Abstract: Improvements in dentin bonding systems have influenced modern restorative dentistry. The desire for minimal invasiveness has resulted in more-conservative cavity design, which basically relies on the effectiveness of current dentin bonding systems. Interaction of adhesives with enamel and dentin is based on two systems, commonly described as etch-and-rinse and self-etch. Priming and bonding agents can be separate or combined, resulting in two- or three-step systems for etch-and-rinse adhesives and one- or two-step systems for self-etch adhesives. Self-etch systems use acidic functional monomers that simultaneously demineralize and impregnate tooth structures. Etch-and-rinse and self-etch systems have advantages and disadvantages, which are primarily related to the simplified bonding procedures required under clinical conditions. Knowledge of the composition, characteristics, and mechanisms of adhesion for each adhesive system is critical in selecting the ideal adhesive materials for clinical use.

Keywords: adhesive systems; self-etch; etch-and-rinse; components; dentin bonding.

1. Current concept of dentin bonding

The acceptance and widespread use of direct-filling composite resin restorative materials have stimulated research on bonding to tooth structures. The fundamental mechanism of bonding to enamel and dentin is an exchange process involving replacement of inorganic tooth substrates by resin monomers that, upon polymerization, become micromechanically interlocked in the created microporosities (1). The micromechanical retention created with the tooth substrate results from diffusion of resin monomers (2). However, because the bond between acid-etched enamel and resin is due solely to micromechanical interactions, leakage at the dentin-resin interface cannot always be resolved. The primary goal of adhesive systems is to provide stable bonding of restorative materials to the tooth structure and to seal the dentin surface (3).

Enamel is composed almost entirely of crystalline hydroxyapatite. These inorganic crystals are arranged in an orderly microstructure that allows acid etching to develop the familiar pattern into which the resin penetrates and interlocks (4,5). Phosphoric acid etching is used to transform the enamel surface from a lower to a higher surface energy and to dissolve and demineralize the inorganic hydroxyapatite, thereby creating micropores that improve mechanical retention (6). The micromechanical interaction of adhesive resins with enamel results from infiltration of resin monomers into the microporosities created by dissolution of enamel and subsequent penetration of the exposed hydroxyapatite crystals with the resin monomers within the pores on the
The ultimate goal of bonded resin composite restorations is to achieve high-quality adaptation to enamel and dentin. Despite the reliability of bonding to enamel, dentin bonding is considered more difficult and less predictable. Dentin has substantial organic content, which varies by depth, and lacks the orderly microstructure of enamel. While enamel is composed of 96\% hydroxyapatite by weight, dentin contains considerable water and organic material, primarily type I collagen (8). The characteristic structural feature of dentin is the tubules, the spacing and orientation of which depend on the location and depth of the dentin surface (9). Dentin is intimately connected with the pulpal tissue by means of fluid-filled dentinal tubules that traverse from the pulp through the dentin to the dentinoenamel junction. When under constant outward pressure, the fluid flow renders the exposed dentin surface moist and intrinsically hydrophilic (10). The organic, hydrophilic, and structural nature of dentin makes bonding to this hard tissue extremely difficult.

The presence of cutting debris on instrumented dental surfaces in the form of a smear layer and smear plugs that obstruct dentinal tubules is also a significant cofactor that should not be underestimated (11,12). The basic composition of the smear layer is hydroxyapatite and altered collagen, with an external surface formed by gel-like denatured collagen (13). This altered collagen may acquire a gelatinized consistency, due to the friction and heat created by the preparation procedure (14). The morphology of the smear layer is determined by the type of instrument that creates it and by the dentin site where it is formed (15). The smear layer should be removed before chemical bonding to the dentin surface is attempted. Despite the different classifications of adhesive systems, current bonding strategies depend on the way they interact with the smear layer (16). Etch-and-rinse systems require two or three steps, depending on whether the primer and bonding agent are separate or combined in a single bottle. Self-etch systems are one- or two-step systems, depending on whether the self-etching primer is separate from the bonding agent or combined with it. Self-etch systems enable a single application procedure, the so-called single-step self-etch system. Figure 1 summarizes the currently available adhesive systems, according to Van Meerbeek et al. (17). Although both systems have shown success in laboratory and clinical studies, their performance is highly product-dependent (18). Knowledge of the composition, characteristics, and mechanisms of adhesion for each adhesive system is critical in selecting the ideal adhesive materials for clinical use.

### 2.1. Etch-and-rinse systems

With etch-and-rinse systems, dentin and enamel are treated with phosphoric acid to remove the smear layer and demineralize the superficial dentin layer. After acid etching, a mixture of resin monomers plus an organic solvent is applied to penetrate the etched dentin and create a bonding interface (19). Three-step etch-and-rinse systems typically include separate etching, priming, and adhesive application steps. Two-step etch-and-rinse systems have been developed to decrease the number of clinical steps and simplify the process by combining the priming and adhesive application steps. Acid etching
promotes dentin demineralization within a depth of 3-5 μm, thereby exposing collagen fibrils without hydroxyapatite (20). To prevent hydrolysis of collagen fibrils, resin monomers should penetrate the water-filled spaces between adjacent dentin collagen fibrils that were previously occupied by hydroxyapatite crystals. After infiltration, the resin monomers are polymerized, resulting in the formation of a hybrid tissue comprising collagen, resin, residual hydroxyapatite, and water, known as the resin-dentin interdiffusion zone (21,22). The micromechanical entanglement of resin monomers with etched dentin may decrease postoperative sensitivity and allow for a better marginal fit of the restorations (23).

### 2.2. Acid etching

Acid etching of enamel is a widely accepted clinical procedure because of its ability to create stable bonding. In addition, it increases the longevity of composite restorations by decreasing the possibility of marginal staining, secondary caries, and postoperative sensitivity (24). However, the effects of etching on dentin vary widely, depending on several factors such as dentin type (sclerotic, caries-affected), depth, and tubule orientation (25,26). After phosphoric acid etching, the tubule access becomes funnel-shaped and the resin tags are elongated. Ideally, the duration of acid etching with 35% phosphoric acid should not exceed 15 s because prolonged application of acid may lead to structural modification of exposed collagen (27).

Opening of the dentinal tubules by acid etching significantly increases dentin permeability, thereby increasing pulpal fluid flow (28). Leakage of pulpal fluids from the tubules under hydrostatic pressure may disrupt attempts at chemical and micromechanical bonding to the dentin substrate. Early attempts to achieve bonding to dentin by extending the enamel acid-etching technique were not successful because air-drying the cavity caused the acid-etched dentin to collapse (29). Because mechanical bonding to etched dentin is not a viable alternative, research has instead focused on forming some type of chemical bond to hydroxyapatite and the collagen fibrils of dentin. The hydrophilic functionality of the adhesive monomer facilitates its permeation into exposed collagen fibrils, leading to formation of a hybridized layer. In contrast, hydrophobic functionality facilitates bonding to resin composites (30). Creation of the hybrid zone is believed to result from infiltration of the resin monomer into the collagen fibrils exposed by dentin demineralization and from in situ polymerization (31).

The collagen network of the demineralized dentin must remain loosely organized before adhesive resin application, to allow adequate infiltration of resin monomers (Fig. 2). Water is required to prevent collagen fibrils within the dentin from shrinking, a concept referred to as wet-bonding technique (32). However, it is difficult to determine exactly how moist the dentin should be to ensure complete penetration of adhesive resins (33). Problems resulting from excess water remaining on
dentin have been reported and are known as over-wet phenomena (34), which appear to cause phase separation of the hydrophobic and hydrophilic components in adhesives, resulting in the formation of voids at the resin-dentin interface. Small voids can be identified by infiltration of silver traces in vitro, referred to as nanoleakage (35). Excessive moisture on the adherent surface may lead to improper polymerization of the resin monomers, resulting in lower mechanical properties of the adhesive layer (36). A certain amount of water is crucial to prevent collapse of the collagen network, while an excessively moist surface may hamper effective bonding to dentin. Determining how moist the dentin should be is a major concern, and this factor is difficult to standardize under clinical conditions (37). Recently, an ethanol wet-bonding technique was developed, wherein ethanol is used instead of water to support the demineralized exposed collagen fibrils (38). Ethanol wet-bonding technique can create higher bond strength, as compared with water wet-bonding; furthermore, it exhibits enhanced bonding durability under chemical challenge (39).

Phosphoric acid etching and penetration into the dentinal substrate led to the idea that etch-and-rinse adhesives are the gold standard for other adhesives when tested in vitro (40). However, concerns remain regarding the degree to which resin monomers contained in etch-and-rinse adhesive systems infiltrate etched dentin (41). The presence of unprotected dentin collagen fibers with resin monomers may be explained by the presence of residual water, which could prevent complete monomer infiltration to the deepest part of the demineralized zone (42). If resin monomers cannot completely infiltrate collagen fibrils, partially exposed fibrils will remain at the bottom of demineralized dentin. The lack of resin protection and the presence of water render demineralized collagen fibrils vulnerable to degradation. Interfibrillar spaces in demineralized dentin contain water and highly hydrated, negatively charged proteoglycans, which form a hydrogel within that space (43). Degradation of collagen fibrils and hydrophilic resin components leads to destruction of the hybrid layer and a decrease in bond strength over time due to collagenolysis (44). This type of degradation of the dentin–resin interface has led researchers to reconsider the conditioners, pH, and association of components in adhesive systems.

2.3. Adhesives in etch-and-rinse systems

Current dentin adhesive systems typically consist of functional monomers, base resin monomers, initiators, solvents, inhibitors, and inorganic fillers (45). The resin monomers are particularly important because their polymerization produces a cross-linked matrix that provides mechanical strength to the adhesive (46). Selection of resin monomers has considerable influence on the properties and durability of the adhesive layer in the oral environment (47).

The hydrophilic methacrylate monomer 2-hydroxyethyl methacrylate (HEMA) is frequently used in adhesives. It is generally accepted that application of HEMA to demineralized dentin, and HEMA-containing etch-and-rinse adhesives, improves bond strength to demineralized dentin (48). HEMA in adhesives functions as a wetting agent and a solvent. These properties improve the stability of adhesives containing both hydrophobic and hydrophilic components and maintain the ingredients in solution without phase separation (49). The hydrophilicity of HEMA may lead to water uptake and subsequent hydrolytic degradation of adhesives over time (50). When the HEMA concentration decreases below a critical level, phase separation will occur between water and the adhesive monomers, and a strong air current is required to remove the water-containing droplets in the adhesive (51). The optimal HEMA concentration to obtain higher bond strengths in primer/adhesive is between 30-40% (52), although the use of HEMA remains controversial.

An increased concentration of hydrophilic components is required in adhesives to enhance their ability to penetrate porous material, particularly the collagen network of demineralized dentin (53). Water, ethanol, and acetone are the most commonly used solvents and must be evaporated from the adhesive; if they remain in the adhesive, polymerization may be compromised and permeability of the adhesive layer may increase (54). Air-blowing of the adhesive is important to achieve optimum strength. The amount of evaporation of the solvents from adhesive resin blends has been studied, and the results indicate that the time specified by manufacturers is too short to remove even half of the solvent (55). After polymerization of the adhesive, residual solvents may be replaced by water, which decreases its mechanical properties (56). To optimize elimination of organic solvents and water, prolonged air-drying and prolonged application times have been proposed (57,58).

Because water is a poor solvent for organic compounds, a secondary solvent such as ethanol or acetone should be added to adhesives. As the vapor pressure of water-based adhesives is lower, rubbing application is required to aid diffusion of the monomer and obtain good clinical performance (59). The type of solvent strongly influences the clinical use of etch-and-rinse adhesive systems (60). Because acetone is a water-chaser, acetone-based systems work well on a moist dentin surface but can
lead to rather poor results on overdried acid-etched dentin surfaces. In contrast, water-based systems are not as sensitive to the moisture concentration in dentin but require a longer evaporation time for the solvent because water has a considerably lower vapor pressure. Vapor pressure is greater for ethanol than for water, which results in better evaporation by air-blowing after application on the tooth surface. Acetone combines the hydrophobic and hydrophilic components in adhesives to prevent phase separation. However, its high volatility may lead to decreased shelf life for acetone-based adhesives, due to solvent evaporation during repeated use of the adhesive vial (61). However, a small number of studies have investigated alternative solvents such as tert-butanol (2-methyl-2-propanol) (62).

### 3.1. Self-etch systems

The latest adhesive systems require fewer and simpler application steps and less application time in clinical situations (63). Self-etch systems do not require a separate etching step, because they contain acidic functional monomers that simultaneously etch and prime the tooth substrate for bonding. The self-etch system is purported to be user-friendly and less technique-sensitive, thereby resulting in reliable clinical performance (64). The acidic functional monomers in self-etch adhesives dissolve the smear layer and demineralize the underlying tooth substrate to create a thin interdiffusion zone, which comprises a surface zone of the hybridized smear layer and a subsurface authentic hybrid layer (65). Self-etch adhesives partially demineralize the dentin and can establish chemical interactions with hydroxyapatite crystals, thus improving long-term bonding durability (66). Because there is no correlation between hybrid layer thickness and bond strength, the existence of thin hybrid layers should not compromise initial bond strength when acidic functional monomers can reach the demineralization front created simultaneously in intact dentin (67).

Self-etch systems were reported to be less technique-sensitive than other systems and resulted in reliable clinical performance (68). Another important clinical benefit of self-etch adhesives is lower incidence of patient-reported postoperative sensitivity, which is due to the fact that these systems leave residual smear plugs that allow less dentinal fluid flow as compared with etch-and-rinse systems (69).

### 3.2. Classification of self-etch systems

Self-etch adhesives are categorized by their interaction with dentin substrates, i.e., according to their acidity or etching aggressiveness. Self-etch adhesives can be classified as strong (pH, <1), intermediate (pH = 1.5), and mild (pH, >2) (70). The morphological features of the dentin–resin interaction zone created by self-etch adhesives depend on the ability of the acidic functional monomers to demineralize the dentin. Strong self-etch adhesives (pH, ≤1.0) completely dissolve the smear layer and form relatively thick transitional layers. The interfacial morphological features promoted by these adhesives on tooth substrates resemble those of etch-and-rinse systems (71). Mild self-etch adhesives (pH, approximately 2.0) superficially demineralize dentin to a depth of <1.0 μm and create a thinner transitional layer (Fig. 3). Mild self-etch adhesives only partially demineralize dentin, leaving a substantial number of hydroxyapatite crystals around collagen fibrils. Ultramild self-etch adhesives have relatively low acidity (pH, approximately 2.7) and expose only very superficial collagen on dentin, with the creation of a nanointeraction zone (72).

Water is necessary to trigger demineralization in self-etch systems. Excess residual water during polymerization may be a reason for poor bond strength (73). Self-etch adhesives with high concentrations of acidic functional monomers behave like permeable membranes and allow water movement from dentin to the composite-adhesive interface (74). This may further compromise durability of the dentin interface and affect bonding of self-etch adhesives to chemical-cured resin composites. Better bonding performance in self-etch adhesives requires the possibility of a chemical interaction between residual hydroxyapatite and functional monomers. A
significant advantage of mild self-etch systems is that they retain more hydroxyapatite crystals around collagen fibers, which may protect collagen against hydrolysis and degradation of the resin-dentin interface (75).

3.3. Adhesives in self-etch systems
Some functional monomers in self-etch adhesives can quickly chemically interact with hydroxyapatite, which results in increased resistance to degradation by preventing nanoleakage (76). In some self-etch adhesives, chemical bonds are created due to the presence of specific functional monomers such as 10-methacryloyloxydecyl dihydrogen phosphate (10-MDP), 4-methacryloyloxyethyl trimellitate anhydride (4-META), and phenyl-P. These monomers contain carboxylic and phosphoric groups that are able to form ionic bonds with calcium in hydroxyapatite (77). Adhesives containing 10-MDP are most commonly used in self-etch systems. After application of adhesives, the self-etching process involves resin infiltration of the enamel. According to the adhesion-decalcification concept, the functional group interacts ionically with calcium in hydroxyapatite. The stability of the resulting calcium-monomer complex in the adhesive suspension determines whether chemical bonding leads to decomposition or demineralization of the tooth surface, while chemical bonding with calcium ions forms a functional monomer-calcium salt layered structure on the hydroxyapatite surface (78). The structure of functional monomers has three distinct components: polymerizable, spacer, and functional groups. The functional group has hydrophilic properties, which enhance the wetting and demineralization of the tooth surface. The spacer group influences the properties of the monomer, including its solubility in water, and its size determines the viscosity, wetting, and penetration behavior of the monomer (79).

The effects of air-drying on the ultimate microtensile bond strength of HEMA-rich and HEMA-free one-step adhesives have been evaluated (80). The results indicate that the degree of evaporation of residual monomers and solvents is higher with prolonged air-drying time. Longer air-drying resulted in higher microtensile bond strength in a HEMA-rich versus a HEMA-free adhesive. Because of its hydrophilicity, HEMA has been used as an adhesion promoter in most self-etch systems (81). However, a high concentration of HEMA in self-etch adhesives may compromise the mechanical properties of the cured adhesive. HEMA also lowers the vapor pressure of solvents; therefore, large amounts may hinder good solvent evaporation from adhesive solutions (82). There is an optimum concentration of HEMA that improves the bonding efficacy of self-etch adhesives. The addition of large amounts of HEMA to self-etch adhesives to prevent phase separation is not recommended because it will not increase bond strength and will result in droplet formation, albeit from a different origin (83).

Water is an indispensable component of self-etch agents because it ionizes acidic monomers and triggers demineralization. However, HEMA retains water in hydrogels, which is difficult to remove by air-drying. A concern is residual water remaining in the adhesive interface, as it cannot be removed completely by air-blowing. Another simple approach to improve bonding efficacy and stability is to enhance solvent evaporation. Warm air-drying of the adhesive may help remove interfacial water and improve bonding effectiveness (84). Cavity geometry is also an important issue and usually differs from the flat adherent surface used in tests of bond strength.

4. Contribution of adhesive systems to clinical dentistry
Good marginal adaptation to the entire tooth surface is believed to decrease marginal discoloration and pulpal irritation related to microleakage. A system that forms a sufficiently strong bond with a tooth and is able to withstand internal and external stresses has long been desired. Because bonding procedures require multi-step clinical techniques, clinical success with these adhesive systems sometimes depends on technique and material-related factors (85). To simplify bonding procedures, several new adhesive systems that rely on simultaneous etching of enamel and dentin with phosphoric acid or a self-etch primer/adhesive have been developed. To achieve optimum clinical performance, the application methods for these newly developed bonding systems have been simplified and manufacturers’ instructions have been clarified. Although the systems are simpler, careful management of the products, and knowledge of the functions of the constituents, are still required. Many clinical studies have clearly shown that, as compared with earlier adhesive systems, total etch and self-etch adhesives result in better clinical performance for class V cervical lesions (86). However, the long-term durability of the resin-dentin interdiffusion zone may be compromised by the presence of some ingredients of adhesives. Challenges for future research include refining the dentin-resin interface to improve adaptation and enhance long-term resistance to hydrolysis (87-90).

References