We are IntechOpen, the world’s leading publisher of Open Access books
Built by scientists, for scientists

3,500
Open access books available

108,000
International authors and editors

1.7 M
Downloads

151
Countries delivered to

TOP 1%
Our authors are among the most cited scientists

12.2%
Contributors from top 500 universities

WEB OF SCIENCE™
Selection of our books indexed in the Book Citation Index in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com
Chapter 5

Adhesive Restorations and the Oral Environmental Behaviour

Egle Milia, Roberto Pinna, Enrica Filigheddu and Stefano Eramo

Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/64973

Abstract

Adhesive restorations are based on the use of materials, which have the capacity to bond tooth effectively. This is possible due to a polymerizing hybrid layer interface created by the use of the Etch&Rinse (ERAs) and self-etching adhesives (SEAs). Bonding using ERAs include the acid-etching removal of the mineral phase from the substrates of enamel and dentine. A hybrid layer results by filling the voids left by minerals by means of adhesive monomers. However, etching dentine may result in too much demineralization and wetness with discrepancies in reinforcement at the bottom of hybrid layer. SEAs avoid the separate etching phase of ERAs using acidic functional monomers. In the two-step SEAs, hybridization is created by the application of a primer of different pH acidity, followed by an adhesive resin. In the ‘One-Step SEAs’, acidic and adhesive monomers are mixed in the same bottle thereby causing hybridization at the same time. 10-MDP mild SEAs represent the better bonding technology in dentistry due to the ability to form a strong chemical bond in tooth tissue. However, adhesive restorations have high vulnerability in the oral environment, which have been attributed to the esterase activity of Streptococcus mutans and hydrolysis by matrix metalloproteinase.

Keywords: 5 max adhesive restoration, Etch&Rinse adhesives, self-etching adhesives, oral biofilm, Streptococcus mutans, MMP

1. Introduction

Adhesion in dentistry is based on the use of materials which have the capacity to bond tooth tissues effectively.

It was the perception of Buonocore [1] who, in 1955, firstly thought to acidify the enamel tissue in order to ‘make the tooth surfaces more receptive to an adhesion process’. During that period,
adhesion was confined to the restoration of carious teeth, whereas today, most of the materials have become adhesive in dentistry completely changing the mind-set in the clinical approach.

In comparison with non-adhesive materials, which spread passively on the tooth surfaces, adhesive materials have the capacity to interlock chemically and micromechanically in tissues allowing a minimal invasion approach in therapy. To a large extent, adhesion concepts are now successfully applied in direct and indirect restorations to allow them to withstand masticatory stress [2], to add to the aesthetic and harmonious parameters in a smile [3–5], as well as to reinforce root canals after endodontic therapy, and, more recently, in the treatment of dental hypersensitivity [6] (Figures 1 and 2).

This huge evolution has been possible due to the presence of a polymerizing hybrid layer interface that is based on an exchange process by which inorganic tooth material is substituted by the synthetic monomers of adhesive systems [7]. On the surface of the tooth, the hybrid layer interlocks chemically and micromechanically to the tooth tissues, and on the surface of the filling, most frequently consisting of a polymerizing resin composite, it becomes integrated into the adhesive. On the composite, adhesion is achieved by a process of co-polymerization involving residual double bonds (-C=C-) in the oxygen inhibition layer of the hybrid layer in the tooth [7] (Figure 3).

However, adhesive resins, particularly dimethacrylates, have shown some adverse biological effects [8], which have directed attention to a possibly low biocompatibility with some mutagenic properties in addition to local cytotoxic effects. Some unreacted residual monomers could dissolve into saliva and be released into the oral environment causing mucosal damage. Moreover, a possible endocrine-disruptive effect of monomers has raised some concern [9, 10].

![Image](image_url)

**Figure 1.** (A) The photograph shows a poorly shaped, IV class direct resin composite restoration in tooth 11 in a young girl. The restored tooth is not in accordance with the other upper maxillary teeth which are part of the smile. Also, the colours and shape of the composite in 11 did not match those of the surrounding unaltered tooth tissues. In addition, the margins of the restoration appear covered by a thick yellow layer, strongly contrasting to the surrounding sound tissues. (B) After replacing the new composite in 11, the incisal and proximal area of the restoration show quite natural opalescence and translucency, similar to the homologous tooth 21. In addition, the restored tooth is now in accordance with the other teeth which comprise the smile.
Adhesion techniques can be widely applied to recover the smile in complex situations, regardless of the age of the patient. (A) A 17-year-old girl, who has an agenesis of the upper maxillary lateral incisors (12 and 22). Until she reaches the age when implants are possible, a zirconia Maryland bridge has been employed (B), adhering to the no-prep palatal surfaces of the upper maxillary central incisors and canines, adjacent to the gaps (C), which supports the artificial porcelain teeth 12 and 22, recapturing the harmony of the smile (D).

Figure 3. Adhesive restorations are based on a polymerizing hybrid layer interface between the tooth surface and the composite surface. (A) A non-decalcified transmission electron microscope (TEM) image showing the surface of a tooth in which the hybrid layer interlocks infiltrating dentin collagen and forming resin tags into the dentinal tubules (empty white arrow). (B) An scanning electron microscope (SEM) image of the bonding between the composite and the hybrid layer (white arrow), which is achieved by a process of co-polymerization involving residual double bonds in the oxygen inhibition layer of the hybrid layer in the tooth. (C and D) The application of composite in the recovery of smiling forces. HL = hybrid layer; RT = resin tag; C = composite.
Also, adhesive restorations have demonstrated a high vulnerability in the oral environment, which explains the high rate of failures [11] and over time the need for frequent replacement. Factors affecting durability could, to some extent, be ascribed to the chemistry of the materials, difficulties in the management of the tissues involved in bonding and on the choice of the most suitable adhesion procedure to be used [2]. In addition, breakdown of adhesive restorations has been attributed to the activity of the oral cariogenic biofilm [12, 13], particularly ascribed to the high susceptibility of resins to be colonized and degraded by the esterase activity of S. mutans. Also, hydrolysis of the bond has been connected to activation of the host-derived proteases matrix metalloproteinase (MMPs).

So, the intention of the present work is to examine adhesive materials and procedures in dental bonding whilst pointing out the main mechanisms of the breakdown of resins within the oral environment.

2. The adhesive systems

2.1. The chemistry of adhesive systems

Dental adhesives, as well as resin composites, both contain a similar mixture of resin monomers in order to ensure good covalent bonds between them. After photo-polymerization, resin monomers provide a structural, chemical-mechanical backbone to the adhesive restoration in teeth.

Like many other bioadhesive materials, adhesive monomers are composed of a mixture of hydrophobic-hydrophilic monomers, which should have (1) a high rate of polymerization; (2) sufficient stability in the monomeric form as well as in the subsequent form of the polymer; (3) minimum capacity of water sorption; and (4) absence of low toxicity in order to avoid damaging effects [14]. To ensure these qualities, monomers are supplemented by the addition of solvents and photo-initiators in adhesives. Some adhesives sometimes contain fluorine fillers and antibacterial agents with the purpose of promoting remineralization and the eradication of residual bacteria, particularly in caries affected dentine (CAD) bonds [15].

Moreover, the hydrophobic-hydrophilic monomers in bonding have the following functions: (1) in the monomer state, adhesive hydrophilicity allows infiltration of the wet, demineralized dentin matrix; and (2) in the polymerized state, adhesive hydrophobicity leads to lower fluid sorption. Also, hydrophobicity confers adequate stiffness to the polymer to minimize swelling and subsequent hydrolytic degradation [16].

Infiltration of the adhesive in tissues is caused by a physical combination of diffusion and convection phenomena, resulting from the external physical energy applied to disperse it in the tooth.

The spatial composition of the adhesive between the surface of the tooth and the resin composite is a conglomerate of many angstrom-scale structural units, which interact through various covalent bonds, forming linear, crosslinks and non-covalent interactions such as van
under Waals and hydrogen bonds, as well as physical interactions [16]. Despite this fact, compositional changes might be experienced by adhesive systems in the oral environment. Compositional changes, which have been related to the chemical composition and network structure of adhesives [17], may cause degradation of the hybrid layer over time [17, 18].

Adhesives are chemically formulated using two main types of monomers: (1) cross-linkers monomers, which have two or more vinyl groups or \(-\text{C}=-\text{C}\-) polymerizable groups, after polymerization form cross-linked polymers with high mechanical strength; and (2) functional monomers, which have only one polymerizable group, mainly added to a functional group. They have the ability to enhance specific properties of the adhesive and after curing lead to linear polymer [19].

The chemical structure of the monomers can be described in the following way: two terminal groups separated by a spacer chain. One of the terminal groups consists of the polymerizable site of the monomer (generally methacrylate); the other terminal consists of a functional group [20].

Methacrylate monomers are widely used in dental adhesives and generally have hydrophobic behaviour. The hydrophobic bisphenol A glycerolate dimethacrylate (BisGMA) is widely utilized as a methacrylate. The hydrophobic aromatic rings in the backbone of BisGMA confer low-chain mobility and deformation under mechanical loading. In addition, the pendant hydroxyl groups along BisGMA chains form hydrogen bonds between molecules increasing the mechanical properties [21] (Figure 4). However, the molecular stiffness and H-bonding formation make BisGMA highly viscous, lowering the infiltration into the wet dentine. Additionally, the ester group (\(\text{R}-\text{CO}-\text{OR}\)), which is typical of all the methacrylate monomers, may render BisGMA susceptible to hydrolysis [22].

![Chemical structures of (A) BisGMA (bisphenol A glycerolate dimethacrylate); (B) HEMA (ethylene glycol methacrylate); (C) 10 MDP (10-methacryloyloxy-decyl-dihydrogen-phosphate); (D) UDMA (urethane dimethacrylate); and (E) TEGDMA (triethylene glycol dimethacrylate).](image)

Figure 4. Chemical structures of (A) BisGMA (bisphenol A glycerolate dimethacrylate); (B) HEMA (ethylene glycol methacrylate); (C) 10 MDP (10-methacryloyloxy-decyl-dihydrogen-phosphate); (D) UDMA (urethane dimethacrylate); and (E) TEGDMA (triethylene glycol dimethacrylate).

These characteristics may lead to adverse reactions, such as phase separation of the hydrophobic/hydrophilic monomers in water, discrepancies in the reinforcement of the deepest
region of demineralized collagen and poor polymerization [23]. Moreover, incomplete infiltration leads to water retention within the collagen/adhesive interface [24] and sub-optimal polymerization leads to loosely cross-linked domains that can be readily penetrated by water [25].

As regards the spacer, the length and composition of the chain between the polymerizable and the functional groups influence some physicochemical properties, such as the viscous solubility and wettability capacities. Sometimes the spacer chain may have effects on the degree of conversion and mechanical strength, as well as lowering water sorption. It usually consists of an alkyl chain, which contains esters, amides or aromatic groups that may be relatively hydrophobic, as in the case of the functional group 10-methacryloxy-decyl-dihydrogen-phosphate (10-MDP) (Figure 4). Moreover, the chain may consist of relatively hydrophilic polyethylene glycols, such as triethylene glycol dimethacrylate (TEGDMA).

As far as the functional group is concerned, it is generally a phosphate, carboxyl acid or alcohol group. All of these have abilities, such as wetting and demineralization, phase separation stabilization, improvement of the penetration of cross-linking monomers, fluoride release and antibacterial properties. Also, due to the hydrophilic properties, functional groups are considered adhesion-promoting agents in dentine, increasing infiltration and bond strength [26].

In particular, some acidic functional monomers of self-etching adhesives (SEAs) play an important role in bonding performance and the physicochemical properties of these adhesives. HEMA (ethylene glycol methacrylate) (Figure 4) is a monomer very frequently used as a functional group. It is an excellent adhesion-promoting agent in dentine and is very soluble in water, ethanol and/or acetone solvents [19]. Also, HEMA has solvent-like properties, which causes stability in hydrophobic and hydrophilic solutions.

However, many adverse reactions have been ascribed to the use of HEMA, especially when added in high concentration. One of the most common is an increase in water sorption parameters in adhesives, particularly at basic pH [27]. Water sorption was reported in the uncured than in the cured state of HEMA [15]. Specifically, before polymerization, HEMA may cause water adsorption and dilution of the monomers affecting polymerization; after curing, the hydrophilic properties of HEMA still lead to water uptake into the polymer chain with consequent permeability of the hybrid layer, hypersensitivity and deterioration of the mechanical properties of the interface. A high concentration of HEMA may also prevent the complete evaporation of solvents from the adhesive due to a lowering of the vapour pressure of water and probably of the alcohol vehicle [7]. Moreover, adverse reactions are related to a possible toxicity of HEMA that, in the case of phase separation, may be trapped as a residual monomer as well as unreacted radicals [24]. The leaching of HEMA into the surrounding tissues may lead to apoptosis and production of reactive oxygen species (ROS) by gingival fibroblasts [28].

Solvents in adhesives are generally water, ethanol and acetone. They are necessary to bond dentine. Firstly, solvent molecules cause monomers to infiltrate the wetness of demineral-
ized dentine [29, 30]. Secondly, solvents are useful in the re-expansion of the fibres in the case of shrunken after demineralization [31].

In particular, a water solvent is essential to the efficiency of both the Etch&Rinse adhesive systems (ERAs) and self-etching adhesive systems (SEAs). Water has a hydroxyl group that can form strong hydrogen bonds and re-expands the shrunken fibres by breaking the H-bonds and other forces, which keep the collagen in a collapsed state [31]. In SEAs, water provides ionization of the medium and leads to the activity of the self-etching monomers [32].

However, the low vapour pressure of water implies that this solvent may be difficult to remove from the adhesive after layering in teeth [25] resulting in sub-optimal polymerization. Although an air-drying procedure is recommended to increase evaporation of the solvent, it can be retained to some extent, hampering perfect conversion with dilution of the monomers, voids and permeability of the interface [15].

Photo-initiators are added to activate a radical polymerization reaction that allows conversion into a completely polymerized form [14]. Nevertheless, the conversion rates in adhesives and dental composites remain quite low and prevent a tight and impermeable resin interface.

Camphorquinone (CQ), 1,7,7-trimethyl-bicyclo[1,2,2]-heptan-2,3-dione, is a typical photoinitiator in dental adhesives and composites. It works in association with a co-initiator, usually a tertiary amine compound, modified by the addition of methacrylate to lower the toxic and mutagenic effects [19]. However, some noxious biological effects can be directly ascribed to CQ, which limit the addition in adhesives. Also, the yellow colour is another adverse effect, which may compromise the matching of the restoration and the tooth [33].

2.2. The chemistry of resin composites

Conventional composite contains a polymerizable organic matrix, inorganic reinforcing fillers and a silane coupling agent, which bond the organic matrix and inorganic fillers usually represented by glass, quartz or ceramic oxides [34] (Figure 5).

![Figure 5](image-url) (A) An environmental scanning electron microscope (ESEM) micrograph of a composite (Vertis Flow, Kerr Corporation, Orange, CA) showing the resin matrix, which is very rich in nanoparticle fillers. Highly visible randomly distributed 5-40 μm particles can also be observed in the matrix. (B) An EDX (X-ray Energy Dispersive Spectrometer) image, which reveals the ionic nature of these filler particles. In this composite, Si, Yb and F are the most abundant elements in the matrix, in which Al, P, Ca and Ba are also present.
The organic matrix consists of several monomers, generally BisGMA and urethane dimethacrylate (UDMA) in addition to ethylene glycol di-methacrylate compounds, such as triethylene glycol dimethacrylate (TEGDMA). Furthermore, the organic matrix contains an initiator/inhibitor polymerization system, which causes conversion through free radical chain polymerization of di-vinyl oligomers, usually initiated by photochemical and chemical means.

BisGMA monomer is the most common monomer used in the polymeric matrix. As in adhesive systems, BisGMA confers to the composite a high capacity to resist deformation and withstand the mechanical loading, due to its hydrophobic aromatic rings and H-bonding capacity. However, the high viscosity of BisGMA rather limits the addition of a high concentration of fillers and the polymerization of the resin mass. In fact, many studies have found that the rigidity of the material has a direct effect on the polymerization stress of composites.

In contrast, low viscous monomers, such as TEGDMA, are added as diluents. By reducing the overall viscosity, the low-molecular weight di-vinyl monomer of TEGDMA enhances the efficiency of polymerization, mixing of the different constituents, as well as handling of the composite. However, restrictions to the addition of TEGDMA are a result of the presence of triethylene oxide spacers that increase water sorption in the composite. Also, TEGMA increases volumetric shrinkage in the composite with the possibility of marginal gaps in restorations.

Gaps and/or tooth distortion still represent quite common negative effects of composite polymerization and are related to nanoleakage and breakdown of restoration till today. This is because conversion is accomplished by replacing the van der Waals spaces in monomers by covalent bonds in polymer and consequently, by a reduction of the free volume of the composite. In addition, the so-called C-factor and compliance of the dental substrate may be considered in the amount of the final polymerization stress. One other cause of degradation connected to the conversion process is the presence of condensation type bonds within the resin. Condensation bonds, which include esters, urethanes and amides, are predominantly found in the di-vinyl monomers and are all prone to chemical hydrolysis catalysed by acids, bases or enzymes.

Different methods have been proposed to reduce shrinkage. Among them, a variety of techniques of cavity filling, such as incremental placement of the composite, the soft-start curing technique and the use of stress absorbing cavity liners. Moreover, modification in composite composition has been studied with the intention of reducing stress. As polymerization shrinkage can be considered indirectly related to the concentration of loaded filler, the mass of filler particles has reached a range of 60–80% of the weight, becoming the major agent of the resin.

Fillers are usually inorganic particles and confer to the composite mechanical properties such as compressive strength and modulus of elasticity. In addition, fillers lower water absorption and the thermal expansion coefficient of composite.

Moreover, a variety of nanomaterials have attracted attention as fillers. Nanomaterials have advantages in higher reduction of the rate of wear, polymerization shrinkage in comparison with traditional fillers.
to traditional fillers, at the same time improving mechanical properties of the composite restoration [42]. The increase in efficiency by the use of nanoparticles has been related to the high specific surface area and richness of functional groups [42].

![Figure 6](image)

Recent studies have been conducted on nanocomposites using calcium-phosphate and calcium-fluoride nanoparticles [43]. Also, amorphous calcium phosphate particles of 116 μm were incorporated into composites. An advantage of the addition of calcium-phosphate particles is the release of supersaturating levels of calcium and phosphate ions at acidic pH with remineralization of initial tooth lesions. More recently, a quaternary ammonium dimethacrylate was incorporated into the calcium-phosphate nanocomposite combining remineralizing with antibacterial properties in the same material [44].

Moreover, nanofibers have become popular as fillers because of the increase in stiffness of composite due to both the high surface area and high aspect ratio of nanofibers. Studies [45] reported that zirconia-silica or zirconia-ytria-silica ceramic nanofibres, as well as hydroxyapatite (HAP) nanofibres [46], are able to improve mechanical properties and fracture toughness of composites. In addition, the associated overlapping of the fibres lowers polymerization shrinkage [47].

More recently, the incorporation of pre-polymerized resin fillers (organic fillers) has been proposed with the advantage of decreasing the volume fraction of the polymerizable resin, at the same time allowing the addition of increased filler volume fraction [48].

2.3. Adhesion techniques

2.3.1. Smear layer

Cutting teeth creates a layer of smear debris, which completely covers the surfaces of the enamel and dentine (49) and plugs the orifices of the dentinal tubules.
Using transmission electron microscope (TEM) and micro-RAMAN spectroscopy, the smear layer was described as a fibrous layer, composed of well-arranged and undisrupted collagen fibrils [49] that because of the inherent weakness can interfere with good adhesion [50].

So, adhesive systems have to interact with the smear to establish high bond strength in teeth (Figure 7). In fact, when the smear was removed by etching there was better adhesion performance [51]. However, the manner of smear creation might be directly related to interferences in bonding [52].

**Figure 7. (A)** A TEM photomicrograph of a dentine surface covered by a porous, amorphous smear layer. The tubule at the front of the dentine is smear plugged. (B) A demineralized TEM image of the hybrid layer formed by an Etch&Rinse adhesive (OptiBond Solo, Kerr Corporation, Orange, CA, USA). In this case, the hybrid layer is completely deprived of the smear layer because of the etching procedure of the Etch&Rinse. The hybrid layer appears as a dense resin micro-infiltration into the totally demineralized collagen, also showing micro-mechanical interlocking in tubules by long resin tags. (C) A demineralized TEM image of the hybrid layer created using a mild self-etching adhesive (Clearfil Protect Bond, Kurary, Osaka, Japan). In this case, the smear layer is included in the uppermost part of this hybrid layer, which is formed by resin infiltration of the water rich channels of the smear reaching the partially demineralized superficial dentine. Short resin tags are present into the tubules by percolation of the smear plug at the orifice. The self-etching hybrid layer in (C) is a dentine resin interaction of approximately 1.5 μm of thickness (between black arrows) and is less deeper than that formed by the Etch&Rinse adhesive in (B), which is about 4.5 μm depth (between black arrows). HL = hybrid layer; T = tubule; RT = resin tag; UD = unaltered dentine.

It was observed that the way smear layer was created has an influence on the thickness, density and attachment of the smear layer to the underlying tissue [53], while composition strongly indicates the characteristics of the tissue and type of cut through which the smear derived [54].

The composition of the smear layer influences the capacity of the etching to dissolve it. This has been justified by the presence of the highly disorganized collagen component of the smear that traps minerals causing a permanence of smear layer on the cavity floor even when acid-etching was used by ERAs [55]. Moreover, a greater quantity of residue, compared with the etched sound dentine, may persist on the surface of carious affected dentine (CAD) in a form of ‘collagen smear layer’ because acids only solubilize the mineral component of the layer [56]. Leaving this collagen smear layer at the bottom cavity, homogeneous infiltration of the monomers in the underlying dentine may be impeded, affecting the quality of bonding, which finally derives from the homogeneity of strengthening in the demineralized dentine [54, 57]. Poor infiltration of demineralized collagen can lead to hydrolysis due to activation of the MMP’s over time [58].

Furthermore, the smear layer might adversely affect homogeneity of hybridization when SEAs are used. SEAs hybrid layer is created by infiltration of the water-rich channels of the
smear layer reaching the underline partially demineralized dentine. This means that the smear is included in the hybrid interdiffusion of SEAs [59]. However, in the case of thick smear layers, superficial demineralization and reinforcement of dentinal collagen might be compromised through early neutralization of the acidic primers of SEAs by the dentine buffering components of the smear [53].

Still, as far as we are currently aware, smear layer interferences remain a controversial issue irrespective of the adhesive techniques [60]. Some studies reported low dentine bond strengths over thick dentin smear layers, [52, 61], while others reported no influence on strength [33, 62], even if using mild SEAs [63], particularly in the early bond strength values [64].

2.3.1.1. ERA bonding

The fundamental processes involved in bonding enamel and dentine using ERAs include the removal of the mineral phase from the substrates without altering the collagen matrix in dentine. The hybrid layer results by filling the voids left by minerals using adhesive monomers that undergo complete in situ polymerization resulting in a tight adhesive interface.

Therefore, bonding by ERAs consists of a first phase of acid etching followed by the rinsing of the acid and then the infiltration of adhesive monomers in the demineralized tissue. The resulting hybrid layer is defined as a sort of dental tissue engineering formed by a mixture of inorganic resin monomers and organic demineralized dental tissue with resin tags in the dentinal tubules [56, 65, 66] (Figure 8). This chemical and micromechanical bonding has the role to seal the surface from leakages of fluids and bacteria [67].

Figure 8. (A) An SEM image of an enamel surface, in which prisms are covered with a smear layer. (B) After the acid-etching procedure, the SEM shows dissolution of the smear layer and of the prism core with residual micro-craters and also of the interprismatic enamel border in a geometrical hexagonal ring (honeycomb appearance). (C) A non-deminer-alized TEM ultrathin section of the hybrid layer in enamel formed by the penetration of a low-viscosity BisGMA resin into the etched prisms. (D) A demineralized TEM section of a dentine surface covered by a smear. (E) An SEM image of acid-etched dentine, which appears completely deprived of the smear layer exposing the intertubular collagen matrix with nanometre-sized porosity and opened tubular apertures. (G) A demineralized TEM image of the fully diffusion of adhesive monomers into the completely demineralized collagen, which leads to the formation of a hybrid layer in which the composite will be able to adhere.
Phosphoric acid treatment completely exposes the enamel morphology of the prisms and interprismatic substance typically creating a honeycomb porosity that can be penetrated by low-viscosity resins by capillary attraction [68]. After polymerization, a durable attachment of the monomers in the enamel is achieved with the evidence of resin enveloping the prisms rendering them acid-resistant (Figure 8).

In dentine, phosphoric treatment exposes the 5–8 μm of the dentinal floor constituted by tubules and intertubular collagen matrix creating a nanometre-sized porosity within the matrix and opens the tubular orifices. In this way, the acid permits infiltration of monomers into and around collagen fibrils and tubular resin tags, gaining the following retention for the composite filling (Figure 8).

However, many problems have been claimed as a result of acid-etching dentine. Firstly, etching dentine may result in too much demineralization compared with the concentration gradient of monomer infiltration with poor resin infiltration and discrepancies in reinforcement at the bottom of hybrid layer [54, 69].

Secondly, removing smear layer and smear plug from the dentine surface, etching increases tubular permeability causing outwards of pulpal fluids into the cavity [54].

Additional factors may interfere with the tight bond using etching when the cavity floor includes the very wet tissue of CAD. The soft, already demineralized collagen [71], the high degree of porosity and wetness [72], a lack of minerals around and within the fibrils [73], as well as spectral changes in the secondary structure of the collagen [49], may cause much aggressive etching in CAD [74]. At the same time, the use of strong acid cannot dissolve intratubular minerals, thus affecting infiltration of monomers and tubular tag formations [72]. Moreover, the low buffer of the tubular minerals may allow high demineralization and increase wetness in peritubular dentine with porosities in interdiffusion [15]. These facts result in a susceptibility of the affected interface to acid and base treatments, with higher degradation of CAD hybrid layers in comparison with sound dentine [75, 76].

Other adverse effects of etching dentine are related to the water-rinsing phase. In fact, the solubilized mineral is replaced by water rinsing, which results in an increase of the global amount of wetness in dentine. This wet dentine has difficulty to be tightly reinforced by the hydrophobic adhesive monomers even if resin tags can be formed in the opened tubules.

It has been shown that water is helpful in keeping the demineralized interfibrillar channels physically expanded allowing monomer percolation [56]. However, at the same time, water may produce (1) a lower degree of resin monomer conversion [49, 77]; (2) interference with the reinforcement of the hydrophobic BisGMA adhesives [15]; (3) phase separations between the hydrophobic and hydrophilic components of adhesives [78]. All of these may result in non-homogeneity and porosities at the interface as an expression of sub-optimal sealing [79–81].

To reduce interference by water, evaporation of the water rinsing in dentine is suggested using air-drying [56]. However, air-drying technique may shrink the demineralized collagen, and narrowing the interfibrillar channels [82] may impede infiltration by the monomers. In this
event, bond strength would be limited to the strength of surface adhesion [56], leaving behind exposed and non-infiltrated fibrils.

This incomplete infiltration appears as voids or microporosity underneath and within the hybrid layer, which have been described through percolation of silver nitrate as nanoleakages [83] and pathway for hydrolytic and enzymatic degradation of the hybrid layer [84–86].

To increase the capacity of the monomers to re-expand the collapsed collagen network, studies evaluated the solubility parameters of chemicals with the intention of breaking collagen inter-peptide hydrogen bonds and then, the stiffened and collapsed state collagen [87]. Interactions were studied using the Hoy’s solubility parameters [88], which provide estimation of the relative contribution of dispersion forces, polar forces and hydrogen-bonding forces to the overall cohesive forces that hold the polymers together. As a result, water and ethanol solvents were suggested to break the inter-peptide hydrogen bonds of the collagen, allowing the softening and expanding of the network in a rapid way [87]. These solvents have been generally blended with HEMA [89].

2.3.1.2. SEA bonding

Avoiding the separate etching phase of ERAs, SEAs seemed to be a good alternative to the problems related with.

SEAs are differentiated in view of the step needed to the hybrid layer formation. In the ‘Two Step SEAs’, hybridization is formed in two different procedures, the first of which is the layering of a primer of different acidity, followed by the application of an adhesive resin, usually BisGMA based. In the ‘One-Step SEAs’, acidic and adhesive monomers are mixed in the same solution, thereby causing hybridization at the same time.

Characteristics of SEAs are the acidic functional monomers in their formulation, which are demineralizing and infiltrating agents at the same time. Specifically, functional monomers have the capacity to interact with HAP and collagen by a series of chemical atomic-level interactions with an advantage of tissue strength. In dentine, these nano-interactions differ from a few hundreds of nanometres in the case of an ultramild self-etching (pH ≥ 2) to one micrometer in the case of a mild (pH ≥ 2) (Figure 9) and between one and two nanometres depth in the case of a strong-self-etching (pH around 1) [26, 90]. However, the resulting bond strength has been inversely related to the pH acidity. The interaction of 10-MDP, mild functional monomer (pH ≥ 2), has shown higher bonding and longevity compared to the strong 4-methacryloxyethyl trimellitic acid (4-MET) and phenyl-P [91, 92]. This is true despite the strong acidity producing a more retentive enamel etching (Figure 10) in comparison to the milder and the resulting hybrid layer is deeper than that of the mild monomer. Also, the retention of unstable calcium-phosphate salts makes the strong SEAs hybrid layer susceptible to hydrolysis [92, 93]. Furthermore, due to the great dissolution of calcium phosphate in intertubular dentine [56, 90, 91], a greater increase in wetness and porosity has to be considered in dentinal collagen, which has difficulty being infiltrated by hydrophobic BigGMA resins [63, 94].
Figure 9. (A) A SEM micrograph of an enamel transversal section obtained by fracture after application of the primer of a two-step, mild-etching system adhesive system (Clearfil SE Bond, Kuraray, Osaka, Japan). This acidic priming is 10 MDP based and produces partial dissolution with infiltration of the core and boundaries of the prisms. (B) SEM section shows the infiltration of the interprismatic spaces in a longitudinal section with initial formation of tags between the prisms (arrow). (C) A non-decalcified TEM image, the application of the adhesive resin BisGMA based completes the hybrid layer in the enamel, which shows a nano-retentive appearance with hybridization of the inter- and intra-crystallite spaces of the prisms. (D) A demineralized TEM image of dentine priming using a 10 MDP primer. (D) A partial demineralization with infiltration of the collagen fibrils, which maintain dense transversal hydroxyapatite banding (arrow). (E) An SEM image, a preliminary tubular tag formation can be observed after priming (arrow). The application of the hydrophobic BisGMA adhesive resin in (F), a demineralized TEM image, completes the formation of the hybrid layer in dentine, which in the uppermost part includes hybridized smear layer residues. The dense appearance of the interdiffusion demonstrates the richness in chemical interactions with hydroxyapatite, which increases bonding of highly insoluble calcium salts. HL = hybrid layer.

Figure 10. SEM images of the enamel-etching pattern obtained using four self-etchings of different pH acidity. (A) A phenyl-P-based primer, pH 0.5, (Resulcin AquaPrime, Merz Dental, Lütjenburg, Germany), which strongly etches the enamel prisms and interprismatic spaces in a similar way to phosphoric acid. (B) Modified methacrylates, phosphoric acid ester primer, pH 1.3 (Artegal One, Merz Dental GmbH, Eetzweg, Lütjenburg), the etching of which produces a geometrical pattern of enamel with shallow, crater-like depressions of the prisms and a less visible boundary wall appearance. (C) The enamel etching of a 10 MDP-based primer, pH 2.8 (Clearfil Protect Bond, Kuraray, Osaka, Japan); and (D) The etch produced by a 10-MDP-based one-step self-etching system, pH 2.7 (Clearfil S3 Bond, Kuraray, Osaka, Japan) both leading to a regular pattern of etching with a microporous appearance of the inter- and intraprismatic surfaces.
However, the mild acidity of MDP causes a regularly layered structure on enamel and dentine, which is rich in chemical interactions with HAP and in highly insoluble calcium salts \([63, 94]\). Also, the stability of the 10 MDP hybrid layer in the oral environment is increased by the presence of the hydrophobic spacer carbon chain that prevents water sorption and degradation of the interface \([20]\).

For this reason, 10 MDP mild SEAs have been suggested as the better bonding technology in dentistry particularly in the case of CAD.

In fact, using mild SEAs the residual HAP crystals in CAD will remain attached around the already demineralized collagen, thus allowing remineralization and at the same time, preventing discrepancies in the reinforcement (Figure 11) \([58, 71, 81, 94–98]\). In addition, the mineral deposits in CAD tubules cannot be dissolved without a high pH level of SEAs \([56, 99]\) and thus resin tags cannot be an advantage to the CAD hybrid layer, neither in the case of mild nor using strong SEAs \([2]\).

**Figure 11.** (A) The clinical appearance of a bottom cavity including the dark, yellow tissue of caries affected dentine (arrow). (B) A demineralized TEM image of a mineral occluded tubule also contains mineralized, residual bacteria (arrow) and (C) The TEM aspect of the partially demineralized fibrils of caries affected dentine with lose transversal banding (arrow). (D) A non-decalcified TEM image shows the hybrid layer in caries affected dentine formed by the use of an Etch&Rinse adhesive (OptiBond Solo, Kerr Corporation, Orange, CA, USA). Despite the use of a strong etching, tubular mineral occlusions cannot be dissolved (arrow) and complete resin tags cannot reinforce the hybrid layer of the Etch&Rinse adhesives. In (E, F and G), there are different decalcified TEM magnifications of the hybrid interface created using a mild self-etching adhesive (Clearfil Protect Bond, Kuraray, Osaka, Japan) in affected dentine. Leaving crystals in and around the already demineralized collagen of caries affected dentine, 10 MDP functional monomer has the ability to interact with the residual hydroxyapatite with a series of chemical atomic-level interactions forming a strong chemical bond. (F) The magnified hybrid layer (between arrows) shows an irregular top of infiltrated smear layer plugging the tubular orifices, which still retain mineral occlusions. Nevertheless, hybridization of peritubular dentine is clearly discernible (asterisk). (G) A higher magnification of (F) shows attached, resin infiltrated hydroxyapatite crystals around the collagen of affected dentine (circle). This fact can prevent the affected fibrils from being exposed and hydrolysed in environmental fluids. MT = mineralized tubule; CAM = caries affected matrix; HL = hybrid layer.

Moreover, the use of mild SEAs in CAD leads to the evidence of an inhibitory effect on secondary caries \([95]\). Morphologically, an electron dense zone was described underlining the hybrid layer created by 10-MDP containing SEAs after exposure to an artificial demineralizing solution (pH 4.5) for 90 mins and then 5% sodium hypochlorite for 20 mins. This ‘acid-base
resistant layer” [95] was attributed to densely packed crystallites, which were probably formed by resin-infiltrated dentine. The observation accredited the chemical reactions that might take place between HAP and 10 MDP in dentine, which have the capacity of increasing the resistance to acid attacks of oral bacteria and, consequently, secondary caries.

As regards the use of one-step SEAs, they are complex mixtures of hydrophilic and hydrophobic components, which lead to acidification, priming and bonding in a same time. These systems result in very thin hybrid layers, which are prone to less polymerization [100] and high permeation by fluids [28, 101, 102] (Figure 12). The incorporation of high concentrations of hydrophilic HEMA monomers [101, 102] explains absorption of water from the dentin fluids towards the interface [103–105]. Particularly, water permeability is enhanced in the case of which the composite interface would not have been immediately polymerized [106].

![Figure 12](image.jpg)

Figure 12. (A and B) Demineralized TEM sections of the very thin hybrid layer (between arrows) formed by a one-step self-etching system (Clearfil S3 Bond, Kurary, Osaka, Japan). In this case, samples were prepared in in vivo conditions of pulpal pressure and were extracted 10 min after completion. The hybrid layer shows a high hydrophilic HEMA appearance and exhibits water channels (white arrow) and porosities within the interface and voids in the tubule, which are a result of the poorly sealed tubules using these HEMA-rich, one-step self-etching adhesive systems. HL = hybrid layer; T = tubule; V = void.

In vitro studies [106] reported that the tubular occlusion in CAD might block the permeation of water fluids in the one-step hybrid layer. However, in clinical conditions of pulpal pressure, OSA’s hybrid interdiffusion in CAD has been shown to be permeable [15]. Thus, it is not surprise that these hybrid layers are likely to be the cause of high hydrolysis [103, 107] and changes in their formulation have been proposed to overcome the problem. Hydrolytically resistant acrylamide-based monomers have been added in the complex mixture of One-steps promising better performance [67]. However, clinical evaluations reported inferior performance using acrylamide-based adhesives in comparison with those obtained in laboratory tests [108].

2.3.1.3. Degradation of adhesive restorations

Nowadays, the reasons for adhesive failure are of two kinds: (1) failures which originate from the surface of the hybrid layer and the upper polymerizing composite restoration; and (2)
failures that take place in the depths of the hybrid layer, in which it interlocks chemically and micromechanically to the tooth tissues.

Failures related to the upper surface of the hybrid layer and to the surface of composite have been mainly correlated to microleakage of salivary fluids and proteins [109, 110]. Also, these failures have been connected to the high susceptibility of BisGMA-containing resins to accumulate dental plaque, which degrades resins as a result of the biofilm of cariogenic bacteria (Finer et al 2004).

Adhesive resins permitted infiltration of salivary fluids and proteins, mainly in the case of poor polymerization. Also, water fluids may be trapped in resins during the curing process. Biological breakdown is due to the addition of water to condensation type bonds within the resin [111]. These bonds, which include esters, urethanes and amides, are all prone to chemical hydrolysis, catalysed by acids, bases or enzymes.

Particularly, hydrolysis of the hybrid layer is linked to the addition of water to the ester bonds of the methacrylate polymer matrix [12]. Water breaks the covalent bonds in ester bonds with production of carboxylic acids, the same functional group that causes demineralization in the presence of lactic acid. Moreover, percolation of water fluids into the hybrid layer promotes the leaching of adhesive components, which have infiltrated the collagen matrix. This reaction is accelerated in pH excursions, which cause an increase of transient acid or base catalysis. Over time, hydrolytic degradation exposes susceptible bonds located deeper within the matrix, as well as allowing the infiltration of salivary enzymes, among which esterase is the most important class which are able to alter the stability of resins in the oral environment [21].

In composites, the main cause of degradation is the gap, which is a result of polymerization shrinkage. When salivary fluids and proteins diffuse into the polymer matrix, this causes a reduction of the glass-transition temperature, polymer plasticization and a decrease in thermal stability [112]. Resin undergoes hydrothermal degradation, hydrolysis and leaching of ions, which ultimately leads to surface softening and mechanical wear during mastication. Additionally, the ion leaching may directly cause permeation of water molecules into the spaces previously occupied by these ions [112–114].

A progressive deterioration of the resin mass permits the leakage of biofilm bacteria, which grow on the surface of composite. In particular, S. mutans has an accelerated growth on composites, which may be due to the leaching out of unreacted monomers or due to the physical property of surface roughness [6, 115]. Esterase activities of S. mutans are able to catalyse enzymatic hydrolysis of the polymer. Moreover, when sucrose from foodstuff is present, adhesion of S. mutans causes the formation of insoluble glucans [116] leading to intense local acidification and chemical hydrolysis [18].

Modification of the resin composition has been examined in an effort to prevent attachment of bacteria to the polymer surface. Quaternary ammonium compounds have demonstrated antibacterial properties and have been incorporated into methacrylate polymers for this purpose [117].
2.4. Activation of MMPs

Failures taking place at the bottom surface of the hybrid layer are related to hydrolytic activity by host-derived proteases. More specifically, MMPs are endopeptidases normally present in human saliva and capable of degrading extracellular matrix proteins [79].

MMPs are a family group of multi-domain calcium- and zinc-dependent endopeptidases that participate in physiological tissue development, remodelling of dentine matrices and remain entrapped in the dentin matrix during tooth development [118–120]. MMPs require metal ions such as calcium or zinc to bind to the active site for their catalytic activation through a so-called cysteine switch [13]. Moreover, MMPs need an acid micro-environment to become active [121, 122]. Activity has been documented during the carious process, in which MMPs digest carious collagen after having been activated by lactate released by the cariogenic bacteria. Furthermore, host-derived hydrolases can degrade sub-optimally infiltrated collagen fibres once they have been activated during bonding procedures.

In fact, it has been reported that acidic priming may induce the necessary low pH micro-environment capable of altering the conformation of the pro-peptide in the active form [119, 120]. More recently, it has been suggested that MMPs may become activated at the tooth and restoration interface by bacterial acid production [80]. In these situations, exposed and not protected collagen of chemical polymers from both the ERA and SEA systems might be degraded by MMPs.

Water is essential for the hydrolytic function of the enzymes because of the hydrolysis of peptide bonds in collagen, resulting in degradation of the polymer. [123]. The importance of water was accredited by experimentations showing no loss of dentine bonding over time when mineral oil was used as a storage medium instead of water [107].

MMP inhibitors have been suggested to treat dentine after acid priming. Among these (1) calcium and zinc chelators from acid-etched dentine, as the presence of calcium and zinc ions is necessary for MMPs to became activated [124, 125]; (2) protein cross-linking agents to cross-link their peptide chains immediately after acid etching [126]; (3) specific and nonspecific inhibitors of proteases added directly to primers [119, 126–129].

Furthermore, the use of the ethanol-wet bonding technique can be useful for preventing hydrolysis [129, 130]. Ethanol acts as a solvated primer to dehydrate the demineralize collagen allowing fibrils to be densely infiltrated by resin, keeping them free of water uptake.

Also, the application of chlorhexidine to acid-etched human dentin can save the collagen fibrils in the hybrid layer when etching and rinsing are used [131]. The addition of chlorhexidine as a primer in ERAs increases the capacity to maintain the structural integrity of the collagen probably by its zinc cation-chelating property [131]. However, it is necessary to define whether its effect is adhesive system specific. In fact, this is dependent upon the composition of the applied adhesive resin and generally results in a statistically significant decrease in the degree of conversion.
3. Conclusions

Despite the great evolution, dental adhesive restorations need to be improved in an effort to obtain stable restorations within the oral environment.

Even if, enamel etching by ERAs can represent the gold standard in enamel bond strength, at the same time, etching dentine may leave exposed and non-reinforced fibrils with all the consequences related to.

The MDP technology of mild SEAs has been suggested as the better bonding technology due to the capacity of increasing the resistance to biological breakdown of adhesion.

However, modification of the resin materials is necessary to antagonize infiltration of salivary fluids and proteins, which are the causes of hydrolysis, particularly by the esterase activities of S. mutans and by MMPs.

Author details

Egle Milia*, Roberto Pinna¹, Enrica Filigheddu¹ and Stefano Eramo²

*Address all correspondence to: emilia@uniss.it

1 Department of Biomedical Science, University of Sassari, Sassari, Italy

2 Department of Surgery and Biomedical Science, University of Perugia, Perugia, Italy

References


[17] Van Krevelen DW, Te Nijenhuis K. Properties of polymers: their correlation with chemical structure; their numerical estimation and prediction from additive group contributions. Amsterdam: Elsevier; 2009.


[34] Nie J, Bowman CN. Synthesis and photopolymerization of N,N'-dimethyl-N,N'-di(methacryloxy ethyl)-1,6-hexanediamine as a polymerizable amine coinitiator for dental restorations. Biomaterials. 2002;23:1221–1226.


