An Overview of Dental Adhesive Systems and the Dynamic Tooth–Adhesive Interface

Ana Bedran-Russo, DDS, MS, PhD[a,*],
Ariene A. Leme-Kraus, DDS, MS, PhD[b],
Cristina M.P. Vidal, DDS, MS, PhD[c], Erica C. Teixeira, DDS, MS, PhD[c]

KEYWORDS

• Dental adhesives • Dentin • Enamel • Bond strength • Biodegradation • Technology

KEY POINTS

- There are 2 adhesive strategies of contemporary dental adhesive systems to bond to enamel and dentin. Strategies can be accomplished in 1 to 3 steps.
- Resin acidity and hydrophilicity increase the susceptibility for degradation of the adhesive interface; altered forms of enamel and dentin can negatively affect bonding to enamel and dentin.
- Adhesive interfaces are susceptible to biodegradation.
- Degradation includes interaction with the dental biofilm, active bacterial enzymes, and activation of endogenous enzymes.
- Some restorative strategies that might influence the long-term outcome of the dynamic tooth adhesive–interface are summarized.

Adhesion has revolutionized contemporary restorative dentistry with 3 groundbreaking research advances:

1. Dental surfaces modification by acid etching,
2. The development of methacrylate-based resin composite chemistry, and
3. The development of hydrophilic resin chemistry.

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[a] Department of Restorative Dentistry, University of Illinois at Chicago College of Dentistry, 801 South Paulina Street, Room 531, Chicago, IL 60612, USA; [b] Department of Restorative Dentistry, University of Illinois at Chicago College of Dentistry, 801 South Paulina Street, Chicago, IL 60612, USA; [c] Department of Operative Dentistry, The University of Iowa College of Dentistry and Dental Clinics, 801 Newton Road, Iowa City, IA 52242, USA
* Corresponding author.
E-mail address: bedran@uic.edu

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Adhesive restorative dentistry affects virtually every dental practice because it is integral to many procedures, including dental sealant placement, bonding of orthodontic brackets, direct composites restorations, intraradicular posts cementation, cementation of inlay or onlay tooth-colored restorations, full-coverage all-ceramic crowns, bonded bridges, and root canal obturation. This review focuses on dental restorative applications of dental adhesives.

CLASSIFICATION OF CONTEMPORARY DENTAL ADHESIVE SYSTEMS

Dental adhesives are often commercially categorized into generations reflecting the handling technique or advances in formulations rather than new adhesion concepts or mechanisms. A close look into the chemistry of dental adhesives and their mechanism of adhesion to dentin yield 2 major adhesive concepts:

1. Reliance on the complete removal of the smear layer (ie, the layer of debris formed after cavity preparation) and superficial demineralization of dentin and enamel, and
2. Partial superficial dissolution and incorporation of the smear layer into the adhesive interface.

Both concepts promote adhesion by micromechanical retention to the underlying dental tissues. However, an additional chemical bond to the substrate is present, particularly in the latter concept.

Multiple or single steps are commercially available within the 2 major categories of systems, being referred to as etch and rinse and self-etch (Fig. 1). Etch-and-rinse systems (also known as total etch) require separate acid etching and rinsing steps followed by the application of the primer and adhesive in 2 separate or one combined step (see Fig. 1). Self-etch systems do not require a separate etching step; rather, acidic primers are used to promote partial dissolution of the smear layer and infiltration of primers by an etching or primer step followed by an adhesive application (2-step systems) or through a single formulation with an adhesive resin (all-in-one system; see Fig. 1). More recently, the term universal systems has been used to define dental adhesive systems that can be applied either in etch-and-rinse or self-etch modes (see Fig. 1).

THE CHEMISTRY OF DENTAL ADHESIVES SYSTEMS

Overall, adhesion is attainable when the following are present: clean dental surfaces, good surface wettability, diffusion of the adhesive resin monomers within enamel and

Contemporary Dental Adhesive Systems					Characteristics			Longevity
System Mode	Delivery	Adhesion Steps			Acidity	Hydrophilicity	Bond Stability[b]	
		Etching	Primer	Adhesive				
Etch-and-rinse	3-step				+	+	++++	Stability ↑ Degree of Conversion Solvent Evaporation ↓ Acidity Hydrophilicity ↓ Degradation
	2-step				++	++	+++	
Self-etch	2-step				+++	++	++++	
	1-step				++++	+++	+	
Universal	1 or 2 steps[a]				+++	++	+ (+) +	

Fig. 1. Current contemporary dental adhesives systems and characteristics affecting the long-term stability of dentin–resin interfaces. Symbol (+) indicates scale ranging from lowest (+) to highest (++++). [a] The adhesive system support optional pre-etching of enamel or dentin (2- step) or self-etching mode (1-step). [b] Depicts relative values of dentin bond strength, note that average bond strengths can greatly vary among brands, studies and application modes (for universal systems). Degree of conversion = polymerization rates of adhesive.

dentin, and adequate resin polymerization. The adhesive systems consist of a blend of methacrylate-based resin monomers with either 2 (cross-linking monomers) or 1 (functional monomers) polymerizable ends, organic solvents, a photoinitiator system, and often nanofillers (Fig. 2).[1] The chemistry of dental adhesive resins must fulfill the requirements for adhesion to different dental substrates: enamel, dentin, and cementum. Functional hydrophilic resin monomers facilitate resin infiltration within the demineralized and moist dentin surface whereas hydrophobic cross-linking resin monomers provide the mechanical strength, stability and compatibility between the adhesive system and the bulk restorative resin or resin cement.[2]

Resin monomers with 2 or more polymerizable groups are necessary to form a highly cross-linked network to provide the strength and stability of the adhesive layer.[1,2] Examples of cross-linking monomers with a more hydrophobic nature are bisphenol A-glycidyl methacrylate, triethylene glycol dymethacrylate (TEGDMA), urethane dimethacrylate, and ethoxylated bisphenol-A dimethacrylate. The difference in molecular weight among the resin monomers is important, because low-molecular-weight monomers dissolve the high-molecular-weight monomers, improving the wettability of the resin blend.

Functional monomers usually have 1 functional group (eg, hydroxyl groups) and a single polymerizable group to form linear polymer chains (see Fig. 2). One example is hydroxyethyl methacrylate (HEMA), a hydrophilic monomer that facilitates resin

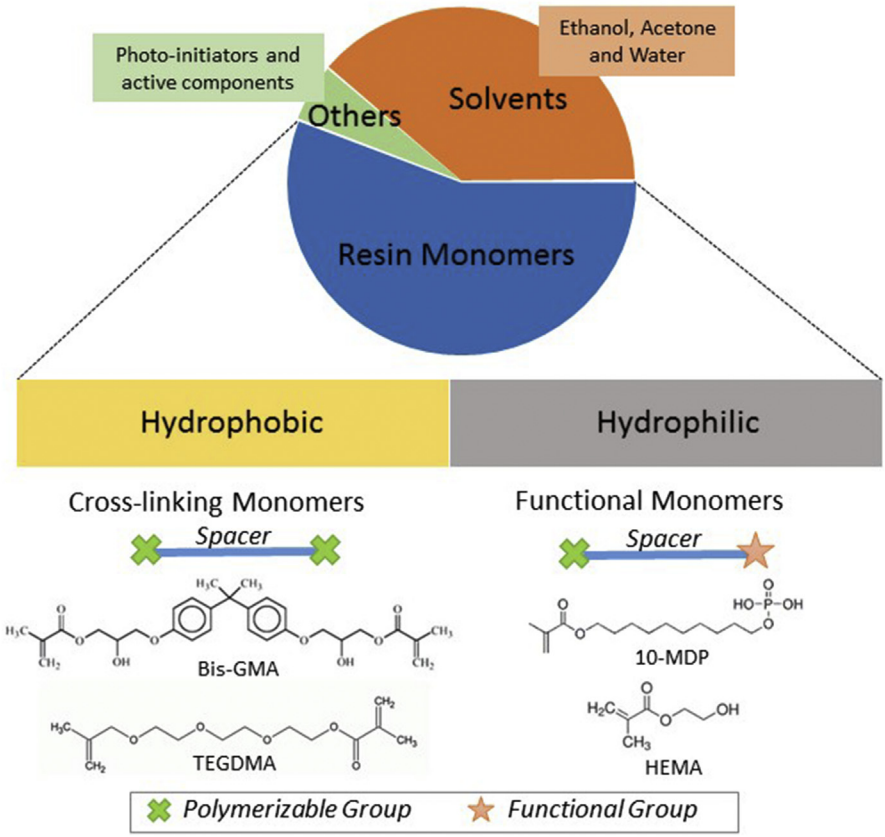

Fig. 2. Composition of dental adhesives and examples of cross-linking and functional monomers used in contemporary adhesive systems.

diffusion within the moist collagen network and is commonly present in contemporary adhesive systems. The importance of HEMA to adhesion in a wet environment is due to its amphiphilic nature, in addition to its low molecular weight that makes HEMA a suitable solvent for high-molecular-weight monomers. As a disadvantage, the incorporation of HEMA to adhesive–resin blends have made dental adhesives too hydrophilic and thus more susceptible to hydrolysis.[3]

In self-etch adhesive systems, the functional groups in the resin monomers are usually acidic, and are also important for etching the enamel and dentin surfaces. Examples of acidic functional resin monomers are 4-methacryloyloxyethyl trimellitate anhydride, 10-methacryloyloxydecyl dihydrogenphosphate (10-MDP), and 2-(methacryloyloxyethyl)phenyl hydrogenphosphate. The functional groups with self-etching ability are either carboxyl or phosphate, and they can also establish ionic bonds with calcium from hydroxyapatite. Overall, 10-MDP is the most popular and highly stable acidic monomer; its stability is attributed to the long carbonyl chain (spacer) between the functional and the polymerizable groups in the monomer structure (see **Fig. 2**). Additionally, the phosphate functional group is capable of forming strong ionic bonds with hydroxyapatite, owing to the low solubility of the resulting calcium salts.[4,5]

Solvents such as ethanol, acetone, and water are added to the adhesive blends to lower viscosity and promote resin infiltration.[1] Solvents are also essential for the effective "wet-bonding" technique of etch-and-rinse systems and dental surface etching by acidic primers in self-etching systems. In etch-and-rinse systems, ethanol plays key roles during the infiltration of the resin monomers within the wet collagen network and further helps in the evaporation of excess water by forming water–ethanol aggregates.[1,6] Remaining solvent within the adhesive layers may impair adhesive polymerization, lowering the mechanical properties and resulting in increased degradation over time.[7,8] Therefore, thorough and careful air drying of the adhesive, exceeding the time recommended by most manufacturers, is necessary to remove excess solvent before the light curing of the adhesive.

Another component that plays significant roles in both the attainment of bond strength and forming a stable adhesive interface is the photoinitiator system. The traditionally used photoinitiator system camphorquinone-amine possesses hydrophobic characteristics and, therefore, may be subjected to phase separation resulting in poor polymerization of the more hydrophilic portion of the adhesive systems.[9,10] Research toward the use of alternative photoinitiator systems have introduced diphenyl(2,4,6-trimethylbenzoyl)phosphine oxide and others like 2-hydroxy-3-(3,4 dimethyl-9-oxo-9H-thioxanthen-2-yloxy)-N,N,N-trimethyl-1-propanaminium chloride (QTX).[10–12] Specifically, the use of QTX has been explored because, as a water-soluble photoinitiator, it may improve the polymerization of the more hydrophilic components of the adhesive resin blends.[10,13]

Active ingredients may also be added to the adhesive resin chemistry for specific functions, such as methacryloyloxydodecylpyridinium bromide in the adhesive resin and benzalkonium chloride in the etching component to impart antibacterial activity.[1] Although the contribution of these specific ingredients have been demonstrated in in vitro studies, more studies are necessary to confirm their clinical efficiency.[14]

Finally, the compatibility and ratio of the various components of adhesive systems is essential to maximize performance. The one-step self-etch systems are chemically more unstable owing to an imbalance between the adhesive blends. The chemistry incompatibility leads to phase separation of the adhesive components, resulting in a porous and poorly polymerized adhesive layer.[9] The sealing ability of these systems is also compromised because of the high amount of hydrophilic monomers that entrap

water within the bonding layer and thus can accelerate the degradation of the adhesive interface.

ADHESIVE BONDING MECHANISMS TO ENAMEL AND DENTIN

Bonding to Enamel

Enamel is the hardest tissue in the human body. It is composed of 96 wt. % mineral, 1 wt. % organic matrix, and 3 wt. % water. Hydroxyapatite crystals are orderly deposited to form highly complex enamel prisms. The enamel prisms run almost perpendicularly from the dentin–enamel junction to the outer enamel surface. An acid-resistant aprismatic enamel surface provides additional protection against enamel dissolution in the oral environment.

Adhesion of methacrylate-based resins to enamel is highly predictable and achievable in most adhesive restorative procedures. The micromechanical bonding mechanism is provided by formation of resin tags and microtags on the superficially demineralized enamel (**Fig. 3**). Phosphoric acid is the acid conditioner of choice for dental tissues. Phosphoric acid increases the surface area, surface energy, and wettability of enamel, which are key physical properties for the infiltration of resin and the formation of resin tags after light curing. Although the bond strength values to enamel are not as high as those to dentin, the bond strength is highly stable because of the nature of the enamel (high inorganic phase and minimal water content). It is unquestionable that pre-etching of the enamel provides the highest enamel bond strength for all contemporary dental adhesives, including self-etching systems.[15]

Bonding to Dentin

Dentin is the bulk tissue of the tooth and thus plays a key role in the clinical outcomes of adhesive restorations. Dentin is highly mineralized, but with lower mineral content

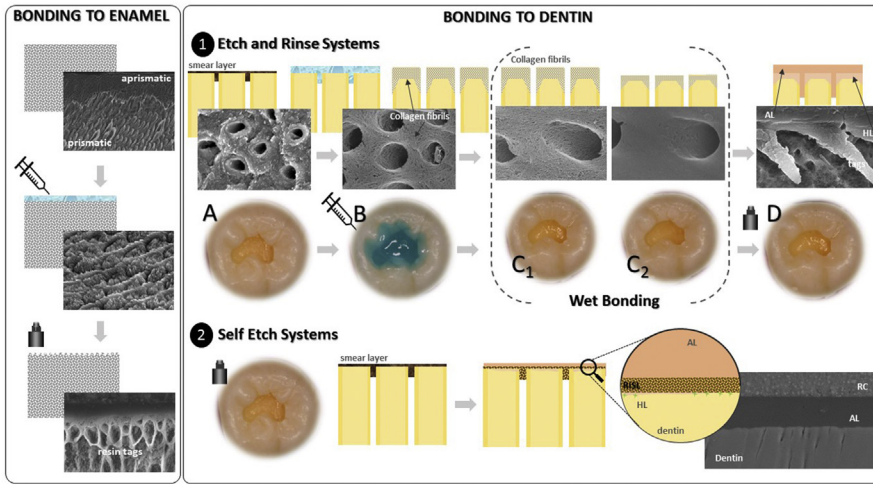

Fig. 3. Mechanism of adhesion of adhesives to enamel and dentin. Bonding to enamel requires superficial demineralization for the formation of resin tags and microtags. Bonding to dentin: (1) (*A*) smear layer on dentin tubules and intratubular and intertubular dentin. (*B*) Etch-and-rinse systems use a separate step of etching, resulting in removal of smear layer and exposure of collagen after superficial mineral removal. (*C1*, *C2*) The importance of surface moisture to maintain the collagen interfibrillar spaces for the infiltration of resin monomers. (*D*) Formation of the hybrid layer. (2) The smear layer is incorporated into the adhesive interface; the hybrid layer is thinner and irregular. Chemical bonding is achievable with certain adhesives brands (*green stars*).

(70 wt. % mineral) and much higher organic composition (20 wt. % organic phase) and water than enamel. The morphology of dentin is highly intricate. Dentin tubules, extending from the pulp complex to the dentin–enamel junction or cementum, are surrounded by a highly mineralized intratubular dentin that is bordered by less mineralized intertubular dentin (see **Fig. 3**). The intertubular dentin is rich in type I collagen fibrils and noncollagenous molecules, both of which are essential components of the dentin–adhesive interface.

There are significant variations in the biochemistry, morphology, and mechanical properties of the different types of dentin, dentin of different ages, within different dentin depths, and between crown and root dentin. Hence, dentin is a dynamic tissue and becomes modified over time owing to physiologic or pathologic conditions. The composition and morphology provides the necessary elasticity and toughness to support the enamel and protect the pulp tissue over a lifespan.

The high fluid content (10 wt. %) in the form of bound and unbound water and the extracellular protein content makes the mechanism of enamel adhesion unachievable in dentin. The dentin is highly hydrophilic and thus not well-suited for the infiltration of hydrophobic resin monomers. As with enamel, surface etching of dentin increases the bond strength owing to the removal of the smear layer (see **Fig. 3**). However, acceptable dentin–resin adhesion is only feasible with the hydrophilic and amphiphilic resin chemistry. Hydrophilic resin monomers can infiltrate the demineralized dentin surface rich in type I collagen fibrils, encapsulating the exposed dentin matrix and forming the so-called hybrid layer.[16] The hybridization of dentin surfaces is the primary mechanism of micromechanical retention of etch-and-rinse adhesive systems. To achieve good adhesion, a wet surface is necessary to maintain the interfibrillar spaces of the exposed collagen network for the infiltration of resin monomers into the demineralized dentin. Thus, the clinician must leave the cavity preparation visually wet, but without excessive water pooling, and immediately place the adhesive systems (see **Fig. 3**). Although this bonding to moist dentin is technique sensitive, it remains the most predictable adhesion mechanism for dentin.

Self-etch adhesive systems can still form hybrid layers, but the incorporation and/or partial demineralization of smear layer at the adhesive interface results in a thin and irregularly formed hybrid layer (see **Fig. 3**). Evidence of chemical bonding between certain acidic primers, such as 10-MDP functional monomer and the mineral phase of dentin, provides additional retention.

There is large variability in the adhesion of self-etching systems to enamel and dentin, reflecting the high variability in performance of various commercially available systems. The clinical performance of self-etching systems continues to improve, particularly with the technique of selective etching of enamel, where phosphoric acid etching of enamel only is performed before using the self-etch adhesive.

THE ORAL BIOFILM AND THE DEGRADATION OF DENTAL ADHESIVE INTERFACES

Microorganisms present in the oral cavity adhere to tooth surfaces (dental plaque), forming a diverse community that functions as a biofilm.[17] The biofilm has physiologic roles; however, changes in the microflora phenotype and genotype can favor the establishment of an acidogenic stage, resulting in the demineralization of enamel and dentin.[18] Biofilms form and interact differently with the various microenvironments in the oral cavity and such interaction is driven by modifications in dental plaque ecology, restorative material, chemistry and surface characteristics.

Oral biofilm formation is greater on resin composites than sound enamel and other restorative materials such as amalgam, glass ionomer cements, and ceramics.[19,20]

The more extensive biofilm formation and acid production on resin composites is a result of increased growth of microorganisms, mainly owing to genetic modifications of bacteria virulence induced by resin components.[21–23] Indeed, different monomers can increase the activity of a variety of cariogenic bacteria species. For example, TEGDMA stimulates growth of *Streptococcus sobrinus* and *Lactobacillus acidophilus*, which have high cariogenic potential for the development of primary and secondary caries, respectively.[24] The cariogenic effect is triggered by high amounts of TEGDMA monomer released from the resin composite matrix owing to increased hydrophilicity and greater unpolymerized content in the material.

Moreover, oral bacteria can induce the biodegradation of resin-based materials by esterase activity, resulting in the release of hydrolyzed byproducts from monomers. For example, triethylene glycol is released from TEGDMA, which stimulates the growth of microorganisms, especially at lower pH levels.[25] In particular for adhesive systems, the esterase activity of cariogenic bacteria can degrade cured resins, especially self-etching systems that present a more hydrophilic chemical composition.[26] However, phosphate derivatives of methacrylates present in those adhesives (such as 10-MDP) can release acidic polymers that actually inhibit bacterial growth owing to a very low pH.[27] Thus, the hydrophilicity of the adhesive system as well as its pH can influence bacterial growth.

Of great importance is that biofilm formation on resin composite is influenced by factors that can be controlled by the clinician, such as the quality of the light curing and finishing procedures.[28] Short light curing times may result in a lesser degree of conversion of monomer to polymer, leaving more residual unpolymerized monomers in the materials and enhancing *Streptococcus mutans* colonization.[29] Also, *S mutans* colonization is lower on polished resin surfaces[30] or nanofilled resin composite.[28] Resin composite surfaces with deep and large depressions or exposure of resin matrix are more prone to biofilm formation,[31] because these features promote a niche for bacteria to better resist shear forces and removal.

DEGRADATION OF DENTAL ADHESIVE INTERFACES: BIOLOGICAL CONSIDERATIONS

The main clinical shortcomings of resin composite restorations are marginal degradation, fracture, debonding, and secondary caries.[32–35] Although the proper handling of materials will maximize their performance, intrinsic (chemistry, bonding mechanism, biology) and extrinsic (oral environment) factors will affect the longevity of adhesive restorations. The mechanisms of degradation of the dental adhesive interfaces are complex, primarily driven by breakdown of the adhesive system, and the underlying dental tissue, potentially mediated by biological or environmental responses. Such mechanisms are described below and are summarized in **Table 1**.

The Stability of Dental Resin Chemistry

The resin chemistry of adhesive systems dramatically influences their stability in the oral environment. The major biological concern is the release of free monomers and/or products from the resin matrix either during the polymerization reaction or over time owing to biodegradation and erosion.[36] Unreacted monomers can diffuse and leach out of the resin matrix,[37] potentially causing cytotoxic reactions in the pulp.[38] This is a concern, particularly in deep cavities owing to increased permeability as a result of the reduced thickness of remaining dentin.[39] Commonly used monomers, such as bisphenol A-glycidyl methacrylate, urethane dimethacrylate, TEGDMA, and HEMA, present cytotoxic potential.[40] Newly developed adhesive formulations, such as the universal systems, have shown favorable results in reducing in vitro

Table 1
Summary of the contributors and the mechanism of the degradation of adhesive interfaces

Structure/Material		Characteristic/ Mechanism	Result	Contribution to Failure
Dental resins	Resin composite	Rough surface	Favors biofilm formation and growth	Resin degradation by esterases
		Leached/ unreacted resins	Favors acidogenic biofilm	Secondary caries
	Adhesive system	Unreacted/ leached resins	Increase water/ saliva sorption	Increases interfacial porosity
			Hydrolysis of resin	Pulp response
			Reach pulp tissue	Susceptibility to degradation
		Incomplete monomer infiltration	Exposed dentin organic matrix	Enzymes degrade anchoring collagen
		Etching technique/pH	Activation of endogenous proteases[a]	Loss of interfacial bonding/seal
Dental tissues	Latent endogenous proteases[a]	Latent enzymes activate at low pH	Degradation of dentin matrix	Increases interfacial porosities
	Inherent moisture	Water trapped at the adhesive interface	Hydrolysis of resin	Loss of interfacial bonding or seal
Oral environment	Bacterial esterases	Enzymatic activity	Resin polymer degradation and release of monomers and byproducts	Enzymes degrade anchoring collagen
	Salivary esterases	Enzymatic activity		Increases interfacial porosities
	Biofilm	Leached or unreacted resins	Favors biofilm formation and growth	Loss of interfacial bonding/seal
			Favors acidogenic biofilm	Secondary caries

[a] Endogenous proteases are matrix metalloproteinases and cysteines cathepsins in dentin.

cytotoxicity.[41] Clinicians should be careful when light curing resin composite and adhesive systems to ensure that the distance between the light curing unit tip and the resin surface is as short as possible and that enough energy is delivered directly to the material to optimize the degree of conversion and reduce cytotoxic effects.

The breakdown and release of unbound monomers from the resin matrix can also take place by enzymatic catalysis,[36] along with pH changes and oxidation, leading to the degradation of resin-based materials.[42] In fact, the hydrolysis of monomers is aggravated by water sorption through nanoporosities within the hybrid layer that accelerates the degradation of the adhesive resin and results in areas of unprotected collagen fibrils and a weaker dentin–resin bond.[43]

The main enzymes involved in the degradation of resin-based materials are believed to be salivary esterases.[44] Esterases are released by salivary glands, gingival crevicular fluid, and oral microorganisms.[42] Esterases can hydrolytically degrade condensation bonds in resin monomers, such as esters and urethanes. Hydrolysis depends on water sorption, which is more likely to occur in adhesive systems composed of hydrophilic and acidic resin monomers acting as semipermeable membranes that allow water movement through the interface, regardless of the etch-and-rinse or self-etch strategy.[3,45,46]

Hence, esterases can act synergistically to promote resin composite biodegradation.[47,48] Therefore, resin composite degradation by esterases are dependent on adhesive or resin monomer formulation and the individual's salivary composition.

The Breakdown of Dentin: Host Response Mechanism

The degradation of the extracellular matrix exposed by the partial demineralization and incomplete infiltration of resin monomers can destabilize the underlying dentin and the hybrid layer. The presence of denuded collagen fibrils is more common in etch-and-rinse systems, owing to discrepancies in depth of acid etching and resin infiltration. For self-etching systems, the dentin matrix can be exposed after hydrolytic degradation of resin monomers.[49] Because collagen breakdown has been shown to take place even in the absence of bacteria, a host response mechanism was proposed to explain such degradation, previously attributed to water hydrolysis, saliva, and/or bacteria.[50]

Matrix metalloproteases (MMPs) were the first enzymes linked to a host triggered degradation of collagen by the cleavage of the extracellular matrix components within the dentin–resin interface.[51] Members of this family of zinc- and calcium-dependent endopeptidases were further identified in dentin,[52–54] whereas a wider gene expression profile for many different MMPs was reported in pulp tissue and odontoblasts.[55] MMPs are synthesized as inactive zymogens that remain trapped within the mineralized dentin and are activated by other proteases or by an acidic environment. However, it is in neutral pH that MMP reach the highest activity.

Cysteine cathepsins (CCs) are another family of host enzymes found in dentin and capable of degrading extracellular matrix components.[56] In contrast with MMPs, CCs are active at slightly acidic pH and most are unstable at neutral pH.[57] Although the role of CCs in the dentin organic matrix degradation was explored mainly in caries disease, a synergy between these 2 families of enzymes was proposed to explain collagen degradation at the adhesive interfaces.[58,59]

The ability of MMPs to contribute to the degradation of the dentin matrix and the hybrid layer was confirmed in vitro and in vivo by the investigation of protease inhibitors as part of the bonding protocol.[60–64] The low pH of phosphoric acid etching and acidic primers can activate MMPs and CCs, whereas the latter can release even more active enzymes, enhancing the proteolytic potency of MMPs.[58] In fact, both etch-and-rinse and self-etch strategies can activate endogenous enzymes.[65–67] When the pH is neutral, MMPs cleave exposed collagen fibrils that anchor the restoration to dentin, resulting in decreased bond strength and increased permeability at the dentin–adhesive interface.

Interestingly, a combined effect of endogenous MMPs and esterases from saliva was reported recently to promote adhesive interface degradation, especially when using an etch-and-rinse adhesive system.[68] Such findings confirm that a complex mechanism is involved in the degradation of hybrid layers. Future research should clarify such interactions to develop novel biomaterials that can inhibit different pathways of degradation.

CLINICAL CONSIDERATIONS WHEN USING CONTEMPORARY ADHESIVE SYSTEMS

The first step in ensuring that the adhesive system placement steps will go smoothly is to review handling instructions. Manufacturers provide easy to follow instructions to maximize the bonding technique steps and indications (ie, direct vs indirect restorations) of individual products. In general, when performing a dental adhesive procedure, the clinician must be aware that bonding to enamel is more predictable than that of dentin or cementum owing to the composition differences among these substrates. Thus, restorations with margins in enamel yield better outcomes.[69,70]

Contamination by saliva and blood during restorative procedure decreases the bond strength[71,72] and must be avoided. If accidental contamination occurs, there are experimentally tested strategies to minimize the negative effects of contamination, including re-etching the surface, rinsing and drying the contaminated surface, and the application of additional coats of adhesive.

Table 2 provides a few strategies and their purpose reported in the literature that might influence the long-term outcome of the dynamic tooth–adhesive interface. Additional considerations are described to maximize performance of adhesive systems.

Table 2
Strategies to optimize bonding and potentially the long-term outcomes of adhesive restorations

Strategy	Purpose	Technique
Field control[73,74]	Prevent contamination of prepared tooth structure (ie, with saliva, blood)	Optimal use of rubber dam isolation
Enamel grinding[73,75]	Expose enamel rods, increase bond effectiveness and durability	Bevel cavosurface of cavity preparation using fine diamond or hand instruments
Selective etching[76]	Improve bond strength and reduce microleakage	Apply phosphoric acid to enamel and rinse before using self-etch system
Wet bonding technique	Prepare dentin for hybridization	Remove excess of water from acid-etched dentin with sponges; apply primer on moist dentin
Dentin desensitizer[77,78]	Occlude dentinal tubules to reduce permeability and sensitivity	Additional step before primer application
Matrix metalloproteinase inhibitors[60,63]	Inhibit activation of endogenous enzymes responsible for the degradation of collagen fibrils	Extra step used as an additional primer of dentin (ie, 2% chlorhexidine) or within exiting primer
Enhanced solvent evaporation[7]	Remove interfacial water	Critical air drying of primer or adhesive layer before light curing
Hydrophobic coating[79]	Reduce water sorption and stabilize hybrid layer over time	Multiple layers of a hydrophobic resin layer might be applied
Dentin impregnation[80]	Enhance dentin impregnation of resin monomer into tubules	Increased application time of adhesive resin with vigorous brushing technique
Extended polymerization[81]	Improve polymerization (degree of conversion) and reduce permeability	Curing times used beyond manufacturer recommendation (ie, from 20 s to 40 s, to 60 s)
Wet ethanol bonding[82,83]	Permits the use of hydrophobic resins that absorb little water	Rub of ethanol in dentin before primer application (ie, 100% for 1 min); protocol is not completely established for clinical user

Substrate

Adhesive systems are formulated to bond to sound tooth structure. However, dental restorative procedures are often carried out on altered forms of enamel and dentin. There are significant compositional and morphologic differences between the dental substrate that impairs adhesion. It is well-known that bonding is higher in superficial dentin than deep dentin because of the increased number of tubules in the latter.[84] Furthermore, tubular fluid percolating from the pulp to the dentin surface can be detrimental to the bonding of certain adhesive systems.[77,85]

In enamel, dental fluorosis decreases the bond strength of etch-and-rinse and self-etching systems.[86] Thus, etching enamel for additional time is recommended. Amelogenesis imperfecta impairs bond strength to enamel, regardless of the adhesive strategy, possibly owing to a very mild etching of the enamel surface.[87] Similarly, bond strength is lower in tetracycline-stained teeth.[88]

Carious dentin is another commonly altered substrate that clinicians manage daily. Studies have shown that dentin with caries has lower hardness and produces lower bond strength owing to the low mineralization and collagen disorganization.[89] With new techniques involving minimally invasive dentistry and selective caries removal, the clinician will often need to bond to these less than ideal substrates when using resin-based materials. However, if the restoration margin is in sound dentin and/or enamel the outcome might not be affected. Therefore, it is crucial for optimization of bonding procedures to have a safe bonding zone containing sound dentin.

Restoration of noncarious cervical lesions are also a challenge, because sclerotic dentin is generally hypermineralized with the presence of intratubular mineral deposits. It has been recommended for noncarious cervical lesion surfaces to be gently mechanically roughened and surface etched with phosphoric acid for additional time (up to 30 seconds) to increase adhesion of selective materials.[90,91] Dentin desensitizers have been suggested to decrease the permeability of the substrate and reduce sensitivity, especially when using the etch-and-rinse approach (see **Table 2**). Desensitizers that do not precipitate at the surface of the tooth do not affect the bond strength of most contemporary systems.[78,92] In addition, the proximity of these lesions to the gingival tissue make class V preparations a challenge for the use of dentin bonding agents. A metaanalysis has shown that field isolation and type of adhesive system are factors that affect the clinical performance of these restorations.[73,74]

In addition, in vitro studies have shown that even the wetness of the acid-etched dentin from the bonding protocol can affect the performance of adhesive systems, and it can be material dependent.[93,94] Therefore, the conditioning of the dentin substrate is important consideration before the application of the primer or adhesive layer (see **Table 2**).

Material

According to most clinical studies, 3-step etch-and-rinse systems and 2-step self-etch systems have shown better performance than other systems with a reduced numbers of steps.[73,95] Self-etch systems are appealing products in clinical practice because of their reduced number of steps and anecdotal evidence of a low incidence of postoperative sensitivity.[96] In addition, they are less sensitive to the application technique as indicated by low variation in bond strength results.[85,97] However, studies have reported poorer clinical outcomes for all-in-one systems. Furthermore, acid etching with phosphoric acid, which has a much lower pH than the acids used in

most self-etching systems, remains the most adequate strategy to achieve high bond strength to enamel.[70,76] Even with self-etching systems, selective etching and enamel grinding are indicated for a variety of clinical procedures, for example, class IV preparations.

With the etch-and-rinse approach, studies have investigated extensively the importance of the hybrid layer and the effective infiltration by resin monomers. The degradation of exposed collagen fibrils is known to be a problem for the tooth–resin interface. A few clinical strategies to overcome this problem are shown in **Table 2**, such as the use of MMPs inhibitors, as mentioned.[61,64]

Compatibility to Luting Cements

The material dependence of the self-etch adhesive systems regarding performance and clinical indications was made clear once these systems began to be used with autocured and dual-cured composites to bond indirect restoration and core buildup restorations on damaged teeth.[98–100] Light-cured resins with the adjunct of an adhesive system are used to bond porcelain or resin composite veneers. On the other hand, bonding all-ceramic restorations onto teeth with short clinical crowns benefit from the advantages of adhesive cementation and a dual-cured cement is usually indicated. The acidic monomers present in self-etch systems might affect the polymerization of dual-cured and self-cured resins.[100] The practitioner must investigate the manufacturers' recommendations before using multiple different systems. Lately, there is a trend to use self-adhesive luting resins, which might change the clinical vulnerability of using incompatible systems.

Preventive and Therapeutic Sealants

Resin-based sealants, used to seal incipient lesions in permanent tooth surfaces, has been shown to be an effective method for preventing and arresting caries. In this procedure, the enamel is etched and a sealant material is applied to fissures and pits acting as a protective layer against plaque retention. A recent clinical article showed that the use of an adhesive system (etch and rinse and self-etch) before placement of sealant (bonded sealant) produced higher retention rates over a 2-year follow-up period than that of the conventional technique, where only acid etching was performed before resin sealant application (no separate adhesive system). The same was not observed with a self-etch system without etching the enamel surface.[101] Additional clinical trials are necessary to investigate the performance of other contemporary adhesive systems for fissure sealing.

THE FUTURE FOR ADHESIVE SYSTEMS: TECHNOLOGICAL AND FUNDAMENTAL TRENDS

Adhesive dentistry continuously evolves fundamentally and technologically. Incremental advances in response to limitations in physical and chemical properties and handling are common and easier to implement than wholesale changes from the development of totally new materials. Innovative strategies for new materials have been aided by the identification of the effects of key biological and environmental factors. Below are examples of new concepts that may drive the development of novel dental adhesives to be implemented in clinical use.

Chemistry of Adhesive Systems

Current efforts are directed toward the modification of the chemistry of traditional monomers and the development of new monomers and resin composite formulations to enhance the chemical stability of resin-based restorations.[102,103] New resin

chemistry free of ester bonds, such as ether-based monomers[102] and methacrylamide-based monomers, show or promise resistance against esterase degradation. Thiolene chemistries are resistant to water degradation and have been explored for the optimization of the physical characteristics and the polymerization mechanism for clinical use.[104–106]

The incorporation of antimicrobials and enzymatic inhibitors has been widely explored and limitations include the lack of substantivity and sustained effects. More recently, the inclusion of bioactive glass fillers, as antimicrobial and remineralizing agents, to an experimental resin showed effectiveness in reducing biofilm formation and penetration within adhesive interfaces.[107] The incorporation of natural-derived plant compounds has also been shown to be an option for obtaining resins with antimicrobial properties.[108] Moreover, novel monomers containing amorphous calcium phosphate have shown the potential to prevent periodontitis-related bacteria and might have potential clinical use to restore class V cavities.[109]

Biologically Driven Strategies

Biologically inspired strategies have been of particular interest to solve the many limitations of dental adhesion. Many of these strategies mimic natural biological processes to develop novel biomaterials. This approach has been particularly used to stabilize and even reinforce the dental substrate in intimate contact with the adhesive interface. Biomimetic analogs, such as polyacrylic acid and sodium trimetaphosphate, have been elegantly shown to regulate mineral deposition in dentin and promote remineralization at the adhesive interface.[110,111]

Other biomimetic approaches use physiologic processes in dentin to mediate physicochemical modification of the dentin matrix using chemical agents. Experimental studies have explored multifunctional synthetic and natural chemical agents to reinforce and stabilize the dentin–adhesive interface. Plant-derived compounds have attracted particular attention owing to their potency, bioavailability, and potential biocompatibility. A range of biological responses are elicited, such as increased collagen cross-linking and inactivation of endogenous and exogenous proteases.[112] Such effects have been shown to increase the mechanical properties of both dentin[113] and the dentin–resin interface.[94] Enrichment of these bioactives has shown remarkably stable adhesion on wet surfaces,[114] as well as the ability to inhibit artificial secondary caries around dentin–resin margins.[115]

Catechol containing molecules are known to adhere to wet surfaces.[116,117] The synergistic role in adhesion of catecholamine functionalized monomers allied to the micromechanical interlocking of the polymerized resin with the dentin collagen network are promising for the future of adhesion to teeth.[118]

SUMMARY

Significant improvements to the chemistry and handling of adhesive systems have broadened the use of adhesive restorative dentistry. However, adhesive systems remain technique sensitive, and proper use of the material is the first step to achieving clinically acceptable bonds to enamel and dentin. Once in service, resin–tooth interfaces are highly susceptible to degradation in the oral environment. Bacteria, endogenous enzymes, and inherent resin chemistry limitations can further determine the longevity of dental restorations. The clinician must be aware of dental tissue variation and optimization strategies for individual decision making of the best adhesive system and bonding technique.

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