The Current Status of Bonding to Dentin Anno 2007

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Abstract

Today, direct composite fillings have reached a satisfactory level, aesthetically and functionally, to replace decayed or lost tooth tissue. However, as the bond degrades with time, the restoration lifetime is limited, depending largely on the type of adhesive used. This review examines the processes involved in the adhesion of biomaterials to enamel and dentin. Contemporary adhesives are categorized upon ultra-morphological, chemical and mechanical features, as well as clinical parameters. Apart from these properties, special attention is given to one-step (self-etch) adhesives, as they are aggressively marketed as the most user-friendly adhesives. Nevertheless, *in-vitro* research has revealed considerable shortcomings related to many of these simplified adhesives. Notwithstanding the amount of *in-vitro* data available, non-carious class-V clinical trials remain the ultimate test method to assess clinical success. In combination with the prior *in-vitro* assessment, the following conclusions were drawn: 1) At present, the three-step etch&rinse approach remains the 'golden standard' in terms of bonding effectiveness; 2) Any kind of simplification in the application procedure results in loss of bonding effectiveness; 3) The today most acceptable trade-off between bonding effectiveness and ease-of-use is a 'mild' two-step self-etch approach that combines micro-mechanical interlocking with additional chemical interaction, the latter definitely contributing to the bond stability on the long term.

Keywords :

dentin bonding, composite resin, glass ionomer, self-etching adhesive, one-step adhesive

Introduction

The use of composite filling materials along with adhesive techniques has revolutionized today's dental practice. The esthetic potential, handling and wear properties of composite fillings have improved tremendously (1). In the hands of a skillful dentist, composite fillings today are able to replace lost tooth tissue in an invisible way. However, no matter how splendid the shape and color, a good composite filling does not last long without a good bond to remaining tooth structure.

Basically, the main bonding mechanism of current adhesives can be regarded as an exchange process involving substitution of inorganic tooth material by resin monomers that upon *in-situ* setting become micro-mechanically interlocked in the created micro-porosities (2). Diffusion is the primary mechanism to obtain such micro-mechanical retention. Recently,

more evidence has corroborated the potentially important role of additional chemical interactions at the biomaterial-tooth interface, especially with regard to bond stability (3, 4).

In this paper, the current status -circa 2007- regarding bonding of dental adhesives to enamel and dentine is reviewed.

The smear layer as an 'OBSTACLE' to bonding

Cavity preparation alters the uppermost layer of tooth tissue, covering the tooth surface with a smear layer. While cutting dentine, the heat and shear forces produced by the rotary movement of the bur cause dentine debris to compact and aggregate. The resultant smear layer is an adherent layer of debris and is revealed by SEM as a 1-2 μm layer of debris with a mainly granular substructure that entirely covers dentine (5). The orifices of the dentine tubules

Table 1. Overview of currently available adhesives categorized according to the classification of Van Meerbeek *et al.* (2).

ADHESIVE	MANUFACTURER
Three-step etch&rinse adhesives (3-E&R)	
Adper Scotchbond Multi-Purpose	3M ESPE, Seefeld, Germany
Adper Scotchbond Multi-Purpose Plus	3M ESPE
All-Bond 2	Bisco Inc., Schaumburg, IL, USA
All-Bond 3	Bisco
Bond-it	Pentron Corporation, Wallingford, CT, USA
Clearfil Liner Bond	Kuraray Medical Inc, Tokyo, Japan
cmf Adhesive System	Saremco, Rebstein, Switzerland
Ecusit-Primer/Mono	DMG, Hamburg, Germany
Gluma Solid Bond	Heraeus Kulzer, Hanau, Germany
Optibond	Kerr, Orange, CA, USA
Optibond FL	Kerr
PAAMA 2	SDI limited, Bayswater, Victoria, Australia
PermaQuick	Ultradent, South Jordan, UT, USA
ProBond	Dentsply, Kontanz, Germany
Quadrant Unibond	Cavex Holland B.V., Haarlem, the Netherlands
Solobond Plus	VOCO, Cuxhaven, Germany
Syntac	Ivoclar Vivadent, Schaan, Liechtenstein
Two-step etch&rinse adhesives (2-E&R)	
Adper Scotchbond 1 XT Adhesive (Single Bond)	3M ESPE
Bond-1	Pentron Corporation
Clearfil Photobond	Kuraray Medical Inc
Clearfil New Bond	Kuraray Medical Inc
Excite	Ivoclar Vivadent
Excite DSC	Ivoclar Vivadent
Gluma Comfort Bond	Heraeus Kulzer
Gluma One Bond	Heraeus Kulzer
Go!	SDI limited
Heliobond	Ivoclar Vivadent
One Coat Bond	Coltene-Whaledent, Altstätten, Switzerland
One-Step	Bisco Inc
One-Step Plus	Bisco Inc
Optibond Solo Plus	Kerr
Optibond Solo Plus Dual cure	Kerr
Peak LC Bond	Ultradent
Polibond	VOCO
Prime&Bond NT	Dentsply
Prime&Bond NT dual cure	Dentsply
PQ1	Ultradent
Quadrant Uni-1-Bond	Cavex Holland B.V.
Solist	DMG
Solobond M	VOCO
Stae	SDI Limited
Superbond C&B	Sun Medical Co, Shiga, Japan
TECO	DMG
XP BOND	Dentsply

2-step self-etch adhesive (2-SEA)	
AdheSE	Ivoclar Vivadent
All-Bond SE (including All-Bond SE Liner)	Bisco Inc
Clearfil Liner Bond 2	Kuraray Medical Inc
(Clearfil Liner Bond II in Japan)	
Clearfil Liner Bond 2V	Kuraray Medical Inc
(Clearfil Liner Bond II S in Japan)	
Clearfil Protect Bond	Kuraray Medical Inc
Clearfil SE Bond (Clearfil Mega bond in Japan)	Kuraray Medical Inc
Contax	DMG
FL Bond (Imperva Fluorobond in Japan)	Shofu Inc., Kyoto, Japan
Frog	SDI Limited
Microbond/Microbond Duo	Saremco
Nano-Bond	Pentron Corporation
One Coat Self Etching Bond	Coltene-Whaledent
Optibond Solo Plus Self-etch	Kerr
One-step Plus/Tyrian SPE	Bisco Inc
Peak Self-Etch	Ultradent
Tokuso Mac Bond II	Tokuyama Dental Corporation, Tokyo, Japan
Unifil Bond	GC, Tokyo, Japan
One-step self-etch adhesive (1-SEA)	
Absolute	Dentsply
AdheSE One	Ivoclar Vivadent
Admira Bond	VOCO
Adper Prompt L-Pop	3M ESPE
All-Bond SE	Bisco Inc
AQ Bond (also Touch&Bond by Parkell, USA)	Sun Medical Co
Bond Force	Tokuyama Dental Corporation
Clearfil S ³ Bond	Kuraray Medical Inc
Futurabond NR	VOCO
G-Bond	GC
Hybrid Bond	Sun Medical Co
iBond	Heraeus Kulzer
James-2	Saremco
OptiBond All-In-One	Kerr
One-up F Bond	Tokuyama Dental Corporation
One-up Bond F Plus	Tokuyama Dental Corporation
Reactmer Bond	Shofu Inc
Tyrian SPE	Bisco Inc
Xeno III	Dentsply
(Xeno CF II in Japan)	
Xeno IV	Dentsply
Xeno V	Dentsply

For more information with regard to composition and pH, see 77.

are obstructed by debris tags, called smear plugs, that are contiguous with the smear layer and may extend into the tubules to a depth of 1-10 μm (6). The smear layer consists of shattered and crushed hydroxyapatite, as well as fragmented and denatured collagen that in clinical conditions may also be contaminated by bacteria and saliva. Early non-acidic adhesives failed, as they did not penetrate profoundly enough to establish a bond with intact dentine. In order to take this 'smear-layer' obstacle, a certain degree of etching is consequently required. There are basically two options, i.e. removal of the smear layer prior to bonding or the use of adhesives that can penetrate beyond the smear layer while incorporating it (7). The first adhesives achieving clinically acceptable results were based on smear-layer removal, and are known as 'etch&rinse' adhesives (8). More recently, smear-layer incorporating or 'self-etch' adhesives have become popular, especially because of their ease of use and faster application procedure (8) (Table 1). Some of those self-etch adhesives interact very superficially with the smear layer and the underlying dentine. In addition to the shallow micro-mechanical interlocking, they can also chemically interact with residual hydroxyapatite following a two-fold bonding mechanism similar to that of glass-ionomers. The latter glass-ionomer bonding strategy can be regarded as the third strategy to bond to tooth tissue (8).

The hybridization process

Micro-morphological characterization of the interface is paramount to gain insight in the bonding mechanism to tooth tissue. As the adhesive interaction process occurs over a couple of micrometers, electron microscopy is preferred on grounds of the high resolution that can be achieved. In particular, the transmission electron microscope (TEM) provides highly informative images of both the interaction zone with intact dentine and with the resin layers.

All categories of adhesives exhibit the common adhesion mechanism of hybridization. This is the process of micromechanical interlocking ensuing a

demineralization, infiltration and polymer setting process, and was first described by Nakabayashi *et al.* (9). A hybrid layer is the resulting resin-infiltrated surface layer of dentine (and enamel).

Etch&rinse adhesives

Etch&rinse adhesives can readily be recognized by an initial etching step, the so-called 'conditioning step', followed by a compulsory rinsing phase. Another frequently used name for this category of adhesives is 'total-etch' adhesives, which is, however, less appropriate because self-etch adhesives also etch and demineralize tooth tissue, and are also applied simultaneously to enamel and dentine (8, 10, 11). This etching step produces etch pits within the enamel, and demineralizes dentine in order to remove the smear layer and smear plugs, and so achieves a micro-porous surface with enhanced bonding receptiveness.

Originally, three-step etch&rinse systems typically consisted of three separate application-steps: 1) conditioning, 2) priming and 3) adhesive resin application. In the search for fewer application steps and simplification, a two-step etch&rinse approach combines the priming and bonding steps into one, frequently being referred to as 'one-bottle adhesives' and misleadingly suggesting a single application step. Both three- and two-step etch&rinse adhesives pursue a similar adhesion mechanism. In the conditioning step, phosphoric acid removes the smear layer while concurrently demineralizing dentine over a depth of 3-5 μm , thereby exposing a scaffold of collagen fibrils that is nearly totally depleted of hydroxyapatite (12, 13). The exposed collagen fibrils function as a micro-retentive network for micro-mechanical interlocking of resin monomers that diffuse into it and polymerize *in-situ*, eventually forming the so-called hybrid layer (Fig. 1). HEMA is often one of the key components for this type of adhesive. Infiltration of the thick (3-5 μm) and potentially collapsed demineralized collagen network requires very hydrophilic and low molecular weight monomers such as HEMA. The re-expansion of the collagen mesh that has collapsed upon post-condi-

Fig. 1. Transmission electron photomicrograph illustrating a non-demineralized, stained section through the interface between the three-step etch&rinse adhesive cmf Adhesive System (Saremco) and dentin. A uniform hybrid layer of about 3 μm is formed, in which typically cross-banded type-I collagen can be observed.

tioning air-drying (14) is especially crucial for bond strength improvement (15).

Neither the thickness of the hybrid layer, nor the length of the resin tags seems to play an important role regarding the bond strength (16, 17). True chemical adhesion between collagen and the methacrylate monomers is unlikely, because of the inert nature of collagen fibrils and the low affinity of the monomers for hydroxyapatite depleted collagen (18). Consequently, the rather poor adaptation and envelopment of resin to the collagen fibrils leave nanometer-sized gaps that have been shown to absorb silver, representing the so-called nano-leakage phenomena (19). This process is thought to be primarily responsible for the gradual degradation of the bond (20, 21).

Bonding to enamel is still today best accomplished using this etch&rinse approach. A 35% phosphoric-acid etch&rinse phase removes the enamel top layer for a few μm , and selectively dissolves hydroxyapatite crystals within prismatic and interprismatic enamel (22). This increases microscopic roughness,

Fig. 2. TEM photomicrographs showing the enamel-adhesive interface produced by, respectively, an etch&rinse adhesive (left: OptiBond FL, Kerr) and a 'mild' self-etch adhesive (right: Clearfil SE, Kuraray). Note the markedly different interfacial ultra-structure with deep (left) versus only shallow (right) resin tags.

surface area and surface energy. The simple application of a hydrophobic low-viscosity resin or ordinary bonding agents efficiently infiltrates the etch pits by capillary attraction. Upon *in-situ* polymerization micro- and macro-tags are formed that are responsible for the durable micro-mechanical interlocking at enamel achieved following this etch&rinse procedure (Fig. 2: left). This bond to enamel not only effectively seals the restoration margin, but even protects the more vulnerable bond to dentine against degradation (21).

So far, *in-vitro* and *in-vivo* research has pointed out that etch&rinse adhesives can achieve high-quality adhesion to both enamel and dentine (2, 8, 23, 24) (Fig. 3). In laboratory and in clinical studies, three-step etch&rinse adhesives commonly perform superiorly to two-step etch&rinse adhesives (16, 23, 25, 26). The latter are also associated with greater technique sensitivity than their three-steps counterparts, which is understandable as a single solution combines the two separate functions of primer and bonding resin (27). Moreover, after aging procedures in durability studies, the bonding integrity of three-step etch&rinse adhesives is better maintained (21, 28). Therefore, three-step etch&rinse adhesives are still today considered as the 'gold standard' amongst adhesives, in spite of the rather elaborate and lengthy working

Fig. 3. Micro-tensile bond strength (μ TBS) of some of today's adhesives to dentine, measured following the Leuven μ TBS protocol.

procedure.

The primer solvent within etch&rinse adhesives is a major factor affecting the handling (29) and performance (15) properties of etch&rinse adhesives. Water-based adhesives are believed to be most forgiving regarding application errors, but the water content in the resultant interface jeopardizes the durability. Acetone-based adhesives on the other hand have water-free formulations, but require the challenging 'wet-bonding' technique (29, 30). Ethanol-based adhesives are believed to be a good compromise regarding user-handling and performance (8). One of the most recent new developments with regard to etch&rinse adhesives was the use of ter-butanol in the recent two-step etch&rinse adhesive XP-Bond (Dentsply) (Table 1). Ter-butanol is a solvent with a similar vapor pressure as ethanol, but a better capability for chemical reaction with monomers. This new etch&rinse adhesive has been recently presented with good micro-tensile bond strength data (Fig. 3) as well as performing well when tested following a conventional shear bond strength test by general practitioners in a so-called 'Battle of the adhesives' series by Degrange *et al.* (31).

Self-etch adhesives

Although the self-etch concept is not new (2), it has only in the last five years come under extensive

scrutiny. First, self-etch adhesives were developed by raising the amount of acidic monomers in HEMA-water based adhesives (10). Self-etch adhesives do not require a separate 'etch&rinse' phase, as they contain acidic monomers that simultaneously condition and prime enamel and dentine. As a result, the dissolved smear layer and demineralization products are not rinsed away, but incorporated in the adhesive resin (32, 33).

Self-etch adhesives can be subdivided according to the number of application steps, and their acidity (pH) and resultant etching aggressiveness (2, 34). Similarly to etch&rinse adhesives, a two-step and a simplified one-step version of self-etch adhesives or so-called 'all-in-one' adhesives exist (35).

The morphological features of the hybrid layer produced by self-etch adhesives depend a great deal on the aggressiveness of the functional monomers (8, 36). Consequently, three categories of self-etch adhesives can be made according to their acidity: mild ($\text{pH} \geq 2$), intermediate ($\text{pH} \approx 1.5$) and strong self-etch adhesives ($\text{pH} \leq 1$) (34, 37) (Fig. 4). 'Mild' self-etch adhesives demineralize dentine only very shallowly, forming a rather shallow hybrid layer with sub-micron dimensions, while leaving hydroxyapatite crystals around the collagen fibrils (Fig. 4: right). TEM images of 'strong' self-etch adhesives applied

Fig. 4. TEM photomicrographs showing the adhesive-dentine interface produced by, respectively, a 'strong' self-etch adhesive (left: Adper Prompt L-Pop, 3M ESPE) and a 'mild' self-etch adhesive (right: Clearfil SE, Kuraray). Note the markedly different interfacial ultra-structure with the formation of a deep (left) versus only shallow (right) hybrid layer. Only in the latter, hydroxyapatite (HAp) still remains.

on dentine strongly resemble the morphological aspect of an etch&rinse adhesive with a thick hybrid layer, which is completely devoid of hydroxyapatite crystals, and with resin tags (Fig. 4 : left). The more aggressive the adhesive, the deeper the hybridization (38). 'Intermediary strong' self-etch adhesives exhibit morphological features that lie between the mild and strong self-etch adhesives. Apart from the pH of the self-etch solution, other factors such as agitation during application, thickness of the smear layer, viscosity and wetting characteristics also account for the obtained depth of infiltration and demineralization by self-etch adhesives (39, 40).

In spite of the small hybrid layer and the absence of resin tags (little micro-mechanical retention), mild self-etch adhesives such as Clearfil SE (Kuraray) can reach satisfactory results as far as bond strength is concerned (8, 16) (Fig. 3). Together with the finding that the thickness of the hybrid layer and the presence of resin tags do not overly influence the bonding performance (16, 17), additional chemical interaction between the monomers and hydroxyapatite may be a plausible explanation for the good performance of some self-etch adhesives (4). One has to keep in mind that the interaction of self-etch adhesives with tooth substrate is dependent to a great extent on the kind of acidic functional monomer and eventually the overall composition of the adhesive. This results generally in a larger variation in bonding performance of the different self-etch adhesives available today than of the etch&rinse adhesives that all rely largely on the use of phosphoric acid and the subsequent infiltration of monomers. The carboxylic and phosphate groups that render these monomers hydrophilic and that function as proton-donors, have been proven to bond ionically with calcium in hydroxyapatite (41). The ability to chemically bond is monomer-specific and depends on the hydrolytic stability of the calcium-monomer bond. Using XPS (X-ray photo-electron microscopy), Yoshida *et al.* has shown that 10-MDP exceeds the bonding potential of 4-MET and phenyl-P (4) (Fig. 5). The hydrolytic stability of the monomer itself is also important, especially with regard to bond durability.

Fig. 5. X-ray Photoelectron Spectroscopy (XPS) of the chemical interaction of three functional monomers with synthetic hydroxyapatite (HAp). The significantly most intense C 1s peak was recorded for 10-MDP, suggesting the most intense chemical interaction with HAp through ionic bond formation.

Whereas micro-mechanical retention is thought to provide resistance to 'acute' de-bonding stresses, the relevance of additional chemical bonding is suggested to lie in durability and survival of adhesion (2, 8).

The composition of self-etch adhesives is unusual in that they contain high concentrations of water and acidic monomers (34). Water is an indispensable ingredient of current self-etch systems; it provides an ionization medium for the functional monomers (42). Two-step self-etch adhesives consist of a hydrophilic aqueous primer solution and a separate hydrophobic adhesive resin. Similar to the combined primer/adhesive resin solution of two-step etch&rinse adhesives, one-step self-etch adhesives are complex mixtures of both hydrophilic and hydrophobic components. In particular, the high concentrations of water have raised questions about potentially harmful effects on polymerization, given that complete water removal is unrealistic (42, 43). This also applies to the high concentrations of solvent that may cause incomplete resin polymerization in case of incomplete evaporation.

When bonding to enamel, the 'strong' self-etch adhesives, in general, perform better than the higher-pH self-etch adhesives (8). Nevertheless, with some 'mild' self-etch adhesives such as Clearfil SE (Kuraray), a quite high and stable bond strength is achieved,

which must most likely be attributed to the good chemical interaction potential of the functional monomer (10-MDP in Clearfil SE, Kuraray). Ultra-structurally, the interaction with enamel is very shallow with the sole formation of micro-tags (Fig. 2: right).

While bonding to enamel may remain a problem, especially for mild self-etch adhesives (25, 40), bonding to dentine has reached results comparable to those obtained by the gold-standard three-step etch&rinse adhesives (16). Recent studies have also reported of good clinical results for some self-etch adhesives. Clearfil SE (Kuraray), which is a mild two-step self-etch adhesive, was reported to have high retention rates in non-carious class V cavities after, respectively, 5 and 2 years (44, 45).

Compared to etch&rinse adhesives, many advantages have been attributed to self-etch adhesives. It has been suggested that they improve the efficiency in clinical procedures by omitting the obligatory rinse phase in etch&rinse adhesives and thus reducing the chairside time (46). Conditioning, rinsing and drying steps, which may be critical and difficult to standardize in clinical conditions, are eliminated in self-etch adhesives (40). Technique sensitivity associated with bonding to dehydrated demineralized dentine is eliminated, as a rinsing and drying phase are no longer needed (47). Collapse of the collagen network is prevented, as monomers infiltrate concomitantly as they demineralize (22, 33, 48). Theoretically, incomplete resin infiltration is prevented in this way as well (33, 36). However, recent nanoleakage observations in the hybrid layer, and especially beyond the hybrid layer have shed doubt upon the concept that self-etch adhesives ensure complete resin infiltration (49). As the smear layer and smear plugs are not removed prior to the actual bonding procedure, rewetting of dentine by dentinal fluid from the dentine tubules is prevented (50) and potential postoperative sensitivity has been reported to be reduced (44, 51). Perdigão (52), however, could not observe any difference in postoperative sensitivity between a three-step etch&rinse adhesive and a self-etch system.

Glass-ionomer Approach

The third adhesive approach is based on the technology of glass ionomers and their auto-adhesive capacity. Glass ionomers are the only true self-adhesive materials as they can adhere to both enamel and dentine by a specific glass-ionomer interaction. Diverse formulas of glass ionomers are on the market, varying in use: glass-ionomer restorative materials, cements and even adhesives to bond composites to tooth tissue.

Glass ionomers have a specific composition, containing polyacrylic acid, alkenoic copolymers, glass-filler particles and water. When resin components are added to glass ionomers, these are called resin-modified glass ionomers. The adhesion reaction to tooth tissue is mainly based on the glass-ionomer components and involves both a micro-mechanical hybridization and a chemical reaction. In the particular case of glass-ionomer adhesives, which are actually resin-modified glass ionomers, the resin components ensure good bonding with the lining composite.

Regarding bonding mechanism, they can be considered a special group of self-etch adhesives based on glass-ionomer technology. Like self-etch adhesives, their mechanism of adhesion is two-fold and depends both on a limited demineralization of enamel and

Fig. 6. Combined TEM photomicrograph and schematic explaining the twofold micro-mechanical (hybrid layer) and chemical interaction mechanism of glass ionomers. On top of the hybrid layer, a typical gel phase is deposited with some glass-ionomers as a polycarboxylate salt with calcium that was released from the underlining dentine.

dentine with subsequent infiltration and mechanical interlocking, and on a chemical adhesion between calcium in hydroxyapatite and polyalkenoic acid (41, 53, 54) (Fig. 6). The demineralization reaction is set off by the high-molecular-weight polyalkenoic acid. This acidic molecule exposes a micro-porous collagen network by selectively dissolving hydroxyapatite crystals. Additionally, ionic bonding takes place between the carboxyl groups of the polyalkenoic acid and calcium of remaining hydroxyapatite crystals. This bond has been proven to be relatively stable, capable of withstanding ultrasonic rinsing (41).

Micro-morphologically, a shallow hybrid layer of 0.5-1 μm in thickness is formed (Fig. 6). Because of a mild and partial demineralization, hydroxyapatite crystals can be distinguished around the collagen fibrils within the hybrid layer. Typically, a 'gel phase' closely attached to the hybrid layer can be observed with some glass ionomers. This amorphous phase on top of the interface has been reported to represent salt of calcium-polycarboxylate (55, 56).

A conditioning step with a weak polyalkenoic acid (PAA) significantly improves the bond strength (57). Its beneficial effect on bond strength lies in a three-fold mechanism: 1) the removal of the smear layer by PAA; 2) a shallow demineralization of the tooth tissue; 3) a chemical interaction of PAA with residual hydroxyapatite (41).

Clinically, the good adhesion of glass ionomers and resin-modified glass ionomers is striking. Very high retention rates of more than 90% have been observed for periods up to 5 year in non-carious cervical lesions (26, 58, 59). Moreover, a recent study has revealed that glass-ionomer retention rates exceed by far the retention rates of other adhesives (23). Other advantages of glass ionomers are their biocompatibility and their fluoride release. The main drawback of glass-ionomer restorations remains their inferior esthetic and mechanical properties as compared to composites.

Current concerns of One-Step adhesives

One-step self-etch adhesives (1-SEAs) are market-

ed as the most user-friendly adhesives. *In vitro* and *in vivo* research, however, revealed considerable shortcomings related to many of these simplified adhesives:

Reduced bond strength

The relatively low bond strengths obtained by 1-SEAs are a main concern (Fig. 3). Compared to multi-step self-etch and etch&rinse versions, one-step self-etch adhesives consistently achieve lower bond strengths (16, 25, 60, 61). Clinically, these lower initial mechanical properties must especially jeopardize their performance in minimally-invasive cavities, and thus narrow and deep cavities. A lot of 1-SEAs might not be able to withstand the resultant high polymerization shrinkage stress, giving rise to early failures and post-operative sensitivity (62).

Reduced bond durability

Due to their high hydrophilicity, cured one-step self-etch adhesives have been demonstrated to act as permeable membranes, permitting water movement across the adhesive layer (63, 64). Reticular patterns of nanoleakage, so-called water trees, have been found within the adhesive layer of 1-SEAs and are considered as sites of incomplete water removal and subsequent sub-optimally polymerized resins (65). The actual clinical relevance of these water trees remains unclear, but as they may function as water ducts, they may contribute to accelerated degradation of tooth-resin bonds (20, 66, 67). The micro-tensile bond strength of some recent-generation one-step adhesives was found to significantly reduce upon water storage of the micro-specimens in water for 6 months.

Technique-sensitivity

All 1-SEAs are very complex mixtures of monomers, solvents and filler particles. These blends of hydrophilic and hydrophobic components have to fulfill all adhesive tasks, namely etching, priming and bonding, in a single step (8). This renders them rather sensitive to application mistakes. Especially the air-drying step subsequent to their application is

crucial to reduce the amount of solvent and water in the adhesive layer as much as possible. It is known that thick adhesive layers of simplified adhesives decrease bond strengths tremendously (69). On the other hand, this air-drying procedure should also be done in such a way that a sufficient amount of monomers is kept at the surface to provide sufficiently good mechanical properties to the adhesive layer. In narrow and complex cavities, the correct balance between too much and not enough air-drying is a tricky thing; while the adhesive may still pool in the cavity corners, the amount of monomers on the cavity walls may already be too low (69).

HEMA-free formulation

More recently, complex processes of phase separation have been shown to occur in one-component, HEMA-free SEAs (69, 70). As soon as such an adhesive was dispensed onto a glass plate and the solvent started to evaporate, simple light microscopy of one-step adhesive solutions revealed a phase separation, yielding a multitude of droplets that slowly emerged towards the top of the adhesive drop and then disappeared. If the adhesive was light-cured, all remaining droplets were entrapped in the adhesive layer. The explanation for these observations must be found in the complex mixture of both hydrophobic and hydrophilic components, dissolved in an organic solvent (usually ethanol or acetone). Gradual evaporation of the solvents sets off the phase-separation reaction, in which water separates from the other adhesive ingredients. HEMA plays a key role in this process, as this monomer acts as a wetting agent due to its hydrophilic character and can prevent water from separating from other adhesive ingredients. It is self-evident that the incorporation of droplets may contribute to bond degradation, but persistence of water in the adhesive layer may also affect the bond strength adversely. However, somewhat surprising no direct negative effect of the entrapped droplets on the ultimate or fatigue strength of adhesive bonds was noted (71). Moreover, these phase separations have been regarded as beneficial, as they offer a way to remove water from the adhesive interface. Air

-blowing of the primed surface will accelerate the evaporation of the solvent (acetone), by which water separates from the other adhesive components. The resultant droplets can then be removed from the adhesive by a prolonged thorough air-blowing (using maximum air pressure). In this way, HEMA-free one-step self-etch adhesives possess a kind of built-in, relatively technique-insensitive, method to achieve a low water-containing adhesive interface.

HEMA-rich formulation

In order to avoid phase-separation, HEMA can be added to the adhesive formulation, as explained in the previous paragraph. One study has demonstrated that a relatively high HEMA concentration is required to avoid phase separation (69). Such HEMA-rich adhesives are however prone to other problems, in particular a higher sensitivity to water absorption from the outside environment as well as from the host dentine. When HEMA is cured in the presence of water, polymerization is incomplete and a porous hydrogel is formed. These areas of increased permeability allow water to permeate through the adhesive layer, compromising especially the long-term bonding effectiveness (42). Another, but related phenomenon is osmosis. The HEMA hydrogel produced upon curing of the all-in-one adhesive can act as a semi-permeable membrane (64), of which the upper layer that is insufficiently polymerized due to oxygen inhibition is a hypertonic fluid. Both effects combined result in an osmotic transfer of water from the underlying dentine towards the adhesive-composite interface. As this is a time-dependent process, postponing the curing of the overlying composite will result in severe droplet formation and premature failure at the adhesive-composite interface (42). Though, in principle, this is valid for all one-step self-etch adhesives, HEMA-rich adhesives are much more sensitive to this osmotic breakdown (70). The fact that due to the higher amount of small (HEMA) molecules, the interface produced by an HEMA-rich adhesive is more permeable; in combination with the high osmotic pressure at the oxygen-inhibition layer this may explain why this osmotic blistering is

a major problem for HEMA-rich adhesives and almost no problem for HEMA-free adhesives (70).

Ultra-mild self-etch adhesive

In particular the low stability of functional monomers in high pH solutions (72, 73) has driven some manufacturers to produce ultra-mild self-etch adhesives, such as Clearfil S³ Bond (Kuraray). TEM revealed that such an adhesive with a relatively high pH (≈ 2.7) decalcified the dentine surface only very superficially for up to a few hundreds of nanometer, with few collagen fibrils exposed at the interface. This particular interfacial feature has therefore been termed a nano-interaction zone (74). The key factor in this ultra-mild approach is the unique property of the functional monomer 10-MDP that has currently been documented with the significantly highest chemical bonding potential (4) (Fig. 5). However, this nano-interaction approach also re-introduced the above mentioned smear layer 'obstacle'. Mild self-etch adhesives (pH ≈ 2) dealt relatively effectively with the smear layer, even when produced by various surface preparation methods such as diamond burs with different grit sizes, air-abrasion and sono-abrasion (32, 75). Due to their increased pH, the newly introduced ultra-mild self-etch adhesives are much more sensitive to the smear layer characteristics. For example, Clearfil S³ Bond performed significantly better when a extra-fine (15 μm grit-size) diamond bur was used, as opposed to a more commonly used regular (100 μm grit-size) bur (76). If this is clinically relevant, it should definitely be investigated.

Reduced shelf-life

Most resins used in dental adhesives are acrylates or methacrylates. The ester groups of these resins are prone to hydrolysis, especially in an acidic environment (72, 73, 77). This degradation results in the formation of acids as such methacrylic acid, enhancing the self-etching aggressiveness that is not necessarily accompanied by the needed deeper resin infiltration (72). Most of the currently commercially available adhesives are prone in some way to such an in-the-bottle monomer degradation (73). A way to

overcome this problem is by producing water-free adhesives (e.g. Absolute, Dentsply-Sankin), as such a monomer degradation is a hydrolytic process that will not take place in a water-free environment. To activate etching, such a water-free adhesive should be applied to a wet surface, which immediately creates the problem how wet the surface should be. Two-component one-step adhesives keep water separate from the functional monomers (e.g. Adper Prompt L-Pop, 3M-ESPE; Futurabond NR, Voco; One-up Bond F Plus, Tokuyama; Reactmer Bond, Shofu; Tyrian SPE, Bisco; Xeno III, Dentsply). More recently synthesized monomers such as amide-linked polymerizable analogues, instead of conventional ester derivatives, and phosphonic-acid monomers instead of phosphoric-acid monomers (both in AdheSE, Ivoclar-Vivadent) are more hydrolytically stable (73), which should improve the shelf life of the adhesives.

Enzymes

Currently, bonding to dentine is achieved primarily through hybrid-layer formation, either relatively deep with etch&rinse adhesives and low-pH 'strong' self-etch adhesives, or relatively superficial with 'mild' and 'ultra-mild' self-etch adhesives. The resultant hybrid layer then, respectively, consists of a completely or partially hydroxyapatite-deprived collagen mesh infiltrated by resin. It has been shown that dental adhesives during the production of this hybrid layer also can release enzymes from the dentine matrix that have a low collagenolytic activity (78). Such host-derived enzymes can hydrolyze the collagen fibrils that make up the hybrid layer and so compromise the long-term clinical bonding effectiveness. Recent enzymographic research revealed that mostly collagenase A is responsible for the hydrolytic breakdown of the hybrid layer (79, 80). The actual relevance of this enzymatic breakdown of the hybrid layer may however clinically be less dramatic than suggested in some papers, as the endogenic enzymes gradually decrease with age, generally disappearing before the age of 40 (81). A way to protect the interface against such enzymatic

degradation process is the use of matrix metallo-proteinases-inhibitors, of which one, chlorhexidine, is already commonly used in dentistry and seems effective *in vitro* as well as *in vivo* (82, 83).

Clinical performance of current adhesives

The ultimate method to test dental adhesives is performing clinical trials. If the study objective is to investigate the bonding effectiveness of adhesives, only studies involving non-carious class-V adhesive restorations should be considered, for which there are many reasons (11). The main reason is that only class-V lesions do not provide any macro-mechanical retention, so that ineffective bonding will result in early restoration loss, which is the only objective parameter available. In a recent systematic review (23), the retention rate of different commercial adhesives that were tested in clinical class-V studies world-wide was registered per category of adhesive approach in order to get an better idea of the clinical effectiveness of today's adhesives. In this study, the following main conclusions were drawn (Fig. 7) :

- Regarding retention rate of class-V restorations, glass-ionomers bonded most effectively and durably to tooth tissue.
- Among the resin-based adhesives, the three-step etch&rinse adhesives and the 'mild' two-step self-etch adhesives showed a clinically reliable and predictably good clinical performance with retention rates generally well above the ADA specifications.

Fig. 7. Annual failure rates of adhesive class-V restorations per adhesive category.

- The clinical effectiveness of two-step etch&rinse adhesives were less favourable than that of their three-step etch&rinse pre-cursors.
- A strongly varying and often inefficient clinical performance was noted for the one-step self-etch adhesives.

Thus, though the one-step adhesives with the most simplified application procedure are clinically faster and easier to use, they generally perform less well. The strongly varying results measured at different research centres point to a relatively high technique sensitivity, in contrast to what is often claimed by manufacturers. It definitely should be mentioned that the most recent generation of one-step self-etch adhesives appear to perform better clinically, as is suggested by a more recent review of class-V clinical data (unpublished data KULeuven) (84, 85, 86, 87). These promising short-term (1-2 year) results are however still far from the near to perfect long-term (7-13 year) results of a 'gold standard' three-step etch&rinse adhesive (88, 89).

Conclusion

A good classification of adhesives is indispensable to keep an overview of the current field. The strength of the proposed classification lies in its simplicity and its scientific basis. Each category in this classification is characterized by a specific bonding mechanism, a specific and distinct application protocol and by a specific interfacial ultra-structure as best imaged using TEM.

With regard to the actual bonding effectiveness, it is now very clear that an adhesive's *in-vitro* and *in-vivo* performance greatly depends on its specific ingredient composition and this is especially so for the more recent one-step self-etch adhesives. In spite of the improved ease-of-use and faster application, a simplified application procedure so far seems to entail a reduced bonding effectiveness, and their advantages should therefore be traded off against their major shortcomings. Presently, the most acceptable trade-off seems to be a 'mild' two-step self-etch adhesive that combines micro-mechanical interlocking to the tooth substrate with additional chemical

interaction that definitely contributes to the bond stability.

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