OBFL being an example of this [25,55]. This observation might help explain why the BS of OBFL did not decline between 24 h and 6 months across all the temperatures tested. As a requirement for an ER OBFL, a 60 °C warm air strategy will be the optimal decision.

Concerning the failures that happened following the μTBS testing, adhesive failure and mixed failures were the most common, while cohesive failures in the resin and dentin were less prevalent. This discovery is in agreement with a previous report by Taguchi et al., [12] who found that warm air specimens had fewer blisters in the adhesive layer than the cold-air ones. Precisely, the BS test employed a load force capable of passing through both the dentin and the resin composite prior to attaining the adhesive interfaces, resulting in an increased stress intensity at these areas [56]; thus, the number of mixed failures increased. It is worth mentioning that after the aging of 6 months, the failure analysis was frequently adhesive. This was due to the aging of the adhesive layer, which caused more adhesive fractures than the baseline mode of fracture (after 24 h) in the samples [25]. After aging, adhesive layer is prone to water uptake, which lowers the tensile strength and the stability of the material, and, consequently, hinders its ability to maintain the bonding of the dental structure to the restorative material [57]. By correlating each mode of adhesive failure with susceptibility to microleakage, risk of secondary caries, and restoration stability over time, clinicians can better understand the clinical implications of different bonding techniques and optimize treatment strategies to enhance the longevity and performance of adhesive restorations. In particular, the predominance of the adhesive or mixed failure modes observed in this study following BS tests between various adhesive systems and dentin underscores the intricate interplay between material properties and clinical application. While these modes of failure are indicative of immediate BS, their implications for long-term adhesive performance warrant a comprehensive examination.

Adhesive or mixed failures may raise concerns regarding the durability and longevity of adhesive restorations. In the context of warm air delivery, the prevalence of such failure modes suggests potential shortcomings in the adhesive interface’s resilience to environmental stressors. Prolonged exposure to oral conditions, including temperature fluctuations and mechanical stresses, could exacerbate these vulnerabilities, leading to compromised adhesive integrity over time. Addressing the underlying mechanisms driving adhesive failure modes is paramount for optimizing the longevity and clinical success of adhesive systems, thereby enhancing the durability of dental restorations and improving patient outcomes [58,59].

In this research, the resin-dentin interface of the three groups tested after 24 h was assessed through SEM. An elevated number of RTs among all the cold and warm air groups was observed for OBFL when compared to the other adhesive systems (PBU, OBU, and CSE). Therewith, resin penetration increased for this ER III (OBFL), where distinguished infiltration was seen in all the temperature tested. The difference in infiltration and tag formation obtained for OBFL was, perhaps, linked to the unique feature of the etching step that preceded the resin infiltration [25]. This etching phase is important in facilitating deeper adhesive penetration into the dentinal substrate, leading to prolonged RTs and a thicker HL development [54]. Taking this into account, regardless of the temperature used for solvent evaporation, using H_3PO_4 for eliminating the smear layer and smear plugs resulted in an increased adhesive penetration. On the other hand, when the temperature of air increased from 20 °C to 60 °C, the thickness of the adhesive layers seemed to have a tendency to decrease, except for OBFL, where the adhesive layer was compact in all the temperatures employed. The formation of dense adhesive layers was accomplished due to the ability of warm air stream to effectively evaporate the solvent contents of the adhesive systems [60]. However, the BS of the resin-dentin interface has been observed to be independent of the thickness of the HL and/or adhesive layer [61]. The current results imply that the bonding performance, particularly degradation during extended water storage, may vary depending on the chemical compositions of adhesives and the type and quality of the functional monomer present. This influence persists regardless of factors such as the adhesive layer thickness and the extent of tag penetration into dentinal tubules. The dentinal tubule orientation varies between samples, as seen from the micrographs. It should be highlighted that tubule diameters and density increase from the dentino-enamel junction to the middle dentin region [62].

Gas chromatography serves as a reliable method for determining the presence of solvents in dental adhesive systems [63]. Through a precise analysis, it enables researchers to assess the impact of warm air utilization on solvent evaporation kinetics, contributing to a deeper understanding of adhesive performance and formulation optimization. In this study, the solvent evaporation rate was used for recording the mass loss of solvents in adhesive systems. So, another explanation of the results from the solvent evaporation rate outcomes would be the type of solvents present in each primer or adhesive tested. For all adhesive systems examined, the use of 40 °C or 60 °C air for solvent evaporation led to an augmented mass loss. At these temperatures, the mass loss for PBU, OBFL, and CSE reached around 90 wt%. Various molecules exhibit differing degrees of attraction between them. By way of explanation, the common attraction among water molecules (in PBU, CSE, and OBFL) and alcohol molecules (in PBU, OBU, and OBFL) is higher compared to acetone (OBU), as it engages hydrogen bonding forces. That being the case, ethanol (with a vapor pressure that is halfway between that of acetone and water) and water have higher boiling temperatures than acetone, making the evaporation more difficult [9,10,13]. This explains why warmer temperatures facilitated the evaporation of water/alcohol and water by increasing their mass loss. Thus, the application of heat via a warm air stream could facilitate the removal of water from the composition more efficiently. On the other hand, from the data on mass loss during solvent evaporation, when a temperature of 20 °C for air streaming was used, in all adhesives systems, the mass loss was around 50 wt%. The warm air stream removed an expressively higher quantity of solvents from all the tested adhesives when compared to normal air stream in a previous investigation [12]. This discovery reinforces the conclusion of this study that warm air drying expedited and simplified solvent vaporization, resulting in advantages for enhancing dentinal BS.

This study is subject to certain limitations that warrant consideration when interpreting the results. First, the inclusion of various quantities and types of adhesive systems introduced potential confounding factors, making it challenging to isolate the specific effects of individual adhesives. Furthermore, the lack of detailed information regarding the exact composition of the adhesive systems used added complexity to the results' interpretation, hindering the ability to attribute observed outcomes to specific components. This uncertainty limited the depth of the analysis and the precision with which conclusions could be drawn. Moreover, in forthcoming studies, it may be beneficial to explore storage options such as water, artificial saliva, or alternative accelerated aging solutions prior to evaluating BS [17]. Including multiple storage times in the experimental design can enhance its rigor and coherence, and this approach could be considered for future analyses. The μTBS method for dentin testing presents challenges including a time-consuming sample preparation and potential damage to the dentin structure, while the interpretation of results requires expertise and a consideration of various factors. Nevertheless, Beloica et al., [64] noted that the adhesive system significantly influences BS irrespective of the testing methodology employed. Adhesion to tooth structure should ideally give retentive strength, provide a marginal seal, be simple to create, and be clinically durable. The authors recommend the μTBS test, particularly following a durability challenge, as a suitable surrogate assessment of dental composite restorative retention (direct restoration). More sophisticated techniques should be employed to assess solvent evaporation, such as gas chromatography [63]. Incorporating quantitative measurements of solvent evaporation rates and their correlation with bonding efficacy would strengthen the validity of the findings. Subsequent studies could employ a precise, safe, and non-destructive technique such as scanning confocal microscopy for the evaluation of the resin-dentin interface [65]. Further studies could explore the temperature rise in the pulp chamber when employing warm air to better understand the practical implications and potential limitations associated with using higher air temperatures in dental procedures. Additionally, in a clinical context, the difficulty in standardizing the temperature of the air emitted from the triple syringe presents a practical challenge. This variability in environmental conditions may compromise the accuracy of the experimental controls, reflecting a potential mismatch between idealized laboratory settings and the dynamic nature of real-world clinical scenarios. Validation procedures, including testing methodologies and results, would be essential for assessing this device's efficacy and reliability in delivering warm air for adhesive applications.

4.5. Conclusions

In summary, higher air-blowing temperatures (40 °C and 60 °C) during application could potentially enhance the dentinal BS of adhesive systems (PBU, OBU, CSE, and OBFL), a variable influenced by specific materials used in clinical settings, indicating the crucial role of warmer temperatures in improving the quality of the HL and promoting better interaction between adhesives and dentin tissue. The efficacy of utilizing a warm air stream for solvent evaporation, though encouraging, necessitates further validation through rigorous randomized clinical trials.

4.6. References

1. Chen, Y.; Yan, X.; Li, K.; Zheng, S.; Sano, H.; Zhan, D.; Fu, J. Effect of air-blowing temperature and water storage time on the bond strength of five universal adhesive systems to dentin. *Dent. Mater. J.* **2021**, *40*, 116–122.
2. Cardoso, M.; de Almeida Neves, A.; Mine, A.; Coutinho, E.; Van Landuyt, K.; De Munck, J.; Van Meerbeek, B. Current Aspects on Bonding Effectiveness and Stability in Adhesive Dentistry. *Aust. Dent. J.* **2011**, *56*, 31–44.
3. Loguercio, A.D.; Luque-Martinez, I.; Muñoz, M.A.; Szesz, A.L.; Cuadros-Sánchez, J.; Reis, A. A Comprehensive Laboratory Screening of Three-Step Etch-and-Rinse Adhesives. *Oper. Dent.* **2014**, *39*, 652–662.
4. Alex, G. Universal Adhesives: The Next Evolution in Adhesive Dentistry? *Compend. Contin. Educ. Dent.* **2015**, *36*, 15–26.
5. Bedran-Russo, A.; Leme-Kraus, A.A.; Vidal, C.M.P.; Teixeira, E.C. An Overview of Dental Adhesive Systems and the Dynamic Tooth–Adhesive Interface. *Dent. Clin. N. Am.* **2017**, *61*, 713–731.
6. Kambaram, M.; Yiu, C.K.Y.; Matinlinna, J.P. An overview of solvents in resin-dentin bonding. *Int. J. Adhes. Adhes.* **2015**, *57*, 22–33.

7. Fontes, S.T.; Fernández, M.R.; Ogliari, F.A.; de Carvalho, R.V.; de Moraes, R.R.; Pinto, M.B.; Piva, E. Tetrahydrofuran as solvent in dental adhesives: Cytotoxicity and dentin bond stability. *Clin. Oral. Investig*. **2013,** *17*, 237–242.
8. Tjäderhane, L.; Mehtälä, P.; Scaffa, P.; Vidal, C.; Pääkkönen, V.; Breschi, L.; Hebling, J.; Tay, F.R.; Nascimento, F.D.; Pashley, D.H.; Carrilho, M.R. The effect of dimethyl sulfoxide (DMSO) on dentin bonding and nanoleakage of etch-and-rinse adhesives. *Dent. Mater*. **2013**, *29*, 1055–1062.
9. Klein-Junior, C.A.; Zander-Grande, C.; Amaral, R.; Stanislawczuk, R.; Garcia, E.J.; Baumhardt-Neto, R.; Meier, M.M.; Loguercio, A.D.; Reis, A. Evaporating Solvents with a Warm Air-Stream: Effects on Adhesive Layer Properties and Resin–Dentin Bond Strengths. *J. Dent.* **2008**, *36*, 618–625.
10. Bourgi, R.; Hardan, L.; Rivera-Gonzaga, A.; Cuevas-Suárez, C.E. Effect of Warm-Air Stream for Solvent Evaporation on Bond Strength of Adhesive Systems: A Systematic Review and Meta-Analysis of in Vitro Studies. *Int. J. Adhes. Adhes.* **2021**, *105*, 102794.
11. Bail, M.; Malacarne-Zanon, J.; Silva, S.; Anauate-Netto, A.; Nascimento, F.; Amore, R.; Lewgoy, H.; Pashley, D.H.; Carrilho, M. Effect of Air-Drying on the Solvent Evaporation, Degree of Conversion and Water Sorption/Solubility of Dental Adhesive Models. *J. Mater. Sci. Mater. Med.* **2012**, *23*, 629–638.
12. Taguchi, K.; Hosaka, K.; Ikeda, M.; Kishikawa, R.; Foxton, R.; Nakajima, M.; Tagami, J. The Effect of Warm Air-Blowing on the Microtensile Bond Strength of One-Step Self-Etch Adhesives to Root Canal Dentin. *J. Prosthodont. Res.* **2018**, *62*, 330–336.
13. Bourgi, R.; Hardan, L.; Cuevas-Suárez, C.E.; Scavello, F.; Mancino, D.; Kharouf, N.; Haikel, Y. The Use of Warm Air for Solvent Evaporation in Adhesive Dentistry: A Meta-Analysis of In Vitro Studies. *J. Funct. Biomater.* **2023**, *14*, 285.
14. Ogura, Y.; Shimizu, Y.; Shiratsuchi, K.; Tsujimoto, A.; Takamizawa, T.; Ando, S.; Miyazaki, M. Effect of Warm Air-Drying on Dentin Bond Strength of Single-Step Self-Etch Adhesives. *Dent. Mater. J.* **2012**, *31*, 507–513.
15. Santana, F.R.; Pereira, J.C.; Pereira, C.A.; Fernandes Neto, A.J.; Soares, C.J. Influence of Method and Period of Storage on the Microtensile Bond Strength of Indirect Composite Resin Restorations to Dentine. *Braz. Oral Res.* **2008**, *22*, 352–357.
16. Yonekura, K.; Hosaka, K.; Tichy, A.; Taguchi, K.; Ikeda, M.; Thanatvarakorn, O.; Prasansuttiporn, T.; Nakajima, M.; Tagami, J. Air-Blowing Strategies for Improving the Microtensile Bond Strength of One-Step Self-Etch Adhesives to Root Canal Dentin. *Dent. Mater. J.* **2020**, *39*, 892–899.
17. Armstrong, S.; Breschi, L.; Özcan, M.; Pfefferkorn, F.; Ferrari, M.; Van Meerbeek, B. Academy of Dental Materials Guidance on in Vitro Testing of Dental Composite Bonding Effectiveness to Dentin/Enamel Using Micro-Tensile Bond Strength (μTBS) Approach. *Dent. Mater.* **2017**, *33*, 133–143.
18. Garcia, F.C.; Almeida, J.C.; Osorio, R.; Carvalho, R.M.; Toledano, M. Influence of Drying Time and Temperature on Bond Strength of Contemporary Adhesives to Dentine. *J. Dent.* **2009**, *37*, 315–320.
19. Hanabusa, M.; Mine, A.; Kuboki, T.; Momoi, Y.; Van Ende, A.; Van Meerbeek, B.; De Munck, J. Bonding effectiveness of a new «multi-mode» adhesive to enamel and dentine. *J. Dent.* **2012**, *40*, 475–484.
20. Tsujimoto, A.; Fischer, N.G.; Barkmeier, W.W.; Latta, M.A. Bond durability of two-step HEMA-free universal adhesive. *J. Funct. Biomater.* **2022,** *13*, 134.
21. Pashley, D.H.; Agee, K.; Nakajima, M.; Tay, F.; Carvalho, R.; Terada, R.; Harmon, F.; Lee, W.; Rueggeberg, F. Solvent-induced Dimensional Changes in EDTA-demineralized Dentin Matrix. *J. Biomed. Mater. Res*. **2001**, *56*, 273–281.
22. Saeed, N.A.; Tichy, A.; Kuno, Y.; Hosaka, K.; Tagami, J.; Nakajima, M. Effect of Surface Moisture on Bur-Cut Dentin on Bonding of HEMA-Free and HEMA-Containing Universal Adhesives with or without Methacrylamide Monomer. *J. Adhes. Dent.* **2021**, *23*, 327–334.
23. Paken, G.; Çömlekoğlu, M.E.; Sonugelen, M. Detection of the hybrid layer biodegradation initiation factor with a scanning electron microscope. *Microsc. Res. Tech*. **2021**, *84*, 2166-2175.
24. Breschi, L.; Maravic, T.; Cunha, S.R.; Comba, A.; Cadenaro, M.; Tjäderhane, L.; Pashley, D.H.; Tay, F.R.; Mazzoni, A. Dentin bonding systems: From dentin collagen structure to bond preservation and clinical applications. *Dent. Mater.* **2018**, *34*, 78-96.
25. Bourgi, R.; Kharouf, N.; Cuevas-Suárez, C.E.; Lukomska-Szymańska, M.; Devoto, W.; Kassis, C.; Hasbini, O.; Mancino, D.; Haikel, Y.; Hardan, L. Effect of Modified Triple-Layer Application on the Bond Strength of Different Dental Adhesive Systems to Dentin. *J. Funct. Biomater.* **2023**, *14*, 522.
26. Hardan, L.; Bourgi, R.; Kharouf, N.; Mancino, D.; Zarow, M.; Jakubowicz, N.; Haikel, Y.; Cuevas-Suárez, C.E. Bond Strength of Universal Adhesives to Dentin: A Systematic Review and Meta-Analysis. *Polymers* **2021**, *13*, 814.

27. Al-Salamony, H.; Naguibb, E.A.; Hamzac, H.S.; Younisd, S.H. The Effect of Warm Air Solvent Evaporation on Microtensile Bond Strength of Two Different Self-Etch Adhesives to Dentin (In Vitro Study). *SYLWAN* **2020**, *164*, 479–497.
28. Van Meerbeek, B.; Van Landuyt, K.; De Munck, J.; Hashimoto, M.; Peumans, M.; Lambrechts, P.; Yoshida, Y.; Inoue, S.; Suzuki, K. Technique-sensitivity of contemporary adhesives. *Dent. Mater. J.* **2005**, *24*, 1–13.
29. Van Landuyt, K.L.; Snauwaert, J.; Peumans, M.; De Munck, J.; Lambrechts, P.; Van Meerbeek, B. The role of HEMA in one-step self-etch adhesives. *Dent. Mater.* **2008**, *24*, 1412–1419.
30. Frassetto, A.; Breschi, L.; Turco, G.; Marchesi, G.; Di Lenarda, R.; Tay, F.R.; Pashley, D.H.; Cadenaro, M. Mechanisms of degradation of the hybrid layer in adhesive dentistry and therapeutic agents to improve bond durability—A literature review. *Dent. Mater*. **2016**, *32*, 41–53.
31. Spencer, P.; Wang, Y.; Walker, M.P.; Wieliczka, D.M.; Swafford, J.R. Interfacial chemistry of the dentin/adhesive bond. *J. Dent. Res.* **2000**, *79*, 1458–1463.
32. Choi, A.N.; Lee, J.H.; Son, S.A.; Jung, K.H.; Kwon, Y.H.; Park, J.K. Effect of Dentin Wetness on the Bond Strength of Universal Adhesives. *Materials* **2017**, *10*, 1224.
33. Spencer, P.; Wang, Y. Adhesive phase separation at the dentin interface under wet bonding conditions. *J. Biomed. Mater. Res.* **2002**, *62*, 447–456.
34. Nagura, Y.; Tsujimoto, A.; Fischer, N.G.; Baruth, A.G.; Barkmeier, W.W.; Takamizawa, T.; Latta, M.A.; Miyazaki, M. Effect of Reduced Universal Adhesive Application Time on Enamel Bond Fatigue and Surface Morphology. *Oper. Dent.* **2019**, *44*, 42–53.
35. Tsujimoto, A.; Shimatani, Y.; Nojiri, K.; Barkmeier, W.W.; Markham, M.D.; Takamizawa, T.; Latta, M.A.; Miyazaki, M. Influence of surface wetness on bonding effectiveness of universal adhesives in etch-and-rinse mode. *Eur. J. Oral. Sci.* **2019**, *127*, 162–169.
36. Han, F.; Dai, S.; Yang, J.; Shen, J.; Liao, M.; Xie, H.; Chen, C. Glycerol Phosphate Dimethacrylate: An Alternative Functional Phosphate Ester Monomer to 10-Methacryloyloxydecyl Dihydrogen Phosphate for Enamel Bonding. *ACS. Omega.* **2020**, *5*, 24826–24837.
37. Sanghvi, M.R.; Tambare, O.H.; More, A.P. Performance of various fillers in adhesives applications: A review. *Polym. Bull.* **2022**, *79*, 10491–10553.
38. Jacobsen, T.; Söderholm, K. Effect of primer solvent, primer agitation, and dentin dryness on shear bond strength to dentin. *Am. J. Dent*. **1998**, *11*, 225–228.
39. Nihi, F.M.; Fabre, H.S.C.; Garcia, G.; Fernandes, K.B.P.; Ferreira, F.B.D.A.; Wang, L. In vitro assessment of solvent evaporation from commercial adhesive systems compared to experimental systems. *Braz. Dent. J.* **2009**, *20*, 396–402.
40. De Munck, J.; Van Landuyt, K.; Peumans, M.; Poitevin, A.; Lambrechts, P.; Braem, M.; Van Meerbeek, B. A critical review of the durability of adhesion to tooth tissue: Methods and results. *J. Dent. Res*. **2005**, *84*, 118–132.
41. Van Meerbeek, B.; Yoshihara, K.; Yoshida, Y.; Mine, A.J.; De Munck, J.; Van Landuyt, K.L. State of the art of self-etch adhesives. *Dent. Mater*. **2011**, *27*, 17–28.
42. Peumans, M.; De Munck, J.; Van Landuyt, K.; Van Meerbeek, B. Thirteen-year randomized controlled clinical trial of a twostep self-etch adhesive in non-carious cervical lesions. *Dent. Mater*. **2015**, *31*, 308–314.
43. Cuevas-Suárez, C.E.; Ramos, T.S.; Rodrigues, S.B.; Collares, F.M.; Zanchi, C.H.; Lund, R.G.; da Silva, A.F.; Piva, E. Impact of Shelf-Life Simulation on Bonding Performance of Universal Adhesive Systems. *Dent. Mater.* **2019**, *35*, e204–e219.
44. Rodrigues, S.B.; Petzhold, C.L.; Gamba, D.; Leitune, V.C.B.; Collares, F.M. Acrylamides and methacrylamides as alternative monomers for dental adhesives. *Dent. Mater*. **2018**, *34*, 1634–1644.
45. Peumans, M.; De Munck, J.; Van Landuyt, K.L.; Poitevin, A.; Lambrechts, P.; Van Meerbeek, B. Eight-year clinical evaluation of a 2-step self-etch adhesive with and without selective enamel etching. *Dent. Mater*. **2010**, *26*, 1176–1184.
46. Loguercio, A.D.; Bittencourt, D.D.; Baratieri, L.N.; Reis, A. A 36-month evaluation of self-etch and etch- and-rinse adhesives in noncarious cervical lesions. *J. Am. Dent. Assoc.* **2007**, *138*, 507–514.
47. Teshima, I. Degradation of 10-Methacryloyloxydecyl Dihydrogen Phosphate. *J. Dent. Res.* **2010**, *89*, 1281–1286.
48. Van Meerbeek, B.; Yoshihara, K.; Van Landuyt, K.; Yoshida, Y.; Peumans, M. From Buonocore's Pioneering Acid-Etch Technique to Self-Adhering Restoratives. A Status Perspective of Rapidly Advancing Dental Adhesive Technology. *J. Adhes. Dent.* **2020**, *22*, 7–34.
49. Luque-Martinez, I.V.; Perdigão, J.; Muñoz, M.A.; Sezinando, A.; Reis, A; Loguercio, A.D. Effects of solvent evaporation time on immediate adhesive properties of universal adhesives to dentin. *Dent. Mater*. **2014**, *30*, 1126–1135.

50. Cho, B.; Dickens, S.H. Effects of the acetone content of single solution dentin bonding agents on the adhesive layer thickness and the microtensile bond strength. *Dent. Mater*. **2004**, *20*, 107–115.
51. Ahmed, M.H.; Yoshihara, K.; Yao, C.; Okazaki, Y.; Van Landuyt, K.; Peumans, M.; Van Meerbeek, B. Multiparameter evaluation of acrylamide HEMA alternative monomers in 2-step adhesives. *Dent. Mater.* **2021**, *37*, 30–47.
52. Fukegawa, D.; Hayakawa, S.; Yoshida, Y.; Suzuki, K.; Osaka, A.; Van Meerbeek, B. Chemical interaction of phosphoric acid ester with hydroxyapatite. *J. Dent. Res.* **2006**, *85*, 941–944.
53. Valsan, D.; Bhaskaran, S.; Mathew, J.; Hari, K.; Joy, J. Comparative Evaluation of the Bonding Efficacy of Multimode Adhesive, Two-Step Self-Etch Adhesive, and a Total-Etch System to Pulpal Floor Dentin—An *In vitro* Study. *Contemp. Clin. Dent.* **2023**, *14*, 104–108.
54. Pashley, D.H.; Tay, F.R.; Breschi, L.; Tjäderhane, L.; Carvalho, R.M.; Carrilho, M.; Tezvergil-Mutluay, A. State of the Art Etch-and-Rinse Adhesives. *Dent. Mater.* **2011**, *27*, 1–16.
55. Moura, S.K.; Lemos, L.V.; Myszkovisk, S.; Provenzano, M.G.; Balducci, I.; Myaki, S.I. Bonding durability of dental sealants to deciduous and permanent teeth. *Braz. J. Oral. Sci*. **2014**, *13*, 198–202.
56. El Zohairy, A.; De Gee, A.; De Jager, N.; Van Ruijven, L.; Feilzer, A. The Influence of Specimen Attachment and Dimension on Microtensile Strength. *J. Dent. Res.* **2004**, *83*, 420–424.
57. Takahashi, M.; Nakajima, M.; Hosaka, K.; Ikeda, M.; Foxton, R.M.; Tagami, J. Long-term evaluation of water sorption and ultimate tensile strength of HEMA-containing/-free one-step self-etch adhesives. *J. Dent.* **2011**, *39*, 506–512.
58. Sano, H.; Chowdhury, A.F.M.A.; Saikaew, P.; Matsumoto, M.; Hoshika, S.; Yamauti, M. The microtensile bond strength test: Its historical background and application to bond testing. *Jpn. Dent. Sci. Rev*. **2020**, *56*, 24-31.
59. Armstrong, S.; Geraldeli, S.; Maia, R.; Raposo, L.H.A.; Soares, C.J.; Yamagawa, J. Adhesion to tooth structure: a critical review of "micro" bond strength test methods. *Dent. Mater*. **2010**, *26*, 50-62.
60. Reis, A.; Klein-Junior, C.A.; de Souza, F.C.; Stanislawczuk, R.; Loguercio, A.D. The Use of Warm Air Stream for Solvent Evaporation: Effects on the Durability of Resin-Dentin Bonds. *Oper. Dent.* **2010**, *35*, 29–36.
61. Kharouf, N.; Ashi, T.; Eid, A.; Maguina, L.; Zghal, J.; Sekayan, N.; Bourgi, R.; Hardan, L.; Sauro, S.; Haikel, Y. Does Adhesive Layer Thickness and Tag Length Influence Short/Long-Term Bond Strength of Universal Adhesive Systems? An in-Vitro Study. *Appl. Sci.* **2021**, *11*, 2635.
62. Sinhoreti, M.A.C.; Soares, E.F.; Abuna, G.F.; Correr, L.; Roulet, J.-F.; Geraldeli, S. Microtensile Bond Strength of Adhesive Systems in Different Dentin Regions on a Class II Cavity Configuration. *Braz. Dent. J.* **2017**, *28*, 474–481.
63. Michelsen, V.B.; Moe, G.; Skålevik, R.; Jensen, E.; Lygre, H. Quantification of organic eluates from polymerized resin-based dental restorative materials by use of GC/MS. *J. Chromatogr. B*. **2007**, *850*, 83–91.
64. Beloica, M.; Goracci, C.; Carvalho, C.-A.; Radovic, I.; Margvelashvili, M.; Vulicevic, Z.-R.; Ferrari, M. Microtensile vs microshear bond strength of all-in-one adhesives to unground enamel. *J. Adhes. Dent.* **2010**, *12*, 427–433.
65. Sahadi, B.O.; Sebold, M.; André, C.B.; Nima, G.; Dos Santos, A.; Nascimento, F.D.; dos Santos Tersariol, I.L.; Giannini, M. Effect of experimental dentin etchants on dentin bond strength, metalloproteinase inhibition, and antibiofilm activity. *Dent. Mater*. **2024**, *40*, e12-e23.

4.7. Publication of Chapter IV

biomimetics

MDPI

Article

Warm Air Delivery in Adhesive Application: Effect on Bonding Performance and Morphological Outcomes

Rim Bourgi [1,2], Naji Kharouf [2,3], Carlos Enrique Cuevas-Suárez [4,*], Monika Lukomska-Szymanska [5], Khalil Kharma [1], Fabienne Hajj Moussa [6], Manar Metlej [7], Youssef Haikel [2,3,8,†] and Louis Hardan [1,*,†]

[1] Department of Restorative Dentistry, School of Dentistry, Saint-Joseph University, Beirut 1107 2180, Lebanon; rim.bourgi@net.usj.edu.lb (R.B.); khalil.kharma@usj.edu.lb (K.K.)
[2] Department of Biomaterials and Bioengineering, INSERM UMR_S 1121, University of Strasbourg, 67000 Strasbourg, France; dentistenajikharouf@gmail.com (N.K.); youssef.haikel@unistra.fr (Y.H.)
[3] Department of Endodontics and Conservative Dentistry, Faculty of Dental Medicine, University of Strasbourg, 67000 Strasbourg, France
[4] Dental Materials Laboratory, Academic Area of Dentistry, Autonomous University of Hidalgo State, San Agustín Tlaxiaca 42160, Mexico
[5] Department of General Dentistry, Medical University of Lodz, 92-213 Lodz, Poland; monika.lukomska-szymanska@umed.lodz.pl
[6] Laboratoire de Pharmacologie, Pharmacie Clinique et Contrôle de Qualité des Médicaments, Faculty of Pharmacy, Saint-Joseph University, Beirut 1107 2180, Lebanon; fabienne.hajjmoussa@usj.edu.lb
[7] Department of Prosthetic Dentistry, School of Dentistry, Saint-Joseph University, Beirut 1107 2180, Lebanon; manar.metlej@net.usj.edu.lb
[8] Pôle de Médecine et Chirurgie Bucco-Dentaire, Hôpital Civil, Hôpitaux Universitaire de Strasbourg, 67000 Strasbourg, France
* Correspondence: cecuevas@uaeh.edu.mx (C.E.C.-S.); louis.hardan@usj.edu.lb (L.H.); Tel.: +52-(771)-72000 (C.E.C.-S.); +961-3700663 (L.H.)
† These authors contributed equally to this work.

Abstract: Solvent evaporation within an adhesive layer is a crucial step during a bonding process. The aim of this current research was to test whether the use of different air temperatures (20 °C, 40 °C, and 60 °C) for solvent evaporation improves the performance of four adhesive systems to dentin. Sixty non-carious human molar teeth were randomly prepared for micro-tensile bond strength (μTBS) tests. Four different adhesive systems, Prime&Bond Universal (PBU), OptiBond Universal (OBU), OptiBond FL (OBFL), and Clearfil SE (CSE), were applied following the manufacturer's instructions. Three groups based on the air-drying temperature were used: solvent evaporation was performed with either of warm (40 °C), (60 °C), and cold air as control group (20 °C) for 10 s at a distance of 5 cm. In all bonded surfaces, three resin composite (Reflectys, Itena Clinical, Paris, France) layers of 2 mm thickness were built up. The resin–dentin samples were kept in distilled water at 37 °C for 24 h and 6 months, respectively, before μTBS testing. Failure analysis, scanning electron microscopy of resin–dentin bonded interface, and solvent evaporation rate were tested as secondary variables. All analyses were conducted using a significance level of $\alpha = 0.05$. Bond strength (BS) values were similar among all the adhesive systems used ($p > 0.05$). Also, the aging factor did not affect the BS ($p > 0.05$). Only the factor of temperature used for solvent evaporation resulted in a statistically significant effect ($p < 0.05$), with the temperature of 60 °C being the highest value ($p < 0.05$). A failure mode evaluation revealed mostly adhesive or mixed modes of failures in all the different temperatures of air used for the solvent evaporation of each adhesive system. The thickness of the adhesive layer and the creation of resin tags varied amongst the temperatures evaluated. For all adhesive systems tested, the use of 40 °C or 60 °C air for solvent evaporation led to an increased mass loss. Warmer temperatures for solvent evaporation contributed positively to bonding performance, enhancing both the quality of the adhesive layer and its interaction with the dentin tissue. Optimizing solvent evaporation with warmer air temperatures (40 °C and 60 °C) significantly improved μTBS, offering a practical means to enhance the quality and longevity of adhesive restorations in esthetic dentistry.

check for updates

Citation: Bourgi, R.; Kharouf, N.; Cuevas-Suárez, C.E.; Lukomska-Szymanska, M.; Kharma, K.; Moussa, F.H.; Metlej, M.; Haikel, Y.; Hardan, L. Warm Air Delivery in Adhesive Application: Effect on Bonding Performance and Morphological Outcomes. *Biomimetics* **2024**, *9*, 194. https://doi.org/10.3390/biomimetics9040194

Academic Editor: Xiang Ge

Received: 22 February 2024
Revised: 14 March 2024
Accepted: 21 March 2024
Published: 24 March 2024

Chapter V: General Conclusion and Future Directions

5.1. General Conclusion

Each adhesive system will have slightly varied protocols and recommended application based on the adhesive's specific composition. To attain improved dentinal BS, adhesive systems must follow a few essential criteria. Based on this thesis, it appears that the AA might be suggested as the gold-standard for applying an adhesive system to dentin. Furthermore, the A method worked well for almost all of the adhesives tested. Notably, a discernable pattern develops, indicating that warmer temperatures (40 °C and 60 °C) for solvent evaporation improve bonding performance, optimizing both HL quality and adhesive interaction with dentin tissue.

More particular, after 6 months of aging, the CV and CVM modalities for PBU and CSE were deemed stable. Furthermore, the combination of ABT and an MLA was a viable solution for the highly filled OBFL. This explains why the LR-MTLA was regarded as an innovative method in the field of adhesive dentistry, with satisfactory bond stability with time. In addition, these intriguing findings indicate the possible advantages of using warmer temperatures during the adhesive application procedure.

However, understanding the composition, properties, and adhesion mechanisms of each adhesive system is critical for developing optimal bonding approaches under clinical circumstances. The use of these methodologies is presently in its early stages, yet it should lead to more awareness of different tricks that improve dentinal adhesion in the oral environment. Continued refinement and enhancement of the procedures, as well as an increased emphasis on their application, are critical to overcoming the challenges that restrict restorative dentistry's success.

5.2. Future Directions

Given that there are still several unresolved problems concerning the longevity of the adhesive interface, it is truly astounding how far adhesive bonding has progressed over the last 50-60 years. Techniques qualified of forming stable resin-dentin bonds while resisting collagenolytic hydrolysis will most likely be available in the coming years, raising the efficacy of dental treatments.

Some future techniques that can be tested in this thesis include:

- SDE for 3 s with the adhesives tested in this study or other adhesives for comparison purposes.
- SE vs ER with UAs. Only SE mode was used in this study.
- Another application. In this study, three main topics were explored (application modalities, different layer application, and various dry-air temperatures). Development of various application strategies to enhance the bond performance of adhesives to dentin will be a future target.
- UA could be included with the application modalities, double coat of adhesive vs MTLA could be performed, in addition a warm temperature between 40 °C and 60 °C might be implemented in further investigations.
- Thick vs thin smear layer. In this study, a thick smear layer was obtained.
- Another brand of UAs. In this study, only two UAs from two manufacturers were used.

- Bonding to enamel with the same protocols used in this thesis should be implemented in future.
- Time of adhesive application. In this study, the primer or the adhesive were applied according to the time (20 s) although in the literature, varying times were used.
- μTBS in "wet" (after 5 min of removal storage) and "dehydrated" states of sticks (tested after 10, 15 min and 24 h). Sticks were directly used for the BS test. Note that sticks were not dehydrated in this study. (Dehydration takes around 2 min, but the researcher can do it for 10 min to 24 h. Other studies dehydrate for varying durations).
- CA analysis of the adhesives via mobile dental photography or Digital Single Lens Reflex. In this study, a CA analyzer was used, but the use of other tools is advised in future tests.
- Pulpal pressure. This study was conducted without a simulated pulpal pressure which can affect the results negatively because the field of work included a condition where dentin is vital.
- *In vivo.* In this *in vitro* study, an extracted tooth was used which is different from a clinical condition. Future clinical studies are important.
- Evaluation of the long-term resin-dentin bond degradation. Only 6 months of aging were assessed.
- Development of the device for warm air-drying. In this study, only a prototype was used.
- A variation in terms of the photopolymerization of each layer should be tested in the future.
- Coming dentin adhesives might also undertake a more instrumental function in therapeutics apart from caries prevention.
- Different methodologies could be explored in further studies including temperature rise in the pulp chamber when using warmer temperatures, cytotoxicity against odontoblastic cells, NL for all the resin-dentin sticks, depth of penetration of the adhesives with different methods used, thickness of HL and length of RTs, micro-CT instead of SEM, gas chromatography for solvent evaporation, biocompatibility, solubility, degree of conversion, shelf-life stability, and polymerization rate of the adhesive applied with different modalities tested.
- Testing a new standard flock-free micro-applicator (ZerofloX) against the micro-brushes used in this thesis. ZerofloX diverges from other applicators presented on the dental market by using fiber-free elastomer bristles rather than the usual fiber flocking with utmost applicator brushes.

Chapter VI: Research Gap

6.1. Research Gap

This study lacks some important points:

- Simulated pulpal pressure: the effect of dentin fluid and the presence of odontoblastic processes throughout most of the tubule length in clinical studies could not be found in *in vitro* conditions. Ideally, when an adhesive is tested *in vitro*, a clinical investigation should be conducted immediately to assess the clinical effectiveness of the adhesive.
- Lack of a comparison of all generations of adhesive systems.
- Bonding to enamel. Only bonding to dentin structure was tested in this thesis.
- The smear layer was standardized using 320 SiC paper wich is clinically considered as a thick layer but not as compared to *in vivo* burs made smear layer.
- Cavity-type sample preparation may be recommended for μTBS testing as a more clinically relevant strategy.
- An increase in the number of adhesive joint failures could be observed when exposed to long-term water storage. Storage in this study was done for 24 h and 6 months only.
- The UAs were only tested in SE mode. Knowing that omitting fillers is advantageous for UAs in both ER and SE modes. Progress in investigation might be of great interest for testing the same adhesives in ER mode.
- Testing of the adhesives under oversaturated phenomenon. Knowing that UAs are generally less sensitive to dentin wetness, future studies testing the same adhesives in such conditions may be of great interest.

Résumé en français de la thèse intitulée : Effet de différentes modalités d'application et de la température d'évaporation de l'air chaud sur la performance de quatre systèmes adhésifs à la dentine

Résumé

La principale visée de la dentisterie adhésive est d'améliorer la compatibilité entre les adhésifs actuels et les substrats dentaires en employant diverses techniques d'application pour assurer l'herméticité et la pérennité des restaurations. Par conséquent, l'objectif de cette thèse était d'évaluer les performances d'adhésion de quatre systèmes adhésifs – Prime&Bond Universal (PBU), Clearfil SE Bond (CSE), OptiBond Universal (OBU) et OptiBond FL (OBFL) – sur la dentine. Le premier facteur étudié était (1) les modes d'application (application passive (PA), application active (AA), application modifiée Compo-Vibes (CVM) et application Compo-Vibes (CV)). Le deuxième facteur étudié était (2) l'impact de l'application triple couche modifiée (MTLA) en conjonction avec la technique de liaison active (ABT) sur la force de liaison (BS) de ces adhésifs au substrat dentinaire. Les adhésifs ont été appliqués selon les stratégies suivantes : application active unique (A) et application de trois couches adhésives incluant Actif-Passif-Passif (APP), Actif-Actif-Passif (AAP) et Actif-Actif-Actif (AAA). Le troisième facteur visait (3) à déterminer si des températures variables de l'air (20 °C, 40 °C et 60 °C) pendant l'évaporation du solvant pouvaient améliorer les performances des systèmes adhésifs testés sur la dentine.

Sur la base des différentes approches utilisées, des molaires humaines non cariées ont été préparées et réparties au hasard pour un test de force de liaison par micro-traction (µTBS) et une analyse du mode de rupture après 24 h et 6 mois. Une évaluation de l'interface composite-dentine a été réalisée à l'aide d'un microscope électronique à balayage (MEB). Pour les différentes modalités d'application, l'angle de contact adhésif (CA) a été mesuré sur les surfaces dentinaires préparées. De même, pour chacune des températures de séchage à l'air, le taux d'évaporation du solvant a été examiné comme variable secondaire dans de petits récipients en verre opaques de poids connu. Une analyse de variance à deux facteurs (ANOVA) a été réalisée pour évaluer la µTBS de toutes les modalités testées. La µTBS a été examinée séparément après 24 h et 6 mois de vieillissement. Le test post hoc de Tukey a été utilisé pour les comparaisons multiples. De plus, les données d'CA ont subi une ANOVA à un facteur avec des comparaisons multiples en utilisant le test de Bonferroni. Un niveau de signification de $\alpha = 0{,}05$ a été utilisé pour toutes les analyses.

Pour (1) : après 24 h, une différence significative avec une valeur de BS plus élevée a été trouvée pour le PBU dans la modalité AA et pour le CSE dans la modalité CVM ($p < 0{,}05$). Cependant, aucune différence significative pour les valeurs de BS n'a été mise en évidence entre les techniques utilisées parmi les autres adhésifs (OBFL et OBU avec $p > 0{,}05$). De plus, à 24 h, seul le PA montrait des différences significatives de BS entre les matériaux testés ($p < 0{,}05$). Après 6 mois, CSE, PBU et OBU présentaient des différences significatives entre les techniques ($p < 0{,}05$), avec une BS plus élevée observée pour le CSE dans les modalités AA et CVM, pour le PBU dans la modalité AA et pour l'OBU dans les modalités AA et PA. Aucune différence significative de BS n'a été trouvée entre les techniques utilisées pour l'adhésif OBFL ($p > 0{,}05$). De plus, seule la technique CVM a démontré des différences significatives de BS entre les matériaux testés après 6 mois ($p < 0{,}05$). CV et CVM ont montré des valeurs diminuées après vieillissement pour le CSE et le PBU, respectivement. Cependant, toutes les modalités ont diminué pour l'OBU et l'OBFL après le vieillissement ($p < 0{,}05$). Tous les adhésifs ont montré une infiltration marquée de résine dans les canalicules dentinaires en AA parmi toutes les modalités testées. Les deux systèmes d'adhésifs universels (OBU et PBU) ont démontré un CA statistiquement inférieur par rapport aux autres systèmes (CSE et OBFL) ($p <$

0,05) lorsqu'ils sont appliqués en mode PA. Concernant le mode AA, seuls les adhésifs CSE et OBFL ont été testés. L'AA a démontré des valeurs d'CA inférieures par rapport aux mêmes adhésifs en PA ($p < 0,05$).

Pour (2) : à 24 h de vieillissement, tous les facteurs testés ne montraient pas de différences significatives de BS ($p > 0,05$) pour le CSE. Pour OBFL, OBU et PBU, des valeurs statistiquement plus élevées ont été observées pour la technique A ($p < 0,05$). De plus, il n'y avait pas de variation significative de BS entre les techniques APP, AAP et AAA ($p > 0,05$) pour OBFL et PBU. Cependant, pour l'OBU, il n'y avait pas de différence significative de BS entre les techniques A et AAA ($p > 0,05$). Après 6 mois de vieillissement, la technique A a montré des valeurs statistiquement plus élevées par rapport aux autres techniques ($p < 0,01$), à l'exception de l'OBFL, où les techniques A et AAA ont montré des résultats prometteurs comparés à APP et AAP ($p < 0,001$). En comparant les valeurs de la BS de 24 h et 6 mois, uniquement pour le PBU, toutes les techniques utilisées ont abouti à une stabilité dans le temps ($p > 0,05$). Des couches adhésives plus épaisses ont été observées lorsque le MTLA a été appliqué. Seul l'adhésif OBFL a montré la formation de tags en résine dans toutes les modalités testées.

Pour (3) : les valeurs de la BS étaient similaires parmi tous les systèmes adhésifs utilisés ($p > 0,05$). En outre, le vieillissement n'a pas affecté la BS ($p > 0,05$). Seul le facteur température utilisé pour l'évaporation du solvant a entraîné un effet statistiquement significatif ($p < 0,05$), la température de 60 °C ayant les valeurs les plus élevées ($p < 0,05$). L'épaisseur de la couche adhésive et la création de tags en résine variaient selon les températures évaluées. Pour tous les systèmes adhésifs testés, l'utilisation d'air à 40 °C ou 60 °C pour l'évaporation du solvant a généré une perte de masse accrue.

L'évaluation des modes de rupture a révélé principalement des modes de ruptures adhésives ou mixtes quels que soient les modalités d'application pour chaque système adhésif testé.

En conclusion, les matériaux et les techniques d'application influencent la BS. La technique AA apparaît comme la référence recommandée pour l'application des systèmes adhésifs sur la dentine. En addition, les modalités CV et CVM, après 6 mois de vieillissement, présentent respectivement une stabilité pour le PBU et le CSE. Les performances d'adhésion dentinaire en utilisant différentes techniques d'application de triples couches variaient en fonction du matériau utilisé. CSE, OBU et PBU ont bénéficié de la technique A; pour l'OBFL, l'utilisation de la technique AAA pourrait être recommandée pour obtenir une meilleure stabilité de la couche adhésive. De plus, l'optimisation de l'évaporation du solvant avec des températures de l'air plus chaudes (40 °C et 60 °C) améliore considérablement le μTBS, offrant ainsi un moyen pratique d'améliorer la qualité et la longévité des restaurations adhésives en dentisterie esthétique.

Mots clés : interface adhésif-dentine, systèmes adhésifs, liaison dentinaire, air chaud.

Introduction générale

Au fil des années, les systèmes adhésifs ont connu des progrès significatifs dans diverses situations cliniques de la dentisterie restauratrice moderne. Cependant, des défis persistent concernant la durabilité à long terme de l'interface de liaison résine-dentine. La liaison à la structure de l'émail est devenue une procédure prévisible et bien établie, tandis que la liaison à la dentine, en raison de sa structure, sa composition et de son histologie, était considérée comme non prévisible. En effet, l'obtention d'une interdiffusion optimale du système adhésif au sein des fibres de collagène et la préservation de la stabilité à l'interface résine-dentine sont d'une importance cruciale. De ce fait, il est fondamental de comprendre le mécanisme d'hybridation de la dentine au cours duquel se forme une zone d'interdiffusion, également appelée couche hybride (CH), conduisant au développement d'une rétention micromécanique de la restauration dentaire. Ainsi, la CH est formée de résidus d'hydroxyapatite (HAp), de solvants, de collagène et de monomères de résine, dont la résistance globale est affectée par la capacité de chaque élément à résister à la dégradation.

Durant le processus d'adhésion, les monomères acides des systèmes adhésifs auto-mordançants (SAM) ou adhésif de mordançage et rinçage (M+R) entraînent une élimination partielle ou totale de la composante minérale. Après que le substrat dentinaire et amélaire ont été totalement mordançés avec de l'acide phosphorique (H_3PO_4), les adhésifs de M+R sont appliqués, éliminant ainsi la couche de boue dentinaire. En revanche, pour la dentine, la phase de mordançage acide n'est pas nécessaire avec les adhésifs SAM car ils comprennent des monomères avec des groupes fonctionnels acides, qui déminéralisent et préparent simultanément le substrat dentaire. Par conséquent, la couche de boue dentinaire est modifiée et incorporée dans le complexe hybride. Les adhésifs de M+R présentent deux ou trois étapes d'application, tandis que les adhésifs SAM se font en une ou deux étapes.

En ce qui concerne les adhésifs de M+R, OptiBond FL (OBFL, Kerr Co., Orange, CA, USA), un adhésif de M+R en trois étapes (M+R3), est largement reconnu comme un standard par de nombreux professionnels dans le domaine. L'adhésif utilisé (OBFL) contient un ingrédient de liaison hautement hydrophobe appelé diméthacrylate de glycéro-phosphate (GPDM), qui réagit chimiquement avec l'HAp présente dans le substrat émail-dentine mordancé et préparé, renforçant ainsi la résistance à la liaison. Par la suite, des adhésifs de SAM ont été développés, éliminant l'usage de l'H_3PO_4 (pour la dentine) et de la phase de rinçage associée. Clearfil SE Bond (CSE, Kuraray Noritake Dental, Tokyo, Japon) est largement reconnu comme un standard dans cette catégorie ; le primer (apprêt dentinaire) et l'adhésif de ce système sont composés de dihydrogénophosphate de 10-méthacryloyloxydécyle (10-MDP), qui établit une liaison forte et stable avec le calcium (Ca), formant ainsi des nanocouches de 10-MDP-Ca. Plus récemment, les fabricants ont développé des systèmes adhésifs offrant une gamme plus étendue d'applications, pouvant être utilisés dans les deux procédures : M+R et SAM, ainsi que pour le mordançage sélectif des marges de l'émail (SEE). Les fabricants recommandent que les praticiens choisissent leurs procédures de liaison en fonction de leurs préférences personnelles et du type de structure dentaire. Ce groupe innovant d'adhésifs dentinaires, également appelés adhésifs "multi-mode" ou "universels" (UAs), représente la dernière évolution des adhésifs dentaires sur le marché.

Actuellement, ces agents de liaison dentinaire sont composés de monomères contenant à la fois des groupes hydrophobes et hydrophiles, ainsi que des modulateurs de polymérisation et des niveaux relativement élevés de solvants organiques. Ces solvants servent de diluants et améliorent l'étalement, le mouillage et la pénétration des monomères dans les microporosités du réseau de collagène exposé et déminéralisé par l'acide. Il est important de noter que plus la concentration de solvant dans le polymère adhésif est élevée, moins la résistance de l'adhésion résino-dentinaire et les propriétés mécaniques de la résine polymérisée sont importantes.

En principe, tout excès de solvant doit être évaporé de la surface dentinaire en séchant à l'air l'adhésif appliqué avant la photoactivation. L'existence de solvant résiduel pourrait compromettre la photopolymérisation des monomères de résine, entraînant une altération de l'intégrité de la liaison et la formation de vides indésirables dans l'interface adhésive. Ces vides peuvent jouer le rôle de sites initiateurs de défauts, ouvrant la voie à des nano-fuites et produisant une réduction de la résistance à l'adhésion résino-dentinaire. L'évaporation du solvant peut être réalisée en incorporant une période d'évaporation entre l'application et la polymérisation de l'adhésif, ou en employant des techniques de séchage à l'air avec une seringue dentaire. Globalement, l'évaporation du solvant d'un adhésif dépend de plusieurs facteurs, notamment le type de solvant, les compétences de l'opérateur, la distance dent-seringue, le type de monomère et la température de l'air qui semble affecter la durée de séchage à l'air d'un système adhésif.

De plus, diverses stratégies existent pour faciliter l'élimination des solvants et renforcer la longévité des systèmes adhésifs, notamment un temps de photopolymérisation amplifié, un temps d'application prolongé, une application active avec frottement (AA) de l'adhésif, plusieurs couches d'adhésif, un séchage à l'air prolongé et l'utilisation d'un séchage à l'air chaud de l'apprêt dentinaire ou de l'adhésif.

En outre, l'AA ou l'agitation ultrasonique (UA) des systèmes adhésifs ont amélioré l'efficacité de l'adhésion dentinaire en promouvant l'infiltration des adhésifs dentaires à l'intérieur des canalicules dentinaires. Essentiellement, l'AA (avec ou sans énergie ultrasonique) des adhésifs conduit à la pénétration d'un nombre élevé de monomères dans la CH, facilite l'évaporation du solvant et améliore ainsi les caractéristiques de l'interface adhésive. De plus, l'UA augmente l'interaction chimique d'un système adhésif avec la structure dentaire, mais nécessite un dispositif spécial pour les vibrations ultrasoniques. Dernièrement, un nouvel appareil appelé Compo-Vibes (CV, Smile Line, St-Imier, Suisse) a été lancé pour un modelage plus facile des composites, plus rapide et plus efficace. Cet appareil émet des micro-vibrations pour une mise en place plus précise du composite, et cela pourrait être possible grâce à différents embouts. Cet appareil génère des micro-vibrations de 0,158 kHz ou 158 Hz avec une tolérance d'environ +/-15%, permettant des applications de résines composites précises avec diverses pointes. De plus, un micro-applicateur, qui a plusieurs fonctions, a remplacé la brossette fournie avec cet appareil. a été fixée à cet appareil. Jusqu'à présent, aucune étude n'a comparé simultanément l'efficacité de liaison de quatre modalités d'application : application passive (PA, application de l'adhésif sans aucune agitation), AA (application de l'adhésif avec agitation active), micro-vibration avec CV (Smile Line, St-Imier, Suisse) (application de l'adhésif à l'aide d'un embout CV (Smile Line, St-Imier, Suisse) servant de pinceau pour le collage), et une application modifiée de CV (Smile Line, St-Imier, Suisse) à l'aide d'un micro- applicateur (CVM).

D'autre part, l'utilisation d'applications multicouches (MLA) a été associée à une augmentation initiale de la résistance à l'adhésion résine-dentinaire, mais cette amélioration n'a pas perduré après vieillissement. Il est donc crucial de déterminer le nombre optimal de couches d'adhésif nécessaire pour maximiser l'efficacité de la liaison. Les pratiques récentes en matière de collage semblent privilégier une application unique des agents adhésifs, bien que cela puisse ne pas être suffisant pour créer une CH ou adhésive suffisamment épaisse pour assurer une rétention micromécanique avec la résine composite sous-jacente. Des études antérieures ont indiqué que l'utilisation de couches d'adhésif doubles ou triples pouvait améliorer la résistance à l'adhésion résine-dentinaire en favorisant une meilleure infiltration des monomères dans la CH et en renforçant les interactions chimiques.

Pour améliorer la dentisterie adhésive, de nouvelles molécules ont été intégrées aux compositions adhésives, notamment le 10-MDP, le N-phényl-p-phénylènediamine (phényl-P) et l'acide 4-méthacryloxyéthyl trimellitique (4-MET). Ces monomères fonctionnels étaient réputés pour leur capacité à se lier chimiquement au Ca présent dans l'HAp. Parmi ces composés, le 10-MDP s'est avéré avoir le potentiel de fixation chimique le plus fort sur l'HAp, ce qui donne lieu à des sels de Ca stables via une nanocouche. En conséquence, une couche supplémentaire d'application doit être reconnue comme une étape clinique importante. Par ailleurs, le monomère 10-MDP nécessite une durée appropriée de 20 s pour qu'un contact chimique se produise néanmoins, l'ajout d'une deuxième couche d'un tel monomère sans polymériser la première permet à la première couche de s'engager de manière appropriée avec l'HAp, favorisant une liaison renforcée. Donc, aucune étude antérieure disponible dans la littérature scientifique ne s'appuie sur l'application d'une couche adhésive incluant les triples couches adhésives en conjonction avec la « technique de liaison active » (ABT), appelée application triple couche modifiée (MTLA). Une présentation de cette méthode innovante pourrait à juste titre susciter l'intérêt pour l'optimisation de l'adhérence du composite résine à la dentine.

Les flux d'air chaud ont été proposés comme un moyen efficace d'évaporer les solvants d'une solution adhésive. De plus, cette technique augmente l'infiltration de résine dans la dentine préparée, ce qui améliore la résistance dentinaire. Il est à noter que le flux d'air chaud dans la zone de tolérance thermique de l'organe pulpaire dentinaire (29 °C-56 °C) n'a aucun effet indésirable sur l'organe pulpaire dentinaire et que la dentine réagit physiologiquement à ces températures d'air chaud. Cependant, selon une revue systématique et une méta-analyse antérieures, la liaison à la dentine par des systèmes adhésifs SAM ou M+R peut être améliorée en utilisant un flux d'air chaud pour l'évaporation du solvant. De nombreuses températures de l'air chaud, englobant 37 °C, 38 °C, 50 °C, 60 °C et 80 °C, ont été identifiées dans une analyse susmentionnée, cependant aucune température standard n'a été préconisée. Des températures plus élevées d'environ 40 °C et 60 °C étaient efficaces pour améliorer l'évaporation du solvant, néanmoins, la température de 60 °C était plus favorable en termes de l'adhésion résine-dentinaire stable et de moindre dégradation de la liaison. Effectivement, une meilleure définition de la température de référence pour le séchage à l'air devrait être sérieusement envisagée.

En conséquence, l'ABT, le MLA (2 couches et plus) et l'utilisation d'air chaud devraient être proposés par les cliniciens dans leur pratique quotidienne afin d'améliorer la résistance à l'adhésion résine-dentinaire des systèmes adhésifs. Le problème est qu'il n'existe jusqu'à présent aucun protocole spécifique pour obtenir une adhésion stable et optimale des systèmes adhésifs à la dentine. De même, l'amélioration de la résistance à l'adhésion peut être réalisée au moyen de plusieurs stratégies en fonction des expérimentations.

Ainsi, le travail de cette thèse vise à : (1) évaluer les performances de liaison de quatre systèmes adhésifs selon différentes méthodes d'application (PA, AA, CV et CVM), (2) explorer l'impact de l'application multicouche de quatre systèmes adhésifs, avec une couche unique en tant que témoin (A), trois couches adhésives avec activation de la première couche (APP), des deux premières couches (AAP) et des trois couches (AAA), tandis que les couches restantes sont passives, ainsi que la corrélation entre ces méthodes et la résistance à l'adhésion résine-dentinaire, et (3) spécifier l'efficacité d'un dispositif d'évaporation du solvant à air chaud sur les performances de quatre systèmes adhésifs. De plus, l'étude cherche à établir une température standard pour le séchage à l'air du solvant en comparant les effets de trois températures différentes (20 °C, 40 °C et 60 °C). Selon l'hypothèse nulle, l'étude vise à vérifier que : (1) la méthode d'application n'a aucun effet sur la résistance à l'adhésion résine-dentinaire immédiate et à long terme (6 mois) des systèmes adhésifs testés sur la dentine, ni sur la mouillabilité dentinaire suite à l'application d'AA et de PA, (2) l'application multicouche des quatre systèmes adhésifs n'affecte pas la résistance à la liaison résine-dentine et la corrélation entre ces paramètres à 24 h et 6 mois de vieillissement, et (3) l'utilisation d'un flux d'air chaud pour l'évaporation du solvant n'affecte pas les propriétés morphologiques immédiates et à long terme (6 mois) des différents adhésifs sur le substrat dentinaire, et que les températures de séchage à l'air de 20 °C, 40 °C et 60 °C n'ont pas d'effet sur la résistance à la liaison et les propriétés morphologiques des systèmes adhésifs testés.

Le premier chapitre de cette thèse est une revue de la littérature sur l'adhésion :

L'adhésion à l'émail et à la dentine

L'émail et la dentine présentent des défis distincts pour le collage. La structure prismatique fortement minéralisée de l'émail sain contraste avec la nature canaliculaire, organique et hydrophile de la dentine. C'est pourquoi une connaissance et une compréhension approfondies des substrats dentaires représentent le pilier essentiel qui contribue à la réalisation d'une liaison réussie. Le mécanisme fondamental de liaison à l'émail et à la dentine est essentiellement basé sur un processus d'échange dans lequel les minéraux extraits des tissus durs dentaires sont remplacés par des monomères de résine qui, lors de la polymérisation, deviennent micromécaniquement imbriqués dans les porosités créées. Ceci est obtenu par la dissolution des tissus dentaires par le mordançage à l'H_3PO_4 qui les conditionne chimiquement.

L'application des adhésifs en dentisterie

Le champ d'application des systèmes adhésifs est très grand et leur apport à l'essor des thérapeutiques plus conservatrices, plus esthétiques et plus biocompatibles est évident. Ces systèmes connaissent actuellement une utilisation vaste non limitée aux applications suivantes : restauration des lésions traumatiques et carieuses de classe I, II, III, IV, V et VI; réparation des restaurations existantes (amalgame, composite, couronne); collage des fragments fracturés des dents antérieures; scellement des puits et des fissures; désensibilisation des surfaces radiculaires exposées; collage des restaurations en céramique (couronnes céramo-céramique, inlays, onlays, facettes); amélioration de la rétention des couronnes céramo-métalliques; collage des tenons moulés ou préfabriqués en métal et en fibre; collage des brackets en orthodontie; et collage des attelles de contention en parodontologie.

Le mécanisme d'adhésion

L'adhésion se manifeste lorsque deux molécules distinctes réagissent au contact, sous l'influence d'une force d'attraction entre elles. Le composé qui induit cette adhésion est désigné sous le terme d'« adhésif », tandis que le support sur lequel l'adhésif est appliqué est appelé « adhérent ».

L'H_3PO_4 est l'agent de mordançage de choix. Il augmente la surface spécifique, l'énergie de surface et la mouillabilité de l'émail qui sont les propriétés physiques clés dans la réussite du collage amélaire. Celui-ci enlève environ 10 µm de la surface de l'émail, créant au-dessous une couche poreuse de 5 à 50 µm de profondeur. La résine de faible viscosité s'écoule par la suite dans la gaine des prismes et les microporosités de cette couche, puis polymérise pour former une liaison micromécanique avec l'émail. Il est à noter que la force de liaison est très stable en raison de la nature de l'émail (phase inorganique élevée environ 96%, teneur réduite en eau 3 à 4% et 1 à 2% de matière organique).

On distingue trois types différents d'émail mordancé :

- Type I : en nid d'abeilles, idéal pour le collage, implique l'élimination des noyaux de prisme d'émail, alors que les périphéries prismatiques (substance interprismatique) restent intactes, c'est le type le plus commun.

- Type II : aspect pavé, bon pour le collage mais rare, c'est le processus inverse du type I : les gaines des prismes sont élargies et les prismes sont laissés intacts.

- Type III : inadéquat pour le collage, consiste en un mélange des deux types précédents ainsi que des zones amorphes, présence d'un émail aprismatique (Figure 1).

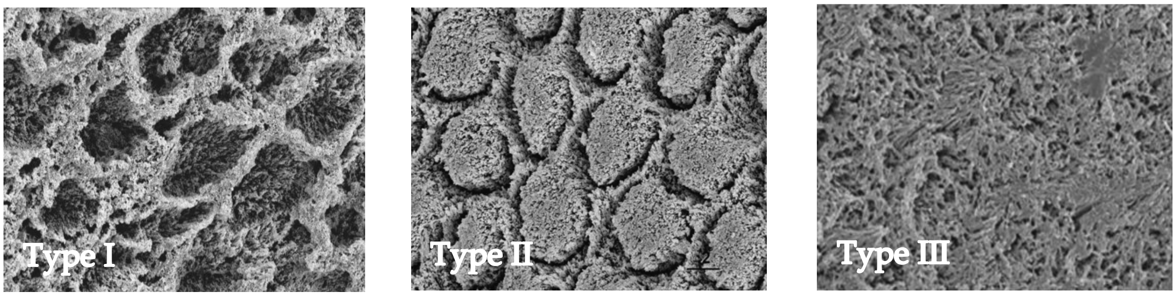


Figure 1 : Différents types d'émail après mordançage.

La dentine est essentielle dans l'utilisation clinique des restaurations adhésives. La dentine est un tissu complexe et, bien que hautement minéralisée, elle a un niveau de minéralisation plus bas (70 % en poids de minéraux et 45 % en volume) et une composition organique plus élevée (20 % en poids de phase organique et 33 % en volume), l'eau constituant le reste. Bien qu'elle soit moins minéralisée que l'émail, la dentine a une teneur en minéraux plus élevée que l'os ou le cément. Le mécanisme de liaison à la dentine concerne un processus de mordançage à l'H_3PO_4 qui déminéralise 5-8 µm de la matrice de dentine intercanalaire pour créer des porosités nanométriques dans la matrice fibrillaire de collagène sous-jacente, (Figure 2a et 2b), un élargissement des canalicules dentinaires, une mise à nu des fibres de collagène (Figure 2c et 2d) et une modification, ou l'élimination de la boue dentinaire.

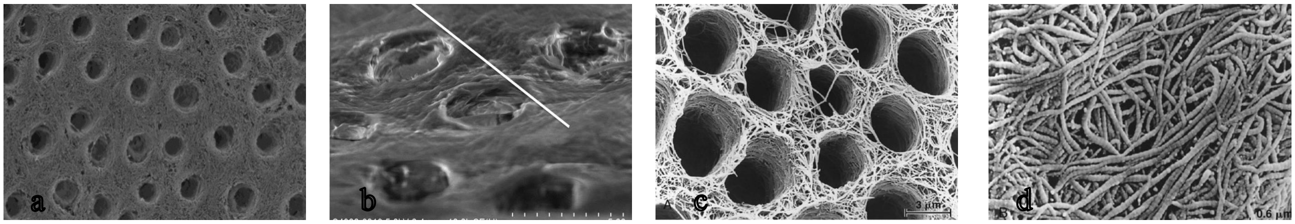


Figure 2 : Mordançage de la dentine avec 37% d'acide phosphorique. (a) et (b) : Les 10 premiers micromètres de dentine sont complètement déminéralisés suite à une attaque avec de l'acide phosphorique. Après rinçage de l'excès d'acide, l'eau élimine le minéral solubilisé et laisse les fibres de collagène insolubles flotter dans environ 70% en volume d'eau. Le but de la dentisterie adhésive est de remplacer ce volume d'eau par des monomères de résine adhésive. (c) et (d) : les fibres de collagène exposées avec un grossissement supérieur en (d) qui montre les striations périodiques caractéristique des fibres de collagène intercanaliculaire.

Il est bien connu que le processus d'adhésion dentinaire repose sur la création d'une CH adéquate et compacte créée par l'imprégnation du substrat de dentine par des mélanges de résines. Ainsi, la CH est un mélange de dentine, d'HAp, de monomères de résines et de solvants résiduels, et sa stabilité dépend en fin de compte de la résistance des composants individuels aux phénomènes de dégradation. En général, plus compacte et homogène la CH, meilleure est la stabilité de la liaison.

Les paramètres intervenant dans le phénomène d'adhésion

L'adhésif, souvent un fluide visqueux, est composé d'un matériau ou d'un film qui réunit deux substrats et les solidifie. Or l'adhérent est le support, le matériau ou le substrat initial sur lequel l'adhésif est appliqué. Les types d'adhérents sont : l'email, la dentine, l'alliage de métal et la céramique. En effet, le contact de l'adhésif avec l'adhérent dépend de la mouillabilité du substrat et de son énergie libre, de la nature du substrat, de l'humidité de la dentine, de l'âge du patient (dentine sclérotique) et de l'histopathologie de la dentine (réactions à la carie ou aux sollicitations mécaniques).

Les composants des adhésifs dentaires

Les composants fondamentaux d'un système adhésif dentaire sont les suivants :

Agent de mordançage : actuellement H_3PO_4 à une concentration comprise entre 30% et 40%. Les gels d'H_3PO_4 courants sont épaissis à l'aide de microparticules de silice, tandis que certains incorporent des épaississants alternatifs comme la gomme xanthane. Pour améliorer la précision de l'application et garantir que tout le gel soit rincé, un colorant coloré doit être intégré. Le glycol est fréquemment utilisé pour augmenter la mouillabilité et réduire la viscosité. L'agent de mordançage est constamment éliminé par rinçage de la surface dentaire.

Dans la technique de M+R, l'agent de mordançage utilisé est l'H_3PO_4 à 35-37%, avec un pH qui varie entre 0.5 et 1. Ce pH devient supérieur à 1 pour la technique de SAM utilisant des monomères acides dérivés de l'estérification de l'H_3PO_4.

Ce pH acide prépare l'émail et la dentine pour être dans une situation apte à recevoir les agents de collage. Le mordançage à l'H_3PO_4 de la dentine permet d'éliminer la boue dentinaire et de déminéraliser la sous-surface. Il s'agit d'une procédure clinique prévisible, mais certains facteurs inhérents au conditionnement du tissu dentinaire peuvent influencer les caractéristiques de liaison des adhésifs. Le collagène dentaire exposé, suite à l'application d'un agent de mordançage, s'est avéré très vulnérable aux processus de dégradation hydrolytique et enzymatique.

L'apprêt dentinaire : Il est composé d'une solution de polymères hydrophiles et hydrophobes, les monomères hydrophiles sont habituellement transportés dans un solvant hydrosoluble (acétone, éthanol, eau) pour favoriser un bon écoulement et une pénétration dans la dentine hydrophile, ce qui peut influencer la BS résultante, tandis que les monomères hydrophobes autorisent la liaison chimique avec la couche sus-jacente de résine. À titre d'exemples on a : hydroxy-éthyl-méthacrylate (HEMA), Bisphenol-A-glycidyl methacrylate phosphate (BPDM) et 4-methacryloxyethyl trimellitate anhydride (4-META). Toutefois, l'apprêt dentinaire le plus couramment utilisé dans de nombreux systèmes adhésifs, y compris les systèmes universels, est l'HEMA. Celui-ci contient un solvant qui agit en éliminant l'eau présente entre les fibres de collagène, et en dissolvant la résine amphiphilique, ce qui augmente la tension superficielle.

Les solvants comprennent l'acétone, l'éthanol et l'eau, dont le temps d'évaporation varie. Par contre, il faut souligner que tout solvant restant doit être évaporé de la surface de la dentine par séchage à l'air de l'adhésif appliqué. Le solvant non évaporé peut compromettre la polymérisation des monomères de résine, créant des vides indésirables dans l'interface adhésive. L'acétone s'évapore rapidement et nécessite le temps de séchage le plus court dans la cavité buccale. L'éthanol s'évapore plus lentement et nécessite un temps de séchage modéré. L'eau s'évapore très lentement et nécessite le temps de séchage le plus long.

Néanmoins, l'évaporation complète du solvant est difficile à réaliser, en particulier dans les adhésifs à base d'eau. Pour cela pour faciliter l'évaporation d'un tel solvant, l'éthanol et l'acétone peuvent être utilisés conjointement avec de l'eau comme co-solvants, ce qui entraîne un mélange azéotropique.

Résine adhésive (Bonding) : Il s'agit par exemple d'une résine à base de bisphénol-A glycidyl methacrylate (Bis-GMA) ou diméthacrylate-uréthane (UDMA). Elle peut être définie comme une fine couche de résine appliquée entre la dentine conditionnée hydrophile et la matrice de résine d'un composite hydrophobe qui favorise la liaison entre l'émail ou la dentine et le matériau de restauration en résine.

L'agent de collage, souvent similaire chimiquement à la matrice de composite de résine sus-jacente, diffuse dans la structure amélaire et dentinaire déminéralisée et, lors de la polymérisation, forme un emboîtement micro ou nano-mécanique à l'aide de digitations internes appelées « tags » dans des porosités minérales, des orifices élargis des canalicules dentinaires et dans le réseau fibrillaire de collagène exposé (la CH). Le problème le plus important de l'interface adhésive est que, même après photopolymérisation, le groupe ester HEMA est le plus vulnérable à la dissociation hydrolytique, formant de l'acide méthacrylique et de l'éthylène-glycol en présence d'eau à pH basique et acide. Une fois la dentine est déminéralisée, la diffusion des monomères adhésifs ne se produit pas dans tout le collagène exposé, ce qui entraîne une zone dans la partie inférieure de la CH où les fibres de collagène risquent de se dégrader et de s'hydrolyser par des enzymes.

Des composants supplémentaires sont présents dans la composition des systèmes adhésifs, notamment des initiateurs (pour un système de résine autopolymérisable avec un initiateur tel que le peroxyde de benzoyle, le processus de polymérisation peut être déclenché à l'aide d'un système photoinitiateur constitué du photosensibilisateur (par exemple, camphoroquinone) et d'un activateur (par exemple, amine tertiaire)), des charges (particules de silice) et d'autres ingrédients (parabène utilisé comme antimicrobien, glutaraldéhyde utilisé comme désensibilisant, fluorure pour la prévention des caries secondaires et chlorhexidine utilisée pour inhiber la dégradation du collagène).

Dans l'ensemble, la chimie d'un système adhésif se résume par la formule suivante M-R-X, où « M » est un groupe méthacrylate qui se combine avec la matrice de résine, « R » est un espaceur et « X » est un groupe fonctionnel pour l'adhérence aux surfaces dentaires.

La classification des systèmes adhésifs

L'approche historique : Cette classification a été proposée pour marquer l'évolution historique des concepts d'adhésion à la dentine. Selon cette classification, on distingue 7 générations (ou familles) d'adhésifs (Figure 3). Puisque la dentine et l'émail sont si radicalement différents, deux systèmes différents d'adhésion sont nécessaires. Lors de la liaison à l'émail, un système de M+R conduit à des meilleurs résultats avec des liaisons plus stable. Lors de la liaison à la dentine, un SAM permet de créer un lien plus fort. Les firmes responsables de la mise au marché des systèmes adhésifs exigeaient la création d'un système de collage qui pouvait être utilisé dans un mode de mordançage total, d'auto-mordançage ou de mordançage sélective. Récemment, plusieurs fabricants dentaires ont lancé des systèmes de collage « universels ». Ces systèmes ont été conçus pour être utilisés avec ou sans une étape de mordançage séparée, ce qui les rend hautement adaptables à toutes les situations cliniques dans lesquelles une liaison à la structure de la dent est requise. Ces adhésifs sont connus sous la classe de huitième génération.

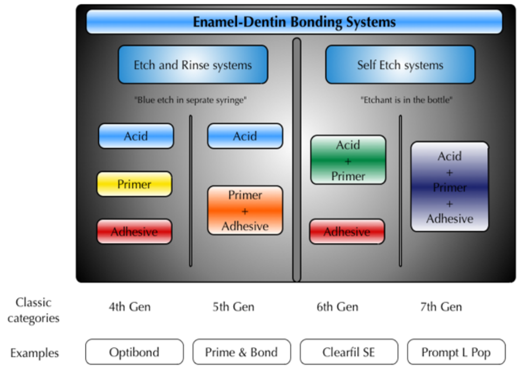


Figure 3 : Classification historique des systèmes adhésifs.

L'approche rationnelle : Il faut souligner que, cette classification en générations, à l'origine historique, a pris un caractère purement commercial depuis une décennie. En effet, si les 4 dernières générations présentent certaines particularités, elles ont presque le même principe fondamental. Par ailleurs, la notion de génération ne tient pas compte ni du principe d'action des adhésifs, ni de leurs performances et il n'apparaît pas évident que chaque génération apporte un bénéfice thérapeutique par rapport à celle qui la précède. En fait, la preuve c'est la présence concomitante des 4 dernières générations sur le marché dentaire actuellement. Il s'avère donc nécessaire d'avoir recours à une classification plus rationnelle.

L'approche selon le nombre d'étapes : Cette classification des systèmes adhésifs reflète leur mode d'utilisation essentiel, plutôt que le développement historique.

1- Trois étapes : impliquant un acide de mordançage, un apprêt dentinaire d'adhésion et une résine adhésive. Ces systèmes sont fournis sous la forme de trois flacons.

2- Deux étapes (1) : utilisation de deux flacons, l'un contenant un agent de mordançage, et l'autre la formulation combinée (apprêt dentinaire et résine adhésive). Ces systèmes nécessitent un mordançage préalable.

3- Deux étapes (2) : utilisation de deux flacons, le premier contenant un apprêt dentinaire auto-mordançant et le second la résine adhésive.

4- Une étape : ceux-ci utilisent un seul flacon contenant une formulation qui combine un apprêt dentinaire auto-mordançant et une résine adhésive.

Classification de Van meerbeeck et Coll. (1999) : Cette classification se base sur le mode de traitement de la boue dentinaire, on distingue ainsi 3 catégories :

- Les adhésifs infiltrant la boue dentinaire : la boue dentinaire est laissée intacte et infiltrée, donc le collage se fait à travers la boue dentinaire.

- Les adhésifs éliminant la boue dentinaire : la boue dentinaire est éliminée par un processus de M+R, donc le collage se repose sur la formation d'une CH.
- Les adhésifs dissolvant sélectivement la boue dentinaire : la boue dentinaire n'est pas éliminée et elle est intégrée en partie dans la CH.

Classification de Degrange (2003) : Elle distingue 2 grandes classes d'adhésifs :

- Celle des produits qui requièrent un mordançage suivi d'un rinçage, en préalable à leur emploi (M+R) divisés en 2 sous-groupes selon le nombre d'étapes (**M+R3** pour les 3 étapes, **M+R2** pour les 2 étapes).
- Celle des produits que l'on applique directement sur les surfaces dentaires sans aucun traitement préliminaire. Cette classe regroupe tous les SAM. Ces derniers sont constitués des systèmes à 2 flacons **SAM2** ou 1 flacon **SAM1**.

Le choix des systèmes adhésifs utilisés dans cette thèse

Quatre systèmes adhésifs ont été utilisés dans cette étude à des fins de comparaison : OBFL (M+R3), CSE (SAM2), OptiBond Universal (OBU, Kerr Co., Orange, CA, USA, Universels) et Prime&Bond Universal (PBU, Dentsply DeTrey GmbH, Konstanz, Germany, Universels).

Après avoir obtenus en laboratoire des résultats prometteurs sur l'efficacité de la liaison, puis confirmées par des données cliniques à long terme sur l'efficacité de la liaison, il est considéré que l'adhésif M+R3 de référence OBFL et l'adhésif SAM2 de référence CSE soient fréquemment utilisés comme contrôle/référence dans des études en laboratoire. Dans l'ensemble, lorsque les recherches en laboratoire et cliniques fournissent des preuves significatives et cohérentes de performances de liaison positives à long terme, les adhésifs commerciaux peuvent être considérés comme GOLD STANDARD. À cet égard, OBFL et CSE ont été utilisés dans la présente thèse.

De plus, les UAs utilisent des monomères d'esters de phosphate fonctionnels acides comme le 10-MDP et le GPDM, qui ont une bonne affinité pour l'HAp. L'idée d'adhésion/décalcification a été proposée pour mieux comprendre la chimie des monomères de phosphate fonctionnel acide avec l'HAp. Cette approche dépend de la stabilité du sel monomère-Ca produit. Le sel 10-MDP-Ca est légèrement plus stable que le sel GPDM-Ca, car le GPDM se décalcifie tandis que le 10-MDP adhère au canal d'adhésion. Il est supposé que l'efficacité de mordançage plus élevée des adhésifs SAM à base de GPDM pourrait aboutir à une liaison tout aussi efficace que le mordançage à l'H_3PO_4. Cela étant, des UAs au moyen d'adhésifs à base de GPDM (OBU) et d'adhésifs à base de 10-MDP (PBU) ont été utilisés dans cette thèse en mode SAM.

Une autre évolution clé pour les systèmes adhésifs a été la rationalisation des procédures cliniques. Les systèmes adhésifs comportant moins de processus cliniques sont plus sophistiqués que ceux comportant plus d'étapes. Dans cette optique, deux UAs différents (OBU et PBU) ont été testés.

Influence des prétraitements et perspectives d'une nouvelle alternative dans la liaison résine-dentine

Pour optimiser les performances et les résultats à long terme des systèmes adhésifs, plusieurs stratégies sont rapportées. De manière appropriée, le clinicien doit utiliser certaines modalités d'application qui diffèrent des recommandations du fabricant pour renforcer la force d'adhésion des matériaux à base de résine à la dentine. Les modalités d'application qui favorisaient la force d'adhésion globale à la dentine étaient : couche de résine hydrophobe, double temps d'application de l'adhésif, plasma atmosphérique non thermique (gaz partiellement ionisés comprenant des atomes et des molécules électroniquement excités , ainsi que des ions et des espèces de radicaux libres pour améliorer la liaison à la dentine), liaison humide à l'éthanol et à l'acétone, application de plusieurs couches d'adhésif (2 couches et plus), flux d'air chaud sur l'apprêt dentinaire ou sur le système adhésif, temps de polymérisation prolongé jusqu'à 40 s, séchage à l'air prolongé, application préalable d'inhibiteurs de protéase, application de différents agents de réticulation, application assistée par une approche d'isolation appropriée, mordançage sélective de la dentine pendant 3 s, technique de frottement, reminéralisation biomimétique et abrasion par particules d'air dans les stratégies d'adhésion spécifiques.

Caractère novateur de la recherche

À ce jour, il n'existe pas d'adhésif ou de technique unique pouvant être considérés comme la norme de référence pour l'adhésion des matériaux à base de résine à la dentine. Dans ce sens, les données de cette étude pourraient aider à améliorer cette procédure standard qui conduit à une adhésion résine-dentine prévisible et durable.

Matériel et méthodes

La thèse actuelle a évalué l'effet de différentes modalités de systèmes adhésifs sur la dentine. À ces fins, diverses méthodes d'évaluation ont été utilisées : résistance de liaison à la micro-traction (μTBS), mode de rupture, microscope électronique à balayage (MEB), l'angle de contact adhésif (CA) et le taux d'évaporation du solvent.

Caractérisation des matériaux à travers les méthodologies suivantes pour les quatre modalités d'application :

- Résistance de liaison à la micro-traction
- Mode de rupture
- Microscope électronique à balayage
- Angle de contact adhésif

Caractérisation des matériaux à travers les méthodologies suivantes pour la technique de liaison active avec des applications de couches multiples :

- Résistance de liaison à la micro-traction
- Mode de rupture
- Microscope électronique à balayage

Caractérisation des matériaux à travers les méthodologies suivantes pour la stratégie d'air chaud :

- Résistance de liaison à la micro-traction

- Mode de rupture
- Microscope électronique à balayage
- Taux d'évaporation du solvent

Dans cette étude, des caractérisations de la résistance à la liaison, ainsi que des caractérisations biologiques et morphologiques des interfaces résine-adhésive, sont réalisées en fonction des facteurs suivants: (1) le système adhésif (adhésif M+R3, OBFL; adhésif SAM2, CSE; adhésif universel sans HEMA, PBU; et adhésif universel contenant du HEMA, OBU); (2) les modalités d'application (PA, AA, CV et CVM); (3) l'application de la couche adhésive (une couche d'adhésif sera appliquée avec la technique active (A); application de la première couche avec la technique active, la deuxième couche sans la technique active, et la troisième couche sans la technique active (APP); application de la première couche avec la technique active, la deuxième couche avec la technique active, et la troisième couche sans la technique active (AAP); application de la première, deuxième et troisième couche avec la technique active (AAA)); (4) la température de séchage à l'air utilisée pour l'évaporation des solvants (20 °C, 40 °C et 60 °C); (5) le vieillissement (24 h et 6 mois).

Le deuxième chapitre est dédié aux protocoles pour les différentes modalités d'application :

Quatre groupes ont été formés en fonction des modalités d'application : (1) PA, application de l'adhésif sans agitation; (2) AA, application de l'adhésif avec agitation active; (3) micro-vibration avec CV (Smile Line, St-Imier, Suisse), application de l'adhésif à l'aide d'un pinceau CV (Smile Line, St-Imier, Suisse) pour le collage (CV); (4) application modifiée de CV (Smile Line, St-Imier, Suisse) à l'aide d'un micro-applicateur (Kerr, Orange, CA, USA) (CVM). La taille de l'échantillon a été estimée sur la base de la littérature antérieure qui a évalué la résistance à la liaison d'un système adhésif utilisant différentes modalités d'application dans un modèle d'étude comparative avec 4 groupes indépendants. En utilisant un α de 0,05, une puissance de 80% et un test à deux côtés, la taille minimale de l'échantillon était de 5 spécimens dans chaque groupe afin de détecter une différence de 5 MPa entre les groupes testés.

Pour PA, tous les adhésifs testés ont été appliqués pendant 20 s et laissés sans agitation; pour AA, tous les adhésifs testés ont été appliqués avec une agitation active pendant 20 s. De plus, pour la micro-vibration avec CV et CVM, tous les adhésifs testés ont été appliqués pendant 20 s avec l'instrument CV (Smile Line, St-Imier, Suisse) (ceci pourrait être possible avec l'aide du pinceau CV (Smile Line, St-Imier, Suisse) utilisé pour le collage dans cette étude (Figure 4a) ou en utilisant un micro- applicateur (Figure 4b)). Il est important de noter que pour la modalité CVM, un micro-applicateur a été coupé comme indiqué dans la Figure 4b. De plus, le bouton rouge sur le manche permettait la micro-vibration des modalités CV et CVM.

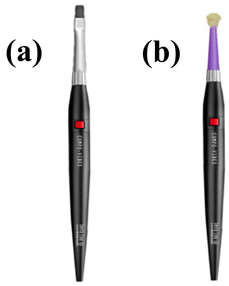


Figure 4 : Images représentatives de l'instrument Compo-Vibes (Smile Line, St-Imier, Suisse) (une modalité d'application pourrait être possible à l'aide du pinceau Compo-Vibes (Smile Line, St-Imier, Suisse) en (a) utilisé pour le collage dans cette étude ou en utilisant un micro-applicateur en (b)).

Le troisième chapitre présente la technique de liaison active avec des applications de couches multiples :

Quatre groupes ont été formés en fonction de l'application de la couche adhésive, comprenant les triples couches adhésives et la "ABT". Une couche (groupe témoin) et trois couches d'adhésifs ont été appliquées selon les instructions du fabricant sans photopolymérisation après chaque application. L'AA des adhésifs sur le substrat dentinaire a été effectuée manuellement à l'aide d'un micro-applicateur (Kerr, Orange, CA, USA). De plus, l'ampleur de la force à appliquer lors de l'action de frottement a été standardisée par un seul enquêteur qui a réalisé le processus d'adhésion. Le nombre d'échantillons par groupe (n=5) a été estimé sur la base d'une étude antérieure ayant évalué l'effet de l'application de MLA sur la résistance à la liaison à la dentine dans un modèle d'étude comparative avec 4 groupes indépendants, une différence minimale détectable de 5,87 en moyenne, un écart-type de 1,54, une puissance de 0,8 et un $\alpha = 0{,}05$.

a- Premier groupe : A.
b- Deuxième groupe : APP.
c- Troisième groupe : AAP.
d- Quatrième groupe : AAA.

La représentation des groupes d'étude est décrite dans la Figure 5.

Figure 5 : Représentation des quatre groupes testés dans cette recherche. Application active unique (A); triple application, Actif-Passif-Passif (APP); triple application, Actif-Actif-Passif (AAP); triple application, Actif-Actif-Actif (AAA).

Enfin, le quatrième chapitre explique la stratégie d'air chaud :

Trois groupes ont été formés en fonction de la température de séchage à l'air : l'évaporation du solvant a été réalisée avec de l'air chaud (40 °C), (60 °C), et de l'air froid comme groupe témoin (20 °C) pendant 10 s à une distance de 5 cm. Dans les trois cas, le flux d'air était généré par un appareil (prototype) pour délivrer de l'air chaud ou froid. La vitesse de l'air du flux était de 5,50 m/s et le débit d'air était de

0,0138 m^3/s. L'appareil est un prototype fabriqué et testé selon la norme organisation internationale de normalisation (ISO). Le nombre de dents par groupe (n=5) a été estimé sur la base d'une étude antérieure ayant évalué l'effet de l'application d'air chaud pour l'évaporation du solvant sur la résistance à la liaison à la dentine dans un modèle d'étude comparative, une différence minimale détectable de 8,8 en moyenne, un écart-type de 2,9, une puissance de 0,8 et un α = 0,05. Le protocole de préparation des échantillons est décrit de manière schématique dans la Figure 6.

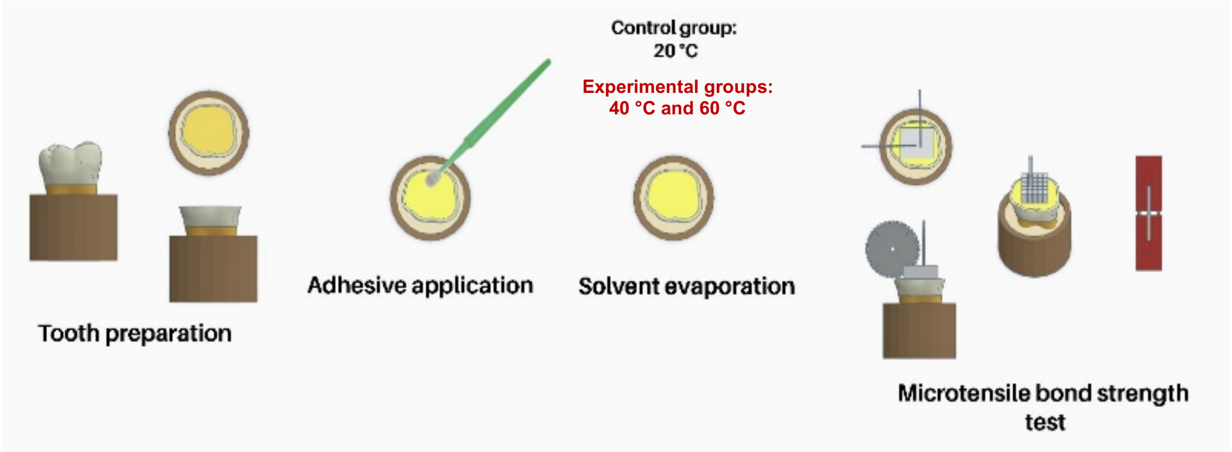


Figure 6 : Protocole de préparation des échantillons.

Publications associées aux différents chapitres de ce travail

applied sciences
MDPI

Review

A Literature Review of Adhesive Systems in Dentistry: Key Components and Their Clinical Applications

Rim Bourgi [1,2,*], Naji Kharouf [2,3], Carlos Enrique Cuevas-Suárez [4], Monika Lukomska-Szymanska [5], Youssef Haikel [2,3,6,†] and Louis Hardan [1,†]

[1] Department of Restorative Dentistry, School of Dentistry, Saint-Joseph University, Beirut 1107 2180, Lebanon; louis.hardan@usj.edu.lb
[2] Department of Biomaterials and Bioengineering, INSERM UMR_S 1121, University of Strasbourg, 67000 Strasbourg, France; dentistenajikharouf@gmail.com (N.K.); youssef.haikel@unistra.fr (Y.H.)
[3] Department of Endodontics and Conservative Dentistry, Faculty of Dental Medicine, University of Strasbourg, 67000 Strasbourg, France
[4] Dental Materials Laboratory, Academic Area of Dentistry, Autonomous University of Hidalgo State, San Agustín Tlaxiaca 42160, Mexico; cecuevas@uaeh.edu.mx
[5] Department of General Dentistry, Medical University of Lodz, 92-213 Lodz, Poland; monika.lukomska-szymanska@umed.lodz.pl
[6] Pôle de Médecine et Chirurgie Bucco-Dentaire, Hôpital Civil, Hôpitaux Universitaire de Strasbourg, 67000 Strasbourg, France
[*] Correspondence: rim.bourgi@net.usj.edu.lb; Tel.: +961-71455529
[†] These authors contributed equally to this work.

check for updates

Citation: Bourgi, R.; Kharouf, N.; Cuevas-Suárez, C.E.; Lukomska-Szymanska, M.; Haikel, Y.; Hardan, L. A Literature Review of Adhesive Systems in Dentistry: Key Components and Their Clinical Applications. *Appl. Sci.* **2024**, *14*, 8111. https://doi.org/10.3390/app14188111

Academic Editor: Bruno Chrcanovic

Received: 11 August 2024
Revised: 27 August 2024
Accepted: 28 August 2024
Published: 10 September 2024

Abstract: The central aim of adhesive dentistry is to improve the compatibility between current adhesives and a range of substrates by employing diverse application techniques. Therefore, the overarching objective of this review is to offer a comprehensive analysis of dentin bonding systems, starting with an introduction to adhesion and a detailed overview of enamel and dentin structures, their histology, and the impact of dentin structure on resin–dentin bonding. It covers the mechanisms of resin–dentin bonding, including resin adhesive application, bonding mechanisms, and factors influencing efficacy. Further, this review explores the composition of resin adhesive systems, including acidic components, cross-linking monomers, solvents, and other critical elements. It also examines various adhesive strategies—etch-and-rinse, self-etch, and universal adhesives—highlighting their applications and advantages. The review extends to clinical applications of dental adhesion, including direct restorations, indirect restorations, and immediate dentin sealing (IDS), demonstrating the practical implications of adhesive systems in enhancing restoration longevity and performance. In conclusion, despite significant advancements, no gold-standard method for optimal adhesion exists. Each adhesive system has distinct strengths and limitations. The review emphasizes the importance of evaluating methods for achieving durable adhesion and staying current with technological advancements in adhesive systems. **Summary:** This review provides a thorough analysis of dentin bonding systems, delving into the structures and bonding mechanisms of both enamel and dentin. By exploring various adhesive systems and their components, it highlights the ongoing challenges in achieving optimal resin–dentin adhesion. The review also addresses the clinical applications of dental adhesion, including direct restorations, indirect restorations, and immediate dentin sealing (IDS), illustrating how different adhesive techniques impact clinical outcomes. It underscores the necessity for continuous innovation and assessment of adhesive systems to enhance long-term bonding effectiveness in clinical practice.

Keywords: adhesion; dental adhesive; dental bonding; dentin bonding agent; etch-and-rinse; self-etch; universal adhesive

Appl. Sci. **2024**, *14*, 8111. https://doi.org/10.3390/app14188111 https://www.mdpi.com/journal/applsci

---

Journal of Functional Biomaterials
MDPI

Review

The Use of Warm Air for Solvent Evaporation in Adhesive Dentistry: A Meta-Analysis of In Vitro Studies

Rim Bourgi [1,2], Louis Hardan [1,†], Carlos Enrique Cuevas-Suárez [3], Francesco Scavello [4,*], Davide Mancino [2,5,6], Naji Kharouf [2,5,*] and Youssef Haikel [2,5,6,†]

[1] Department of Restorative Dentistry, School of Dentistry, Saint-Joseph University, Beirut 1107 2180, Lebanon; rim.bourgi@net.usj.edu.lb (R.B.); louis.hardan@usj.edu.lb (L.H.)
[2] Department of Biomaterials and Bioengineering, INSERM UMR_S 1121, University of Strasbourg, 67000 Strasbourg, France; mancino@unistra.fr (D.M.); youssef.haikel@unistra.fr (Y.H.)
[3] Dental Materials Laboratory, Academic Area of Dentistry, Autonomous University of Hidalgo State, San Agustín Tlaxiaca 42160, Mexico; cecuevas@uaeh.edu.mx
[4] IRCCS Humanitas Research Hospital, 20089 Rozzano, Milan, Italy
[5] Department of Endodontics and Conservative Dentistry, Faculty of Dental Medicine, University of Strasbourg, 67000 Strasbourg, France
[6] Pôle de Médecine et Chirurgie Bucco-Dentaire, Hôpital Civil, Hôpitaux Universitaire de Strasbourg, 67000 Strasbourg, France
[*] Correspondence: francesco.scavello@humanitasresearch.it (F.S.); dentistenajikharouf@gmail.com (N.K.); Tel.: +33-66752-2841 (N.K.)
[†] These authors contributed equally to this work.

check for updates

Citation: Bourgi, R.; Hardan, L.; Cuevas-Suárez, C.E.; Scavello, F.; Mancino, D.; Kharouf, N.; Haikel, Y. The Use of Warm Air for Solvent Evaporation in Adhesive Dentistry: A Meta-Analysis of In Vitro Studies. *J. Funct. Biomater.* **2023**, *14*, 285. https://doi.org/10.3390/jfb14050285

Academic Editors: Ping Li, Guojiang Wan, Shulan Xu and An Li

Received: 20 April 2023
Revised: 15 May 2023
Accepted: 17 May 2023
Published: 20 May 2023

Abstract: Any excess solvent from dental adhesive systems must be eliminated prior to material photopolymerization. For this purpose, numerous approaches have been proposed, including the use of a warm air stream. This study aimed to investigate the effect of different temperatures of warm air blowing used for solvent evaporation on the bond strength of resin-based materials to dental and nondental substrates. Two different reviewers screened the literature in diverse electronic databases. In vitro studies recording the effect of warm air blowing to evaporate solvents of adhesive systems on the bond strength of resin-based materials to direct and indirect substrates were included. A total of 6626 articles were retrieved from all databases. From this, 28 articles were included in the qualitative analysis, and 27 remained for the quantitative analysis. The results of the meta-analysis for etch-and-rinse adhesives revealed that the use of warm air for solvent evaporation was statistically significantly higher ($p = 0.005$). For self-etch adhesives and silane-based materials, this effect was observed too ($p < 0.001$). The use of a warm air stream for solvent evaporation enhanced the bonding performance of alcohol-/water-based adhesive systems for dentin. This effect seems to be similar when a silane coupling agent is submitted to a heat treatment before the cementation of a glass-based ceramic.

Keywords: dentine; silane; solvent-based; total-etch; warm air

1. Introduction

Adhesive systems contain resin monomers with hydrophilic and hydrophobic characteristics, polymerization modulators, and a high concentration of solvents [1]. Organic solvents act as diluting agents that improve wetting and the infiltration of resin monomers into the dentinal surface [2]. It is crucial that any excess solvent must be eliminated from the dental substrate by means of air drying prior to the photopolymerization of the applied adhesive, in addition to allowing time between these two processes [3]. A presence of residual solvents might affect the polymerization of monomers and hinder the integrity of the bond, creating unwanted pathways for voids inside the adhesive interface and causing a decrease in the bond strength [4,5].

J. Funct. Biomater. **2023**, *14*, 285. https://doi.org/10.3390/jfb14050285 https://www.mdpi.com/journal/jfb

---

polymers
MDPI

Article

Effectiveness of Different Application Modalities on the Bond Performance of Four Polymeric Adhesive Systems to Dentin

Rim Bourgi [1,2], Louis Hardan [1,†], Carlos Enrique Cuevas-Suárez [3], Walter Devoto [4], Cynthia Kassis [1], Khalil Kharma [1], Ryan Harouny [1,5], Tarek Ashi [2], Davide Mancino [2,6,7], Naji Kharouf [2,6,*] and Youssef Haikel [2,6,7,†]

[1] Department of Restorative Dentistry, School of Dentistry, Saint-Joseph University, Beirut 1107 2180, Lebanon; rim.bourgi@net.usj.edu.lb (R.B.); louis.hardan@usj.edu.lb (L.H.); cynthia.kassis@usj.edu.lb (C.K.); khalil.kharma@usj.edu.lb (K.K.); ryaneliott.harouny@net.usj.edu.lb (R.H.)
[2] Department of Biomaterials and Bioengineering, INSERM UMR_S 1121, University of Strasbourg, 67000 Strasbourg, France; tarekachi@live.com (T.A.); mancino@unistra.fr (D.M.); youssef.haikel@unistra.fr (Y.H.)
[3] Dental Materials Laboratory, Academic Area of Dentistry, Autonomous University of Hidalgo State, San Agustín Tlaxiaca 42160, Mexico; cecuevas@uaeh.edu.mx
[4] Independent Researcher, 16030 Sestri Levante, Italy; walter@walterdevoto.com
[5] Craniofacial Research Laboratory, Division of Biomaterials, School of Dentistry, Saint-Joseph University, Beirut 1107 2180, Lebanon
[6] Department of Endodontics and Conservative Dentistry, Faculty of Dental Medicine, University of Strasbourg, 67000 Strasbourg, France
[7] Pôle de Médecine et Chirurgie Bucco-Dentaire, Hôpital Civil, Hôpitaux Universitaire de Strasbourg, 67000 Strasbourg, France
[*] Correspondence: dentistenajikharouf@gmail.com; Tel.: +33-66752-2841
[†] These authors contributed equally to this work.

check for updates

Citation: Bourgi, R.; Hardan, L.; Cuevas-Suárez, C.E.; Devoto, W.; Kassis, C.; Kharma, K.; Harouny, R.; Ashi, T.; Mancino, D.; Kharouf, N.; et al. Effectiveness of Different Application Modalities on the Bond Performance of Four Polymeric Adhesive Systems to Dentin. *Polymers* **2023**, *15*, 3924. https://doi.org/10.3390/polym15193924

Academic Editors: Matej Par and Katarzyna Mańka-Malara

Received: 7 September 2023
Revised: 22 September 2023
Accepted: 25 September 2023
Published: 28 September 2023

Abstract: One of the major goals of adhesive dentistry is to improve the interaction of the already-existing adhesives with different substrates by using different application techniques. Thus, the objective of the present in vitro study was to assess the bond performance of four adhesive systems, Prime&Bond Universal (PBU), Clearfil SE Bond (CSE), OptiBond Universal (OBU), and OptiBond FL (OBFL), to dentin using various application modes: passive application (PA), active application (AA), Compo-Vibes modified application (CVM), and Compo-Vibes application (CV). Eighty extracted human molars were allocated into four groups based on the application modalities tested. The micro-tensile bond strength as well as fracture mode were tested in accordance with ISO/TS 11.405 after 24 h and 6 months of aging. Adhesive contact angle (CA) and scanning electron microscope analysis were also performed ($n = 3$). Statistical tests were performed with $\alpha = 0.05$. After 24 h, a significant difference with a higher bond strength value was found for PBU in the AA modality and for CSE in the CVM modality ($p < 0.05$). However, no significant difference was shown between the techniques used among the other adhesives (OBFL and OBU). Moreover, at 24 h, only the PA demonstrated significant differences between the tested materials ($p < 0.05$). After 6 months, CSE, PBU, and OBU demonstrated significant differences between the techniques ($p < 0.05$), with a higher bond strength for CSE in AA and CVM modalities, for PBU in AA modality, and for OBU in AA and PA modalities. No significant differences were found between the techniques used among the OBFL ($p > 0.05$). In addition, only the CVM technique demonstrated significant differences between the tested materials after 6 months. CV and CVM showed a decreased value after aging for CSE and PBU, respectively. However, all the modalities decreased for OBU and OBFL after aging. All the adhesives showed marked resin infiltration into dentinal tubules in AA among all the modalities tested. Both universal adhesive systems (OBU and PBU) demonstrated statistically lower CA when compared to the other systems (CSE and OBFL) ($p < 0.05$) when applied in the PA mode. Concerning the AA mode, only CSE and OBFL were tested. The AA demonstrated lower CA values compared to the same adhesives in PA ($p < 0.05$). It could be concluded that the bond strength could be influenced by both materials and application techniques. It seems that the AA technique could be recommended as a gold standard for the application of an adhesive system to dentin. Plus, the CV and CVM modalities

Polymers **2023**, *15*, 3924. https://doi.org/10.3390/polym15193924 https://www.mdpi.com/journal/polymers

Journal of Functional Biomaterials

Article

Effect of Modified Triple-Layer Application on the Bond Strength of Different Dental Adhesive Systems to Dentin

Rim Bourgi [1,2,*], Naji Kharouf [2,3,*], Carlos Enrique Cuevas-Suárez [4], Monika Lukomska-Szymańska [5], Walter Devoto [6], Cynthia Kassis [1], Omar Hasbini [7], Davide Mancino [2,3,8], Youssef Haikel [2,3,8,†] and Louis Hardan [1,†]

[1] Department of Restorative Dentistry, School of Dentistry, Saint-Joseph University, Beirut 1107 2180, Lebanon; cynthia.kassis@usj.edu.lb (C.K.); louis.hardan@usj.edu.lb (L.H.)
[2] Department of Biomaterials and Bioengineering, INSERM UMR_S 1121, University of Strasbourg, 67000 Strasbourg, France; mancino@unistra.fr (D.M.); youssef.haikel@unistra.fr (Y.H.)
[3] Department of Endodontics and Conservative Dentistry, Faculty of Dental Medicine, University of Strasbourg, 67000 Strasbourg, France
[4] Dental Materials Laboratory, Academic Area of Dentistry, Autonomous University of Hidalgo State, San Agustín Tlaxiaca 42160, Mexico; cecuevas@uaeh.edu.mx
[5] Department of General Dentistry, Medical University of Lodz, 92-213 Lodz, Poland; monika.lukomska-szymanska@umed.lodz.pl
[6] Independent Researcher, 16030 Sestri Levante, Italy; walter@walterdevoto.com
[7] Department of Prosthetic Dentistry, School of Dentistry, Saint-Joseph University, Beirut 1107 2180, Lebanon; omar.hasbini@net.usj.edu.lb
[8] Pôle de Médecine et Chirurgie Bucco-Dentaire, Hôpital Civil, Hôpitaux Universitaire de Strasbourg, 67000 Strasbourg, France
* Correspondence: rim.bourgi@net.usj.edu.lb (R.B.); dentistenajikharouf@gmail.com (N.K.); Tel.: +33-66752-2841 (N.K.); +961-71455529 (R.B.)
† These authors contributed equally to this work.

Citation: Bourgi, R.; Kharouf, N.; Cuevas-Suárez, C.E.; Lukomska-Szymańska, M.; Devoto, W.; Kassis, C.; Hasbini, O.; Mancino, D.; Haikel, Y.; Hardan, L. Effect of Modified Triple-Layer Application on the Bond Strength of Different Dental Adhesive Systems to Dentin. *J. Funct. Biomater.* **2023**, *14*, 522. https://doi.org/10.3390/jfb14100522

Academic Editor: Conrado Aparicio

Received: 20 September 2023
Revised: 10 October 2023
Accepted: 12 October 2023
Published: 17 October 2023

Abstract: The goal of this article was to assess the effect of modified triple-layer application (MTLA) in conjunction with the active bonding technique on the bond strength of four adhesive systems to dentinal substrate. The adhesives tested were Prime&Bond Universal (PBU), OptiBond Universal (OBU), OptiBond FL (OBFL), and Clearfil SE (CSE). The adhesives were applied according to the following strategies: single active application (A) and triple adhesive layer application including Active–Passive–Passive (APP); AAP; and AAA. The micro-tensile bond strength test was evaluated following 24 h or 6 months of storage. The composite–dentin interface morphology was investigated using scanning electron microscopy. The data were statistically analyzed with a significance level of $\alpha = 0.05$. At 24 h of aging, all of the factors tested were not significant ($p > 0.05$) for CSE. For OBFL, OBU, and PBU, statistically higher values were observed for the A technique ($p < 0.05$). Plus, there were no significant variances between the APP, AAP, and AAA techniques ($p > 0.05$) for OBFL and PBU. However, for OBU, there were no significant differences between the A and AAA techniques ($p > 0.05$). After 6 months of aging, the A technique showed statistically higher values when compared to the other techniques ($p < 0.01$), except for OBFL, where the A and AAA techniques showed promising outcomes. When comparing the bond strength values of 24 h and 6 months, only for PBU, all of the techniques used resulted in bond strength stability over time ($p > 0.05$). Thicker adhesive layers were observed when MTLA was applied. Only the OBFL adhesive showed the formation of resin tags in all of the modalities tested. The bonding performances of the different application techniques used were material-dependent.

Keywords: active application; aging; bond strength; etch-and-rinse adhesives; self-etch adhesives; universal adhesives

J. Funct. Biomater. **2023**, *14*, 522. https://doi.org/10.3390/jfb14100522 https://www.mdpi.com/journal/jfb

biomimetics

Article

Warm Air Delivery in Adhesive Application: Effect on Bonding Performance and Morphological Outcomes

Rim Bourgi [1,2], Naji Kharouf [2,3], Carlos Enrique Cuevas-Suárez [4,*], Monika Lukomska-Szymanska [5], Khalil Kharma [1], Fabienne Hajj Moussa [6], Manar Metlej [7], Youssef Haikel [2,3,8,†] and Louis Hardan [1,*,†]

[1] Department of Restorative Dentistry, School of Dentistry, Saint-Joseph University, Beirut 1107 2180, Lebanon; rim.bourgi@net.usj.edu.lb (R.B.); khalil.kharma@usj.edu.lb (K.K.)
[2] Department of Biomaterials and Bioengineering, INSERM UMR_S 1121, University of Strasbourg, 67000 Strasbourg, France; dentistenajikharouf@gmail.com (N.K.); youssef.haikel@unistra.fr (Y.H.)
[3] Department of Endodontics and Conservative Dentistry, Faculty of Dental Medicine, University of Strasbourg, 67000 Strasbourg, France
[4] Dental Materials Laboratory, Academic Area of Dentistry, Autonomous University of Hidalgo State, San Agustín Tlaxiaca 42160, Mexico
[5] Department of General Dentistry, Medical University of Lodz, 92-213 Lodz, Poland; monika.lukomska-szymanska@umed.lodz.pl
[6] Laboratoire de Pharmacologie, Pharmacie Clinique et Contrôle de Qualité des Médicaments, Faculty of Pharmacy, Saint-Joseph University, Beirut 1107 2180, Lebanon; fabienne.hajjmoussa@usj.edu.lb
[7] Department of Prosthetic Dentistry, School of Dentistry, Saint-Joseph University, Beirut 1107 2180, Lebanon; manar.metlej@net.usj.edu.lb
[8] Pôle de Médecine et Chirurgie Bucco-Dentaire, Hôpital Civil, Hôpitaux Universitaire de Strasbourg, 67000 Strasbourg, France
* Correspondence: cecuevas@uaeh.edu.mx (C.E.C.-S.); louis.hardan@usj.edu.lb (L.H.); Tel.: +52-(771)-72000 (C.E.C.-S.); +961-3700663 (L.H.)
† These authors contributed equally to this work.

Citation: Bourgi, R.; Kharouf, N.; Cuevas-Suárez, C.E.; Lukomska-Szymanska, M.; Kharma, K.; Moussa, F.H.; Metlej, M.; Haikel, Y.; Hardan, L. Warm Air Delivery in Adhesive Application: Effect on Bonding Performance and Morphological Outcomes. *Biomimetics* **2024**, *9*, 194. https://doi.org/10.3390/biomimetics9040194

Academic Editor: Xiang Ge

Received: 22 February 2024
Revised: 14 March 2024
Accepted: 21 March 2024
Published: 24 March 2024

Abstract: Solvent evaporation within an adhesive layer is a crucial step during a bonding process. The aim of this current research was to test whether the use of different air temperatures (20 °C, 40 °C, and 60 °C) for solvent evaporation improves the performance of four adhesive systems to dentin. Sixty non-carious human molar teeth were randomly prepared for micro-tensile bond strength (μTBS) tests. Four different adhesive systems, Prime&Bond Universal (PBU), OptiBond Universal (OBU), OptiBond FL (OBFL), and Clearfil SE (CSE), were applied following the manufacturer's instructions. Three groups based on the air-drying temperature were used: solvent evaporation was performed with either of warm (40 °C), (60 °C), and cold air as control group (20 °C) for 10 s at a distance of 5 cm. In all bonded surfaces, three resin composite (Reflectys, Itena Clinical, Paris, France) layers of 2 mm thickness were built up. The resin–dentin samples were kept in distilled water at 37 °C for 24 h and 6 months, respectively, before μTBS testing. Failure analysis, scanning electron microscopy of resin–dentin bonded interface, and solvent evaporation rate were tested as secondary variables. All analyses were conducted using a significance level of $\alpha = 0.05$. Bond strength (BS) values were similar among all the adhesive systems used ($p > 0.05$). Also, the aging factor did not affect the BS ($p > 0.05$). Only the factor of temperature used for solvent evaporation resulted in a statistically significant effect ($p < 0.05$), with the temperature of 60 °C being the highest value ($p < 0.05$). A failure mode evaluation revealed mostly adhesive or mixed modes of failures in all the different temperatures of air used for the solvent evaporation of each adhesive system. The thickness of the adhesive layer and the creation of resin tags varied amongst the temperatures evaluated. For all adhesive systems tested, the use of 40 °C or 60 °C air for solvent evaporation led to an increased mass loss. Warmer temperatures for solvent evaporation contributed positively to bonding performance, enhancing both the quality of the adhesive layer and its interaction with the dentin tissue. Optimizing solvent evaporation with warmer air temperatures (40 °C and 60 °C) significantly improved μTBS, offering a practical means to enhance the quality and longevity of adhesive restorations in esthetic dentistry.

Biomimetics **2024**, *9*, 194. https://doi.org/10.3390/biomimetics9040194 https://www.mdpi.com/journal/biomimetics

1. **Bourgi, R.;** Hardan, L.; Cuevas-Suárez, C.E.; Scavello, F.; Mancino, D.; Kharouf, N.; Haikel, Y. The Use of Warm Air for Solvent Evaporation in Adhesive Dentistry: A Meta-Analysis of In Vitro Studies. *J. Funct. Biomater*. **2023**, *14*, 285. https://doi.org/10.3390/jfb14050285
2. **Bourgi, R.;** Hardan, L.; Cuevas-Suárez, C.E.; Devoto, W.; Kassis, C.; Kharma, K.; Harouny, R.; Ashi, T.; Mancino, D.; Kharouf, N.; Haikel, Y. Effectiveness of Different Application Modalities on the Bond Performance of Four Polymeric Adhesive Systems to Dentin. *Polymers* **2023**, *15*, 3924. https://doi.org/10.3390/polym15193924
3. **Bourgi, R.;** Kharouf, N.; Cuevas-Suárez, C.E.; Lukomska-Szymańska, M.; Devoto, W.; Kassis, C.; Hasbini, O.; Mancino, D.; Haikel, Y.; Hardan, L. Effect of Modified Triple-Layer Application on the Bond Strength of Different Dental Adhesive Systems to Dentin. *J. Funct. Biomater*. **2023**, *14*, 522. https://doi.org/10.3390/jfb14100522
4. **Bourgi, R.;** Kharouf, N.; Cuevas-Suárez, C.E.; Lukomska-Szymanska, M.; Kharma, K.; Moussa, F.H.; Metlej, M.; Haikel, Y.; Hardan, L. Warm Air Delivery in Adhesive Application: Effect on Bonding Performance and Morphological Outcomes. *Biomimetics* **2024**, *9*, 194. https://doi.org/10.3390/biomimetics9040194
5. **Bourgi, R.;** Kharouf, N.; Cuevas-Suárez, C.E.; Kassis, C.; Monjaras-Avila, A.J.; Qaddomi, M.; Abi Raad, S.; Al Hasani, M.; Haikel, Y.; Hardan, L. Assessment of Clinical Performance of Universal Adhesives Versus Other Adhesive Systems: A Systematic Review and Meta-Analysis of Clinical Trials. *Int. Arab J. Dent.* **2024**, *15*, 204-230. https://doi.org/10.70174/iajd.v15i2.1046
6. **Bourgi, R.;** Kharouf, N.; Cuevas-Suárez, C.E.; Lukomska-Szymanska, M.; Haikel, Y.; Hardan, L. A Literature Review of Adhesive Systems in Dentistry: Key Components and Their Clinical Applications. *Appl. Sci.* **2024**, *14*, 8111. https://doi.org/10.3390/app14188111

Vous trouverez ci-joint le certificat d'acceptation du cinquième article.

USJ 1875
Université Saint-Joseph de Beyrouth
Faculté de médecine dentaire
fmd

THE INTERNATIONAL ARAB
JOURNAL OF DENTISTRY

SCOPUS INDEXED

CERIFICATE OF ACCEPTANCE

The article entitled:
“Assessment of Clinical Performance of Universal Adhesives Versus Other Adhesive Systems: A Systematic Review and Meta-Analysis of Clinical Trials”

Authored by:
Rim Bourgi, Naji Kharouf, Carlos Enrique Cuevas-Suárez, Cynthia Kassis, Ana Josefina Monjaras-Avila, Mohammad Qaddomi, Sophie Abi Raad, Mohammed Al Hasani, Youssef Haikel, Louis Hardan

Has been accepted in “*International Arab Journal of Dentistry*” (ISNN:2218-0885)
and will be published in Vol 15, issue 2, in November 2024.

Résultats et conclusion générale

Les différentes fonctions et applications cliniques des systèmes adhésifs sont devenues une partie fondamentale de la dentisterie restauratrice. Le plus grand défi pour de tels systèmes est de fournir une adhérence adéquate aux différents tissus, qui peuvent être de nature très diverse.

Lors du choix du système adhésif approprié, le dentiste doit être familiarisé avec l'origine, la composition, le mécanisme d'action et la méthode d'application de chaque système. Les produits disponibles sur le marché et leur haute technicité ont permis au clinicien de développer une philosophie de conservation maximale des tissus, une esthétique optimisée, des concepts et des procédures modernes et une fonction complète de l'élément restauré, compatible avec la théorie biomimétique.

En conséquence, le succès de toute technique de collage dépend de la bonne sélection du système adhésif et pour que ce choix soit pertinent, chaque système adhésif aura des protocoles légèrement variés et une application adaptée en fonction de la composition spécifique de l'adhésif. Pour obtenir une meilleure force de liaison dentinaire, les systèmes adhésifs doivent suivre quelques critères essentiels

Sur la base de cette thèse, il semble qu’une application active avec frottement pourrait être suggéré comme la référence en matière d'application d'un système adhésif sur la dentine. En addition, la méthode d’application active unique a bien été adaptée pour presque tous les adhésifs testés. Notamment, un modèle perceptible se développe, indiquant que des températures plus chaudes (40 °C et 60 °C) pour l’évaporation du solvant améliorent les performances de liaison, optimisant à la fois la qualité de la couche hybride et l’interaction adhésive avec le tissu dentinaire.

Plus particulièrement, après 6 mois de vieillissement, les modalités (application Compo-Vibes et application modifiée Compo-Vibes) pour le Prime&Bond Universal et le Clearfil SE Bond ont été jugées stables. En outre, la combinaison de la technique de liaison active avec une application triple couche modifiée s'est révélée être une solution viable pour l’OptiBond FL très rempli. De plus, ces découvertes surprenantes indiquent les avantages possibles de l’utilisation de températures plus chaudes lors de la procédure d’application de l’adhésif.

Cependant, il est essentiel de bien comprendre la composition, les propriétés, et les mécanismes d’adhésion de chaque système adhésif afin de développer des approches de liaison optimales dans des conditions cliniques. L’utilisation de ces méthodologies en est actuellement à ses débuts, mais elle devrait conduire à une meilleure connaissance des différentes « astuces » qui améliorent l’adhésion dentinaire dans l’environnement buccal. Le perfectionnement et l'amélioration continus des procédures, ainsi que l'accent accru mis sur leur utilisation, sont essentiels pour surmonter les défis qui limitent le succès de la dentisterie adhésive.

Perspectives

Étant donné qu'il existe encore plusieurs problèmes non résolus concernant la longévité de l'interface adhésive, il est vraiment impressionnant de voir à quel point le collage a progressé au cours des 50 à 60 dernières années. Des techniques capables de former des liaisons résine-dentine stables tout en résistant à l’hydrolyse collagénolytique seront très probablement disponibles dans les années à venir, augmentant ainsi l’efficacité des traitements dentaires.

Certaines techniques en perspective pouvant être explorées pour compléter ce travail de thèse :

- Mordançage sélective de la dentine pendant 3 s avec les adhésifs testés dans cette étude ou d'autres adhésifs à titre de comparaison.
- SAM et M+R avec les UAs. Seul le mode SAM a été utilisé dans cette étude.
- Une autre application. Dans cette étude, trois sujets principaux ont été explorés (modalités d’application, application des différentes couches et différentes températures de l’air). Le développement de diverses stratégies d'application pour améliorer les performances d'adhérence des adhésifs à la dentine sera un objectif futur.
- Couche de boue dentinaire épaisse ou mince. Dans cette étude, une couche épaisse de boue dentinaire a été obtenue.
- Une autre marque d'UAs. Dans cette étude, seuls deux UAs provenant de deux fabricants ont été utilisés.
- Le collage à l'émail avec les mêmes protocoles utilisés dans cette thèse devrait être mis en œuvre à l'avenir.
- Temps d'application de l'adhésif. Dans cette étude, l’apprêt dentinaire ou l'adhésif ont été appliqués en fonction du temps (20 s) bien que dans la littérature, des temps variables aient été utilisés.
- μTBS à l'état « humide » (après 5 min de stockage) et « déshydraté » des bâtons (testé après 10, 15 min et 24 h). Les bâtons ont été directement utilisés pour le test de résistance d’adhésion. Notez que les bâtons n’ont pas été déshydratés dans cette étude. (La déshydratation prend environ 2 min,

mais le chercheur peut la faire pendant 10 min à 24 h. D'autres études déshydratent pendant des durées variables).

- Analyse de l'CA des adhésifs via mobile ou reflex numérique à objectif simple. Dans cette étude, un analyseur d'CA a été utilisé.
- Pression pulpaire. Une étude précédente a été menée sans simulation de pression pulpaire, ce qui peut affecter négativement les résultats car le domaine de travail incluait une condition dans laquelle la dentine est vitale.
- *In vivo*. Dans cette étude *in vitro*, une dent extraite a été utilisée, ce qui est différent d'un état clinique. Les futures études cliniques sont importantes.
- Évaluation de la dégradation à long terme de la liaison résine-dentine. Seuls 6 mois de vieillissement ont été évalués.
- Développement du dispositif d'évaporation d'air chaud. Dans cette étude, seul un prototype a été utilisé.
- Une variation en termes de photopolymérisation de chaque couche devrait être testée dans le futur.
- Les prochains adhésifs dentinaires pourraient également jouer un rôle plus instrumental dans le domaine thérapeutique en dehors de la prévention des caries.
- Différentes méthodologies pourraient être explorées dans des études ultérieures, notamment l'augmentation de la température dans la chambre pulpaire lors de l'utilisation de températures plus chaudes, la cytotoxicité contre les cellules odontoblastiques, les nano-fuites pour tous les bâtonnets résine-dentine, la profondeur de pénétration des adhésifs avec les différentes méthodes utilisées, l'épaisseur de la CH et la longueur des tags en résine, la tomodensitométrie (micro-CT) au lieu du MEB, la biocompatibilité, la solubilité, le degré de conversion, la stabilité de la durée de conservation et le taux de polymérisation de l'adhésif appliqué avec différentes modalités testées.

USJ 1875
Université Saint-Joseph de Beyrouth
جامعة القدّيس يوسف في بيروت

Université de Strasbourg

École doctorale
Physique, chimie-physique
ED 182
Université de Strasbourg

Rim BOURGI

Effect of different application modalities and temperature of warm air evaporation on the bonding performance of four adhesive systems to dentin

Résumé

Les lignes directrices de cette thèse consistent à utiliser différentes stratégies pour améliorer les performances de liaison des systèmes adhésifs à la dentine. Actuellement, il n'existe pas de protocole spécifique pour obtenir une adhésion optimale entre l'adhésif dentaire et la dentine. Cependant, la combinaison d'une modalité active, d'une application monocouche, et de températures plus élevées pour l'évaporation du solvant dans l'adhésif dentaire a été proposée comme moyen d'optimiser le collage et de simplifier l'application, ce qui améliore la durabilité des liaisons résine-dentine. Il semble que l'obtention d'une forte liaison adhésif-dentine, réalisable grâce à des modalités d'application appropriées et une exécution correcte, puisse renforcer la force d'adhésion et assurer une durabilité à long terme. Ainsi, les procédures analysées dans cette thèse sont essentielles au succès durable des traitements de restauration dentinaire. Les étapes importantes de l'application de divers matériaux adhésifs nécessitent une compréhension approfondie de la chimie de l'adhésif utilisé. Cette thèse propose aux cliniciens des modifications novatrices des modalités actuelles pour les aider à maintenir la force de l'adhésion à la dentine. Il est intéressant de noter qu'aucun agent ne peut surpasser les méthodes inefficaces.

Mots clés: interface adhésif-dentine, systèmes adhésifs, liaison dentinaire, air chaud.

Résumé en anglais

The guidelines of this thesis are to employ different strategies to enhance the bond performance of adhesive systems when bonding to dentin. Currently, there is no specific protocol to obtain optimal adhesion between dental adhesive and dentin. However, the combination of an active modality, a single-coat application, and warmer temperatures for solvent evaporation in the dental adhesive has been proposed as a means to optimize bonding and simplify application, thereby improving the durability of resin-dentinal bonds. It appears that achieving a strong and reliable adhesive-dentin bond, using feasible application modalities and proper execution, can promote bond strength and durability over time. Therefore, the procedures analyzed in this thesis are essential for the long-term success of dentin restoration treatments. The important steps in the application of various adhesive materials require a thorough understanding of the chemistry of the used adhesive. This thesis proposes innovative adjustments in current techniques to assist clinicians with maintaining the strength of adhesion to dentin. Interestingly, no agent can outperform inefficient methods.

Keywords: adhesive-dentin interface, adhesive systems, dentin bonding, warm-air.