

ADHESIVE STRATEGIES TO PREVENT DEGRADATION OF ADHESIVE/ DENTIN INTERFACE: LITERATURE REVIEW

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ABSTRACT

The main purpose of this review was to evaluate different strategies that have been developed to prevent bond interface degradation over time. Studies evaluating the degradation of dentin-bonding interfaces were identified. The search was restricted to articles written in English between January 1966 to May 2018. The source of the published studies used was the PubMed database with the search strategies: “((((resin-dentin bonds) OR dentin bonding) OR adhesive systems)) AND ((hybrid layer degradation) OR collagen) AND ((((((polymer hydrolytic stability) OR Acrylamides) OR 10-MDP) OR calcium-chelation dry bonding) OR ethanol wet-bonding) OR hema free) OR ((adhesive stability) OR monomer stability))”. In

addition, the references of all identified articles were manually searched for further relevant studies. The use of functional monomers that are more hydrolytically stable, monomers that chemically bond to the dentin substrate, adhesive systems that induce mineral deposition and modifications during the adhesive procedure to decrease the amount of remaining water in the substrate are described as strategies for greater restorative clinical longevity. Numerous strategies proposed in the literature attempt to reduce the degradation of the adhesive interface. Although the adhesive systems reduced the clinical restorative time and facilitated the operative technique, most of the proposed strategies add another step in the clinical restorative protocol, which can often need a more sensitive technique due to lack of experience. With the facilitation of the operative technique, the search for new monomers that have higher hydrolytic stability, a chemical interaction with the dentin substrate and lower aqueous content remaining at the adhesive interface seems to be the pathway for less hydrolytic degradation and operative facility.

KEYWORDS:

Dentin-bonding agents.
Hydrolysis. acrylamides.
methacrylates.

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INTRODUCTION

Recent advances in dentistry such as the development of the etch-and-rinse and self-etching adhesive systems have enabled treatments that previously depended on mechanical retention to be replaced by minimally invasive treatments. These new treatments allow a greater preservation of dental tissue during the restorative procedure. An adhesive interface is a form of tissue engineering in which the dentin collagen matrix is used as a scaffold for monomers to infiltrate and form a micromechanical bond between the collagen and polymer. This hybridization is possible due to an increase in superficial enamel area¹ and in dentin² after the surface is conditioned by acids. With the acid application, the removal of an inorganic part of the substrate will leave the collagen fibers exposed and that can be filled by monomers present in the adhesive systems after polymerization forms the hybrid layer.³ The characteristics and formation of this hybrid layer are related to the use of the etch-and-rinse or self-etching adhesive systems.⁴

Independent of the adhesive system, the etch-and-rinse or self-etching components can be present in the same bottle or separated. In the etch-and-rinse adhesive, demineralization occurs in 37% of phosphoric acid application (pH 0.1–0.4), resulting in a hybrid layer of 5–8 μm and resin tags inside the dentin.⁵ The bond between the dentin substrate, which is a hydrophile, and an adhesive resin that contains hydrophobic monomers occurs by *primer* application since it has hydrophilic monomers that dissolve in organic solvents. The adhesives are a compound of a mixture of co-monomeric blends with low viscosity that has acrylate monomers, methacrylates and ether vinyl;^{5,6} can form polymers with high crosslinked density and mechanical properties and forms chemistry bonds with composite resin.^{7,8}

In self-etch adhesives, dental etching occurs by the acid monomers, 2-methacryloyloxyethyl dihydrogen phosphate (HEMA-P) and 10-methacryloyloxydecyl dihydrogen phosphate (10-MDP).⁹ Commonly, acid monomers stay in the same bottle as the *primer*, and thus, the use of a solvent—as water is indispensable—ensures the ionization of monomer acids on dentin.⁹ The demineralization depth of self-etch system will depend on the adhesive system's pH and acid monomer, pKa. Classification is according to the strength of the monomer acid: strong (pH<1.5 with demineralization of $\pm 4 \mu\text{m}$), mild (pH~2 with demineralization of $\pm 500 \text{ nm}$) and ultra-mild (pH>2.5 with demineralization less than 500 nm). In addition, resin tags are not made into the hybrid layer.¹⁰

The type of adhesive systems used is directly related to the degradation of the adhesive interface and/or collagen matrix exposed over time.¹¹⁻¹³ The water remaining in demineralized dentin must be completely replaced by adhesives blends; however, the complete infiltration of monomers into the wet and demineralized dentin is not consistently achieved, leaving incompletely infiltrated zones along the bottom of the hybrid layer. Denuded collagen fibrils surrounded by rinse water is directed related to the activation of dentin collagenolytic enzymes during the restoration procedure of chemical agents by dentin

fluids, saliva, and bacterial products.¹¹⁻¹⁵ Different methods and the inhibitors substances of matrix metalloproteinases and cathepsins present on collagen, such as chlorhexidine, polyphenols, ethylenediaminetetraacetic acid (EDTA) and ammonium quaternary, have already been evaluated. However, no consolidated long-term evidence implementing these restorative procedures with use of these substances currently exists.

The degradation of the adhesive resin is related to the remaining water in the adhesive procedure, hydrophilicity of functional monomers and water sorption.¹⁶ Degradation occurs due to the rupture of covalent bonds between functional monomers and noncured monomer elution, provoking premature losses and consequently interfering in the longevity of restorative treatment.¹⁷⁻²¹ Even with the development of simplified adhesive systems and knowledge of the chemical interactions between acid monomers and dentin substrates,^{22,23} simplified adhesive systems still suffer degradation in adhesive interfaces over time²⁴⁻²⁸ seem to be more relevant than collagenolytic degradation. Therefore, the main purpose of this systematic review is to evaluate different strategies that have been developed to prevent bond interface degradation over time.

SEARCH STRATEGY

Studies evaluating the degradation of dentin-bonding interfaces were identified. The search was restricted to articles written in English between January 1966 to May 2018. The source of the published studies used was the PubMed database with the search strategies: “((((resin-dentin bonds) OR dentin bonding) OR adhesive systems)) AND ((hybrid layer degradation) OR collagen)) AND ((((((polymer hydrolytic stability) OR Acrylamides) OR 10-MDP) OR calcium-chelation dry bonding) OR ethanol wet-bonding) OR hema free) OR ((adhesive stability) OR monomer stability))”. In addition, the references of all identified articles were manually searched for further relevant studies.

In this literature review, we aim to present the main strategies for more adhesive interface stability. The use of functional monomers that are more hydrolytically stable, monomers that chemically bond to the dentin substrate, adhesive systems with mineral deposition capacity and modifications during the adhesive procedure to decrease the amount of remaining water in the substrate are described as strategies for greater restorative clinical longevity.

ADHESIVES STRATEGIES

Polymer hydrolytic stability

A lasting adhesive bond strength is achieved between a dental substrate and restorative materials adhesive when agents are used due to bifunctional molecules with a polymer group. To achieve a durable adhesive bond strength between the dental substrate (enamel and dentin) and restorative materials, bonding agents are used²⁹ due to constitute bifunctional molecule contains a polymerizable group, a spacer and a polar functional group.³⁰ The polymerizable group, methacrylates, can be copolymerized with restorative material and exhibit hydrophobic behavior.³¹ The spacer, alkyl chain as well may contain an ether group or amines or aromatic groups, maintains the polymerizable group and the functional group separated.³² The hydrophilicity of the spacer can determine water solubility and, in other solvents, influence water absorption. As a result, monomer hydrolysis, as well as swelling and discoloration of polymerizable resin, occurs. The spacer size determines polymer flexibility, viscosity and, consequently, wettability.²⁹ The functional group of monomers usually present hydrophilic properties and can improve the wetting and reaction of dentin tissue, improving the bond strength.³³ The following are

examples of functional groups: phosphates, carboxylic acid and alcohols. Basically, two monomers types, functional monomers and crosslinks, can be distinguishable. Functional monomers present only one polymerizable group and result in linear polymers.⁴ Crosslinks show two or more polymerizable groups (vinyl groups) and result in crosslinked polymers, presenting better mechanical properties than linear polymers.^{34,35}

Acrylates and methacrylates are usually used in dental adhesive systems due to their high reactivity, and when associated with correct photoinitiations, they result in insoluble polymers with crosslink bonds.⁴ They have shown high mechanical properties including flexural strength and longitudinal bond strength.^{36,37} The methacrylates have distinct characteristics. Bisphenol A-glycidyl methacrylate presents high reactivity because it is a dimethacrylate, with carbon double bonds, high weight molecular viscosity and aromatic rings. The hydroxyl groups in our molecular structure have hydrogen bonds, are hydrophobic and have lower water solubility.²⁹ Therefore, obtaining polymers with a high degree of conversion should be associated with flexural monomers, low molecular weight, low viscosity and as high solubility as triethylene glycol dimethacrylate (TEGDMA).³⁴ Currently, the hydrophilic methacrylate, 2-hydroxymethyl methacrylate (HEMA), is used due to

its low molecular weight and low viscosity, which increases miscibility and solubility with polar and nonpolar adhesive components.³⁸

The ester group of methacrylate monomers suffers hydrolysis when in an acidic environment, such as, for example, in self-etching adhesive systems when the acid monomer is together with the functional monomer.^{32,39} The hydrolysis of methacrylate monomers in an acidic environment occurs within 14 days and results in a subproduct formation that compromises the polymer's mechanical properties, such as flexural strength, bond strength^{27,40} and adhesive shelf time.⁴ Not only is the ester group susceptible to hydrolysis, but also the phosphate and carboxylic groups used in functional monomers are vulnerable to hydrolysis in water as well.⁴

Hydrophobic monomers present low water sorption, while hydrophilic monomers present high water sorption. Thus, a simplified adhesive system with a high hydrophilic monomer concentration creates a hybrid layer that can pass fluids as the membrane is semipermeable.¹⁶ Furthermore, all adhesive systems showed an incomplete polymerization that is associated with fluid permeability and is even higher in a simplified adhesive system.^{20,41} The permeability of the adhesive interface results in resinous mass loss and a decrease in the elastic modulus of the adhesive resin, as well as bond strength,⁴² compromising the longevity of restorative treatment.²⁸

Monomers with high hydrolytic stability

Monomers with high hydrolytic stability were developed as acid phosphate monomers (MDP), surfactant monomers, acrylamides and methacrylamides to result in adhesive systems with over two-year shelf lives at room temperature^{4,42,43} and that have not degraded hydrolytically in an adhesive interface. However, some phosphate monomers and acid phosphate monomers were stable hydrolytically but were not indicated to include radical polymerization due to lower reactivity when compared with methacrylates.^{42,44}

10-MDP

The 10-MDP is a functional acid monomer used in mild self-etching adhesives. It is a long hydrophobic spacer chain with ten carbons that are present at the end of the phosphate group that has a chemical ionic bond with the calcium of residual hydroxyapatite.²³ The salt formed between 10-MDP and the calcium, 10-MDP-Ca, is more stable than other monomers evaluated, such as 4-MET and phenyl-P. Furthermore, salt has the capacity to form self-assembled nanolayers with 4 nm between them.^{10,45} These nanolayers are responsible for protecting the collagen fibers of hydrolytic degradation due to hydrophobicity and increasing the apatite crystals dentin resistance to acid bacterium dissolution.⁴⁶ The nanolayer of 10-MDP-Ca was demonstrated in adhesive interfaces produced with commercial adhesive systems such as Clearfil SE Bond (Kuraray) and Single Bond Universal (3M ESPE).⁴⁷ However, because the 10-MDP has a low capacity to crosslink, when compared to dimethacrylates, the stability of 10-MDP-Ca salt can be limited over time. This also explains why nanolayers have never been observed for transmission electron microscopy (TEM) in completed

demineralized samples. Furthermore, these nanolayers were not found in all adhesive interface extensions, and some regions stayed without a chemistry bond between the monomer and dentin substrate subject a polymer and hydrolytic collagen degradation.⁴⁶ The presence of HEMA in the adhesive systems, together with 10-MDP, promoted a reduction in nanolayer formation already decreased once by a demineralization tax, which is a requisite before the formation of 10-MDP-Ca salts.⁴⁸ Although there is still no consensus about the extension this nanolayer has over an adhesive interface, ClearFil SE Bond shows a low annual failure rate (2.2%) in the restoration of noncarious cervical lesions over time. Moreover, 1-step self-etch adhesives with 10-MDP also results in low annual failure rates: 2.6% for Clearfil S3 Bond (Kuraray Noritake), 1.3% for G-Bond (GC), and 4.0% for Scotchbond Universal (3M ESPE).²⁸

Surfactants Monomers

The surfactant monomers were used to substitute the HEMA monomer in self-etch adhesive systems. They resulted in immediate bond strength values similar to the groups with HEMA. The molecular structure has both hydrophilic and hydrophobic groups, are soluble in organic solvents, facilitate monomer penetration in demineralized dentin, have high bond strength, lower phase separation and are less susceptible to hydrolysis.^{43,49-52} Even without longitudinal evidence about experimental adhesive systems with surfactant monomers, *in vitro* studies have shown that some monomers can substitute HEMA and result in better mechanical properties, low cytotoxicity and similar degree of conversion and bond strength compared to the HEMA group.⁵³⁻⁵⁵

Acrylamides and methacrylamides

As described in the literature, carbamides are more stable hydrolytically than esters due to the lower reactivity of carbonyl. Therefore, to occur, hydrolysis is a necessary strong condition as an environmental acid concentrate of sulfuric acid or phosphoric acid.³⁸ Acrylamides and methacrylamides were synthesized to present amide group (RNH-CO- or -CO-NR1R2) instead the ester group (-COOR) present in methacrylates to increase the hydrolytic stability of adhesive systems.^{4,56-58} Moreover, an explanation for the

growing interest in acrylamides may involve its similarity to the amino acids composed of collagen fibers that have hydrolytic stability in acidic environment up until 18 months, good mechanical properties, good solubility in organic solvents and 35 time less cytotoxicity when compared to TEGDMA.^{32,42,59-64} However, some acrylamides were synthesized and resulted in a solid product, making the incorporation with other monomers or lower water solubility difficult.⁶⁵

Acrylamides degrade in the acid concentrate environment and for this are indicated in self-etch adhesives simplified, monomers acids and functional monomers in the same bottle.⁶³ Studies development *primers* with bis(acrylamides) and acids bis(acrylamides) for self-etch and evaluated the bond strength using resin adhesives with methacrylates, which makes it difficult to characterize the adhesive interface.^{38,60-63,66-71}

Hydroxyethyl acrylamide (HEAA), together with BisGMA, has already been used in an adhesive resin without HEMA and presents inferior mechanical properties when compared to the control group (HEMA and BisGMA).⁷² The HEAA reacted six times more than BisGMA during the polymerization process and resulted in a polymer with low mechanical properties, forming a polymer with linear chains instead of being crosslinked. Bis(acrylamides) are found in the commercial adhesive system, Adhese (Ivoclar Vivadent), a mild 2-step self-etch adhesive that has a resulting annual failure rate of 3.6% and high shelf life, since the *primer* does not contain acid monomers and HEMA in the same bottle.^{4,28}

Adhesive resin with incorporation of fillers

Nanometric particles were incorporated in adhesive systems with the aim to increase mechanical and chemical properties of adhesive systems. The high degree of conversion for adhesive resin was found when nanoparticles of dioxide titanium were functionalized with carboxylic acid, silver nanoparticles, boron nitride nanotubes, nanostructured hydroxyapatite and niobium pentoxide, zirconium dioxide, were incorporated in the adhesive systems.⁷³⁻⁷⁹ More conversion resulted in less water sorption and hydrolytic degradation. A copper incorporation into a 2-step etch-and-rinse adhesive system that did not interfere with the system's properties resulted in antimicrobial action against *Streptococcus mutans*, a decrease in nanoleakage and a significant reduction in longitudinal bond strength (1 year) when compared to the control group, which had no copper particles.⁸⁰ Clearfil Protect Bond (Kuraray) is a commercial adhesive with an antimicrobial agent. This mild 2-step self-etch adhesive system presented a 12-methacryloyloxy dodecyl pyridinium bromide (MDPB) monomer,⁸¹ resulting in an annual failure rate of 2.6%²⁸ and a decrease in enamel demineralization around of brackets after 30 days and was not significant for dentin.⁸² Other promising antibacterial agents were added to an adhesive system of laboratory studies as [2-(methacryloyloxy)ethyl]trimethylammonium chloride,⁸³ triazine compound,⁸⁴ 2-[3-(2H-benzotriazol-2-yl)-4-hydroxyphenyl] ethyl methacrylate⁸⁵ indomethacin- and triclosan-loaded nanocapsules have potential to prevent recurrent caries.^{86,87}

Zinc oxide nanoparticles preserve the adhesive interface and integrate the polymerization shrinkage of experimental adhesive resin.⁸⁸ In addition, it does not form clusters when sized between 1 and 10 nm, particles known as quantum dots; these result in a polymer with less susceptible fractures.^{89,90} These quantum dots have not yet been incorporated into commercial adhesive systems.

Remineralization

The combination of 40% calcium silicate nanoparticles in adhesive resin with primers contend biomimetic analogs, as polyaspartic acid or sodium trimetaphosphate, promoted a biomimetic remineralization in the adhesive interface.⁹¹ Other fillers such as halloysite aluminum silicate nanotubes were also incorporated into the adhesive resin and reinforced the adhesive interface. Once these nanotubes penetrated the dentin and resin tags, they increased the chemical bonds between the dentin and resin.^{92,93} These nanotubes were incorporated and evaluated in the 2-step etch-and-rinse and 1-step self-etch adhesives, improving the properties of the adhesive interface. Boron nitrate nanotubes were included in an experimental 3-step etch-and-rinse adhesive. Besides promoting an improvement in the physical-chemical properties of the adhesive system, it also promoted a mineral deposition in the adhesive interface when 0.15% of the filler was incorporated. It contributed to bond stability between the dentin

and resin.⁷⁷ Hydroxyapatite, α -tricalcium phosphate, octacalcium phosphate, triclosan-loaded halloysite nanotubes and niobium pentoxide were incorporated in an adhesive resin and an orthodontic adhesive resin, these fillers may be a promising strategy to achieve therapeutic remineralization at the composite-dentin interface besides improve bond strength.^{78,94-97} Although many fillers being used in *in vitro* tests with promising results, these fillers were not evaluated in the *in vivo* studies.

Ethanol wet-bonding

Ethanol

Ethanol wet bonding is a concept that replaces the amount of residual water into the interfibrillar and intrafibrillar spaces of demineralized dentin collagen with ethanol, thus avoiding the excess of dentin water. Dentin is more susceptible to hydrolysis and prevents phase separation in simplified adhesives due to its hydrophobic nature.^{4,98,99} Furthermore, ethanol has high vapor pressure when compared to water, resulting in fast evaporation and allowing for better resin infiltration due to the early evaporation of water molecules from the interfibrillar spaces of collagen fibrils. Ethanol also facilitates adhesive polymerization, thus improving the resin-dentin bonds and blocking collagenolytic degradation by the matrix metalloproteinase.^{28,100}

The success of ethanol wet bonding adhesion is due to its positive results in immediate and post-6-month bond strength compared to water adhesion. This result is due to the high degree of conversion of the resin matrix when monomeric propagation continues to occur from low environment viscosity and high monomeric mobility.¹⁰¹ In the clinical protocol for the application, prior to the bonding procedure, the dentin is dehydrated by the application of 50% ethanol for 10 s, followed by 100% absolute ethanol for 10 s. Ethanol excess was then dried.¹⁰¹ Intraradicular dentin treated with 100% ethanol prior to the bonding procedure reduced the amount of residual water in the root canal as well as at the hybrid layer level, thus improving resin-dentin bond.¹⁰²

DMSO

Dimethyl sulfoxide (DMSO) is a polar aprotic solvent that dissolves polar and nonpolar components, has two hydrophobic methyl groups and is miscible in many solvents and monomers used in adhesive dentistry.^{97,103,104} It is a polyfunctional molecule with the ability to dissociate the highly crosslinked collagen into a sparser network of apparent fibrils. It increases wettability in demineralized dentin and increases monomeric diffusion into the collagen matrix. It also concomitantly re-expands the collapsed collagen and bonds with lower water content in the adhesive interface.¹⁰⁵⁻¹⁰⁸ DMSO is being used as a pretreatment between acid etching and the *primer* application, with the objective to reduce the water remaining from the etch-and-rinse adhesives as well as to increase the interaction between dentin and resin to dry dentin. A pretreatment with DMSO/H₂O and DMSO/ethanol, independent of a dry or wet dentin bond in a 3-step etch-and-rinse system, resulted in an improvement in bond strength.¹⁰⁴

Hydrophobic resin coating

After the bonding steps, a hydrophobic resin was applied in the substrate, followed by an air blower to achieve an optimally thin layer of adhesive. This insoluble hydrophobic layer adds hydrophobic monomers to the adhesive interface, decreasing retained solvent concentrations and noncured monomers. Consequently, the adhesive interface will be more densely packed, more resistant to tensile forces and less prone to degradation over time.^{109,110} For universal adhesives, resin coating improved the adhesive performance of enamel bond strength when used with the selective enamel strategy and dentin bond strength when self-etching. The in situ degree of conversion increased independently of the strategy used (self-etch or etch-and-rinse).¹¹¹

CONCLUSION

Numerous strategies have been proposed in the literature attempt to reduce the degradation of the adhesive interface. Although the modern adhesive systems reduced the clinical restorative time and facilitated the operative technique, most of the proposed strategies add another step in the clinical restorative protocol, which can often create a more sensitive technique. With the facilitation of the operative technique, the search for new monomers that have higher hydrolytic stability, a chemical interaction with the dentin substrate and lower aqueous content remaining at the adhesive interface seems to be the pathway for less hydrolytic degradation and operative facility.

Nowadays, the 2-step self-etch adhesive system may be the best adhesive system of choice for clinical restorative use because it presents more benefits than the 3-step etch-and-rinse adhesive system. When the acid monomers were separated from the hydrophobic monomers, they avoided phase separation and technical operative facility, had less remaining aqueous content (because they do not need to condition the dentin with phosphoric acid), had monomers that were ionically bound to the dental substrate (such as 10-MDP), had low annual failure rates and formed nanolayers with higher hydrolytic stability. However, the 3-step etch-and-rinse adhesive system—when used with the correct technical operative such as slightly wet dentin after acid etching with an active primer application and evaporating the remaining solvent—is still widely used and demonstrates high survival rates over time.

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