AdheSE® / AdheSE® Activator

Scientific Documentation

ivoclar vivadent

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1. Introduction

At the beginning of the 1990s, the adhesive technique opened up new perspectives in dentistry. Since this technique allows restorative materials to be bonded to the remaining tooth structure, it is no longer necessary to prepare surfaces for mechanical retention (Leinfelder, 1996). Consequently, healthy tooth structure can be preserved. Some of the pioneering products, such as Syntac, are still considered to be among the clinically most successful adhesive systems (Folwaczny *et al.*, 2000; Mazer *et al.*, 1994; Pröbster *et al.*, 1996). The clinical success of these multiple-bottle adhesives can be attributed to the fact that they take into account the requirements of the different bonding substrates, *i.e.*, enamel and dentin. The requirements that a dentin adhesive must fulfil are recapitulated below:

- To achieve an etching pattern in the enamel and expose the dentin tubules and collagen, hydroxyapatite must be removed by etching. An aqueous acid is used for this purpose.
- Etched enamel can be dried. Therefore, it can be directly wetted using a hydrophobic bonding agent.
- Conditioned dentin is hydrophilic and moist. Consequently, a bond between a hydrophilic substrate and hydrophobic composite material must be achieved.

For research chemists, therefore, it is easier to develop a product that comprises several components, which are sequentially applied to establish a bond between the tooth and the composite, rather than a product that is made up of only one or two components. Table 1 shows the different “tasks” of the components of multi-bottle bonding systems (Syntac) and one-bottle total etch adhesives (Excite). Nevertheless, adhesives featuring fewer bottles and application steps have been developed in response to the demand of dental professionals for

- a reduced number of components;
- a reduced number of working steps;
- faster application procedures.

The efforts to develop bonding systems using a reduced number of components have proceeded in two directions. Many products combine the function of the primer and the bonding agent in one component. These products are known as one-bottle adhesives and are used with the total etch technique. Unfortunately, these streamlined products are not as easy to use as they were intended to be. The following problems may arise when using a one-bottle adhesive.

- Dentin may be etched too deeply. If this is the case, the exposed collagen will not be infiltrated with adhesive throughout the demineralized layer.
- Dentin may be excessively dried. The exposed collagen collapses and hinders the penetration of the adhesive into the dentin tubules and the collagen network.
- If the dentin is too moist, the adhesive may become diluted with water.
- The adhesive may be dispersed with too much air pressure, leaving a very thin layer, which cannot be polymerized because of oxygen inhibition.

In the meantime, these one-bottle adhesives have become known as being technique sensitive (Frankenberger *et al.*, 2000). The discussions about how moist dentin should be are familiar to everyone (Gwinnett, 1992). Undoubtedly, these one-bottle adhesives can achieve equally successful results as multi-bottle systems if they are used precisely as directed. Nevertheless, multi-bottle systems are more tolerant of application errors than one-bottle adhesives. Thus, the dental profession has great expectations for adhesive systems that no longer involve phosphoric acid etching.

The second approach has been to reduce the number of bottles and combine the conditioning and wetting agents in what are known as self-etching primers. Our new product AdhesSE has been developed along these lines.

Working step	Task of the step	Syntac	Excite	AdheSE
Enamel conditioning	Exposure of the retentive etching pattern	H_3PO_4	H_3PO_4	AdheSE Primer
Dentin conditioning	Exposure of the collagen network and dentin tubules	Syntac Primer	H_3PO_4	
Wetting	Transition between hydrophilic and hydrophobic tooth structure	Syntac Adhesive	Excite	
Bonding	Bond to the composite	Heliobond		AdheSE Bond

1.1 Fundamentals of primers

Dentin contains 25 vol% water (Schroeder, 1991). Therefore, it is moist as well as hydrophilic. Hence, the primer must contain hydrophilic polymerizable components, which will thoroughly wet this substrate. Self-etching primers must have a low pH and contain enough acid to dissolve the smear layer as well as superficial enamel and dentin mineral.

At the same time, it should be possible to polymerize the monomers of the primer together with the bonding component to allow a firm resin layer to infiltrate into the exposed dentinal collagen. This function can only be successfully fulfilled if the primer also contains a cross-linking monomer that is adequately hydrophilic so that it dissolves in water, but hydrophobic enough to enable it to bond with the more hydrophobic adhesive.

1.2 Challenges for the research chemist

In the development of a self-etching primer, chemists are faced with a considerable problem of a fundamental nature. To dissolve the smear layer and expose the retentive enamel pattern as well as the dentinal collagen, hydroxyapatite has to be removed by etching. A strong water-based acid has to be used for this purpose. Under these chemical conditions, however, most monomers are unstable. Phosphoric acid ester and methacrylic acid ester compounds in particular can by hydrolized by aqueous solutions with an acid pH value (Moszner *et al.*, 2001).

Most of the manufacturers of self-etching adhesives have managed to circumvent this problem in two different ways:

- The acid monomers of the primer and water are mixed just before they are used.
- The product has to be refrigerated to retard hydrolysis.

Clearly, this problem can only be solved if adhesive monomers that retain their hydrolytic stability in conjunction with highly acidic pH values are used. This type of composition would eliminate the necessity of having to mix two components and ensure that the quality of the material remains unchanged, even if it is not transported or stored correctly on its way from the manufacturer to the customer.

1.3 Hydrolytically stable monomers from Ivoclar Vivadent

Most manufacturers use what are known as phosphoric acid ester compounds as the acid monomer. Such compounds, however, have one drawback: The C-O-P bond is not hydrolytically stable (Fig 1). Ivoclar Vivadent has been developing and patenting hydrolytically stable monomers for some time. A phosphonic acid compound, for example, was used as the acid monomer for the first time ever in the one-bottle adhesive Excite. This compound is decidedly more stable, as the phosphorous atom directly bonds with a carbon atom (C-P) (Fig 1).

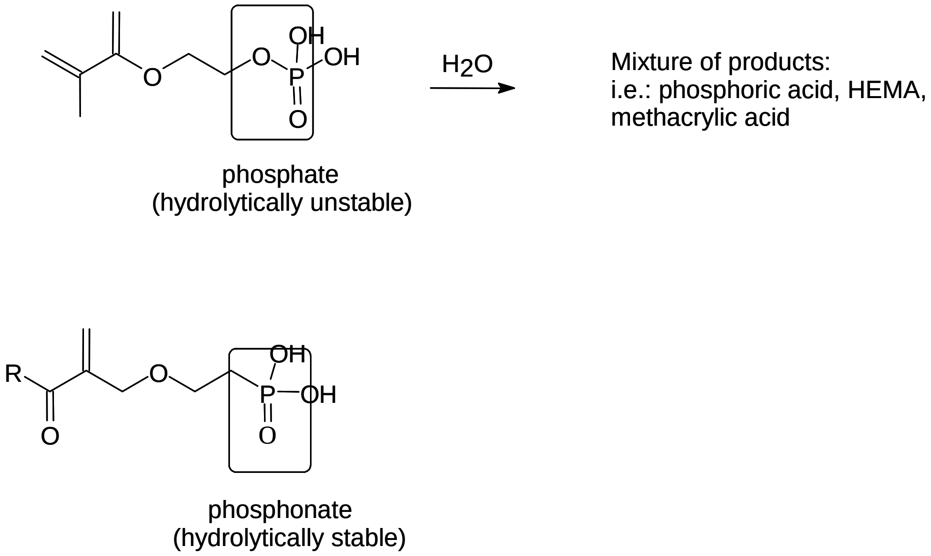


Figure 1: Structural formula of phosphonic acid acrylate (adhesive monomer in Excite) compared with that of a phosphoric acid ester compound.

In most monomers used for resin-based dental materials, the methacrylate group is attached to the rest of the molecule by an ester bond. This bond is also not hydrolytically stable. If monomers such as these are used in highly acid primers, they slowly decompose, releasing methacrylic acid (Fig 2).

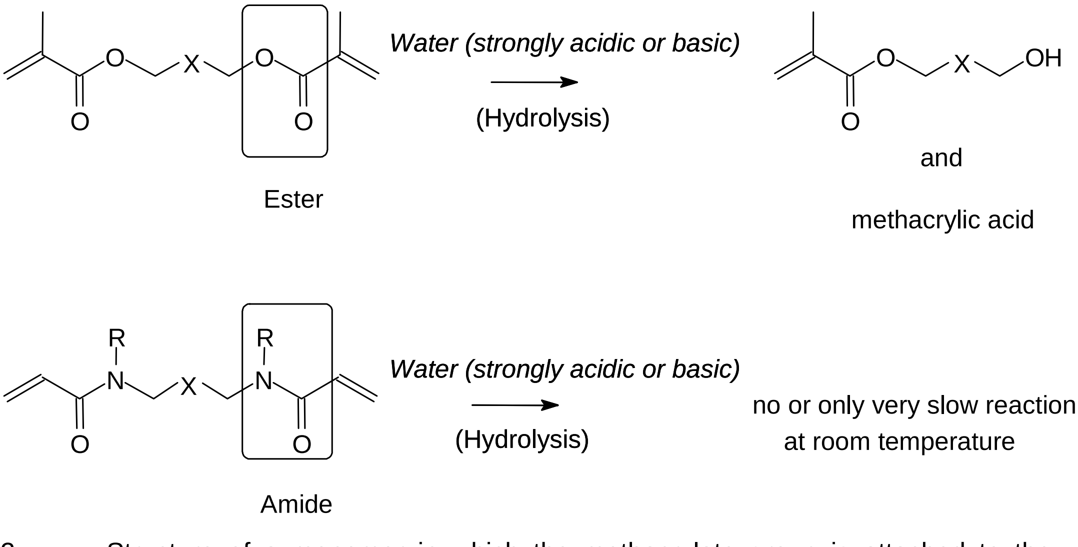


Figure 2: Structure of a monomer in which the methacrylate group is attached to the hydrocarbon structure with an ester bond and the hydrolytically stable bis-acrylamide compound, which is used in AdheSE.

Therefore, Ivoclar Vivadent has consistently pursued the goal of developing hydrolytically stable monomers for dental materials. The current result of this endeavour is a bis-acrylamide compound (Fig 2) that dissolves in water as well as in organic solvents. This type of monomer is ideal for the primer of dentin adhesives. Figure 3 shows the results of a study in which the hydrolytic stability of triethylene glycol dimethacrylate (TEGDMA), glycerol dimethacrylate (GDMA) and the new bis-acrylamide was examined in two experimental primer formulations.

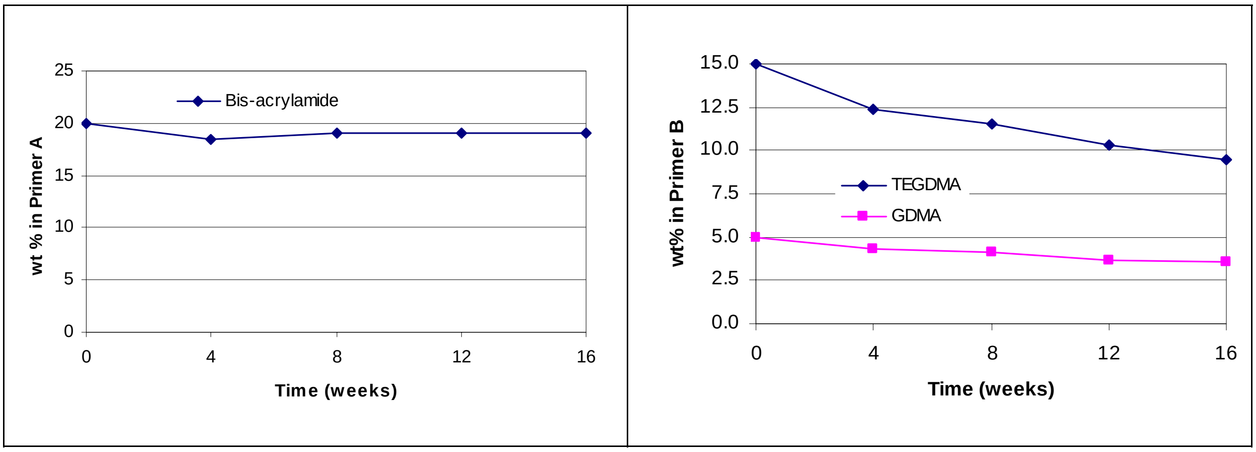


Figure 3: Two experimental self-etching primers were fabricated. Primer A contains 40% phosphonic acid acrylate, 20% bis-acrylamide and 40% water, while Primer B contains 30% phosphonic acid acrylate, 15% triethyleneglycol dimethacrylate (TEGDMA), 5% glycerine dimethacrylate, hydroxyethyl methacrylate and water. The primers were stored at room temperature (23°C). The dimethacrylate content was measured at base line and after 4, 8, 12 and 16 weeks.

Investigated by R&D Ivoclar Vivadent, Schaan, Liechtenstein

These investigations show that the bis-acrylamide compound used in AdheSE Primer is hydrolytically stable at room temperature. By contrast, TEGDMA and GDMA had hydrolized to a large extent under these conditions after four months.

1.4 The product AdheSE

AdheSE is the new self-etching adhesive from Ivoclar Vivadent. It is composed of a primer and a bonding component which are successively applied. Subsequently, the adhesive is cured with light. AdheSE is indicated for use with direct light-curing composite restoratives.

1.5 AdheSE DC as variant for dual and self-curing cementation procedures

The bonding agent can be mixed with the activating liquid (AdheSE Activator), which has been developed especially for this purpose, in a 1:1 ratio. This liquid contains a solution of initiators for self-curing. After dispersing the solvent, the modified bonding agent cures on its own. This version can be used for all indirect applications in conjunction with self and dual-curing luting composites.

2. Technical data

<u>Standard composition</u>

<u>Primer</u>	Phosphonic acid acrylate
	Bis-acrylamide
	Water
	Initiators and stabilizers
<u>Bond</u>	Dimethacrylates
	Hydroxyethyl methacrylate
	Highly dispersed silicon dioxide
	Initiators and stabilizers
<u>Activator</u>	Solvent
	Initiators

<u>Physical properties:</u>

After light curing (of AdheSE):

Shearbondstrength on dentin	>20 N/mm²
Shearbondstrength on enamel	>20 N/mm²

After self-curing (of AdheSE and AdheSE Activator):

Shearbondstrength on dentin	>20 N/mm²
Shearbondstrength on enamel	>20 N/mm²

3. Investigation of the material (*in vitro*)

In vitro investigations form the basis for all materials tests during the development phase of a dental product. Naturally, thorough *in vitro* investigations are not capable of predicting clinical success. Nevertheless, they represent the most important instrument during the development phase for testing different formulations and optimizing them. It goes without saying that only once an adhesive has shown good performance *in vitro*, will it be clinically tested in humans.

In the development of dental adhesives, the adhesive strength of the material is of primary importance. Marginal quality tests are conducted with the most successful formulations. In most cases, extracted teeth are used for this purpose.

3.1 *In vitro* examination of application procedures

Not only the chemistry of the adhesive is important for achieving a sound bond between the tooth structure and a restorative material, but also the way in which the dentist applies the adhesive. Therefore, the manufacturer must provide accurate information about how the product must be used. This will help the operator to achieve optimal results.

As self-etching adhesives do not require the enamel to be conditioned with phosphoric acid, the correct application of the primer is immensely important to achieving a retentive etching pattern. For this purpose, various ways of applying the primer have been examined.

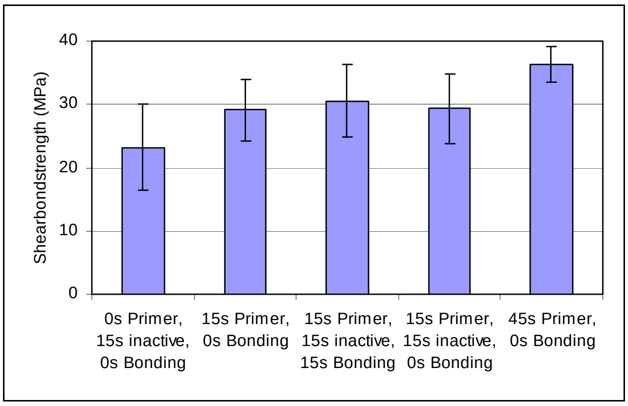
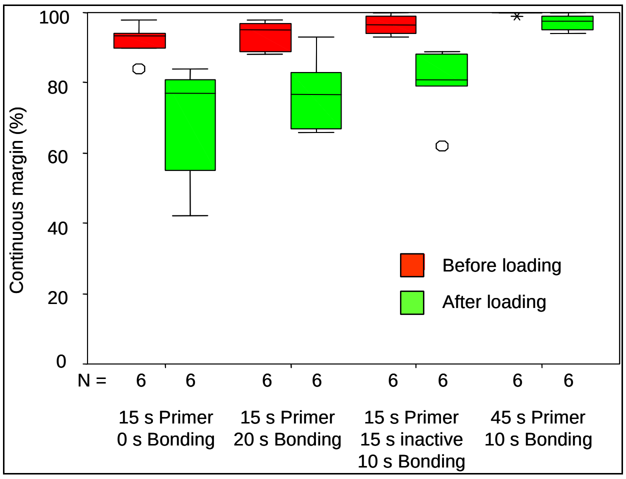


Figure 4:

Shearbondstrength and the quality of margins were examined as a function of the application procedure of AdheSE Primer and AdheSE Bond.

Dentin shearbondstrength was measured after 24 h immersion in water at 37°C.



The quality of the margins was determined at the enamel margin in Class V cavities. The restorations were immersed in water for 1 week at 37°C. The marginal quality was established on the basis of impressions examined under the electron microscope (before loading). After the restored teeth had been exposed to 640,000x occlusal load cycles and 1,500x thermocycles between 5 and 55°C, the quality of the margins was examined again on the basis of impressions (after loading).

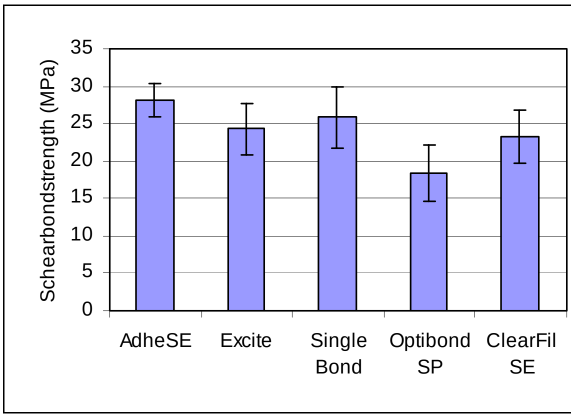
The shearbondstrength values on dentin and marginal results in enamel are shown as a function of the application of the primer and the bonding component in Figure 4. The following application methods were examined:

1. Apply AdheSE Primer as quickly as possible (0 s Primer), wait (inactive), apply AdheSE Bond as quickly as possible (0 s Bond) and light cure immediately
2. Apply AdheSE Primer for 15 s (15 s Primer),apply Bond and light cure
3. Apply AdheSE Primer for 15 s, wait 15 s and apply Bond and light cure
4. Apply AdheSE Primer for 45 s, apply Bond and light cure

The investigations of the shearbondstrength and the analysis of the margins indicate that the active application of the Primer for 15 seconds and a total reaction time of the Primer of 30 s are necessary to achieve optimal bond strength values and marginal quality. Longer application of the Primer has even been shown to improve the material's performance. By contrast, no significant difference was noted when the bonding component was immediately cured after its application or if another 10 s were allowed to elapse.

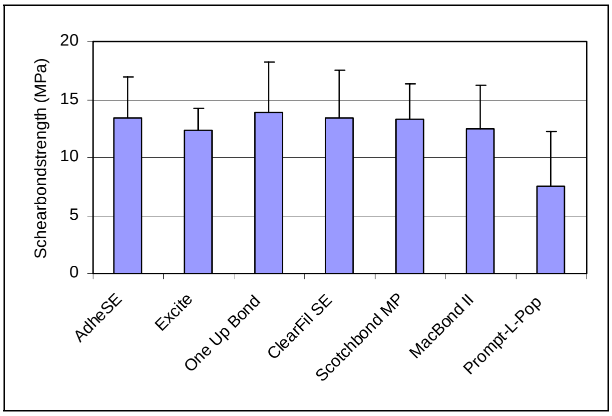
3.2 Shearbondstrength

In general, two test principles are applied in bond strength tests. In the shearbondstrength test, a composite test specimen that has been bonded to a substrate with the adhesive to be tested is sheared off parallel to the bonding surface. In the tensile strength test, the load is applied at a right angle to the bonding surface. Bond strength tests have been conducted with AdheSE at a number of test centres. The gathered data are summarized below:



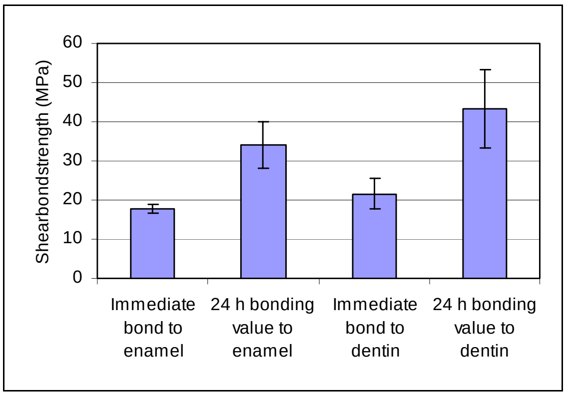
Shearbondstrength on dentin compared with competitive products

Head of study: Prof Dr Powers, University of Texas, USA



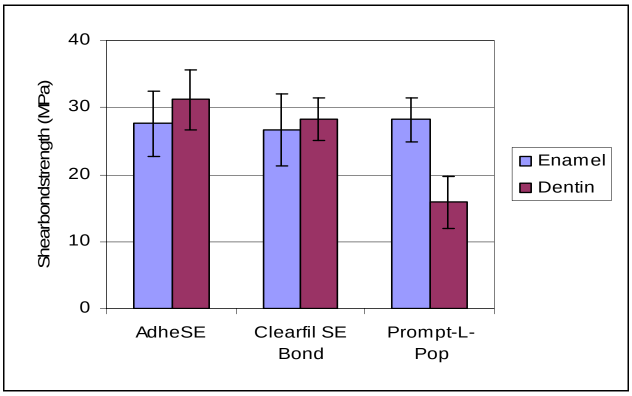
Shearbondstrength in a "one-bottle bond" test in which 55 practising dentists fabricated a total of 400 test specimens

Head of study: Prof Dr Degrange, University of Paris, France



Bonding values immediately after the fabrication of the test specimen and bond after 24 h.

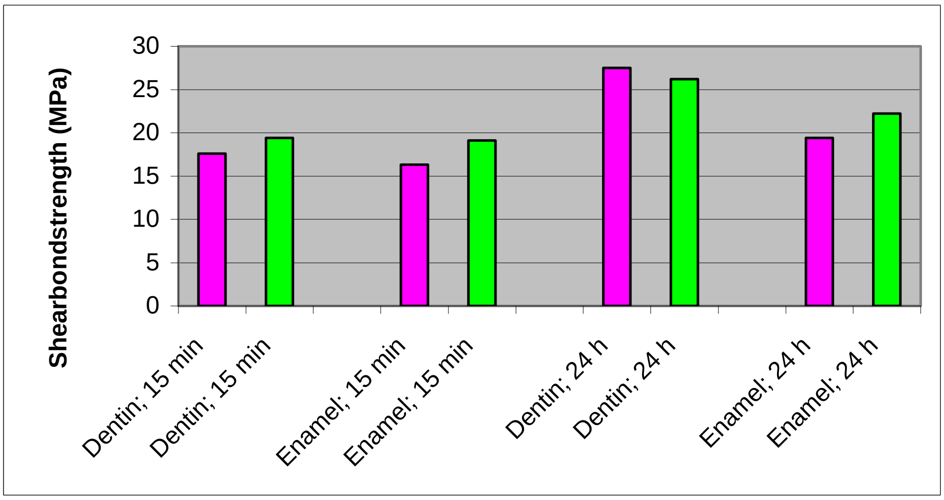
Head of study: Prof Dr Carlos Munoz, Loma Linda University, USA



Shearbondstrength on enamel and dentin

Head of study: Prof Dr K-J Reinhardt, University of Münster, Germany

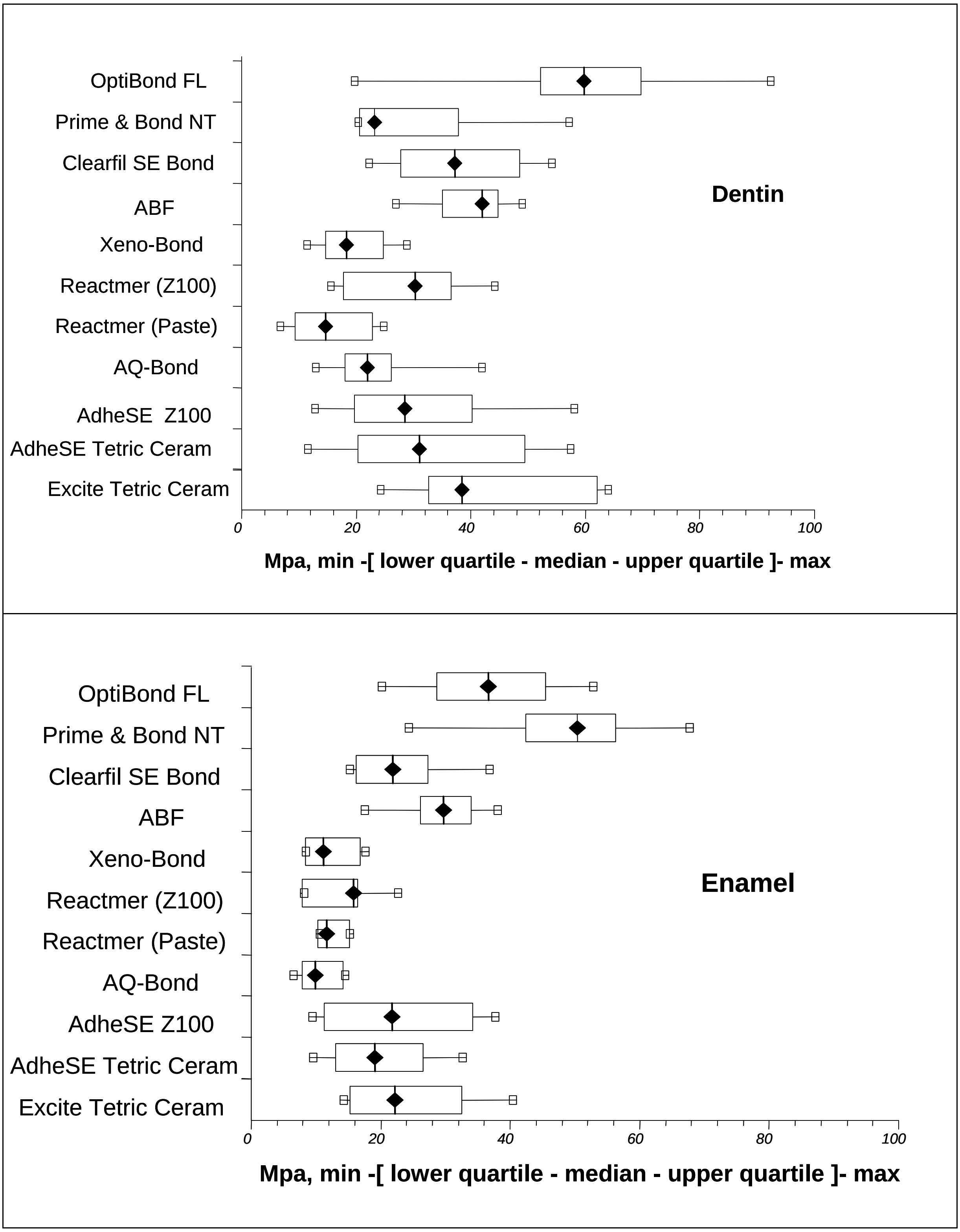
Dual-curing composites with the chemically curing AdheSE DC have been used for the cementation of indirect materials. For this purpose, AdheSE Bond is mixed with the activator in a 1:1 ratio. After application on conditioned dentin or enamel, the bonding agent cures on its own. Subsequently, a plug of Variolink II is applied and light cured for 40 seconds. The following shear bond values have been determined according to the Ultradent method.



Shear bond values on dentin and enamel after 15 min and 24 h. The results of Prof. M. Latta (Creighton University, Omaha) are violet, the results of Prof. Munoz (Loma Linda University) are green.

3.3 Tensile bond strength

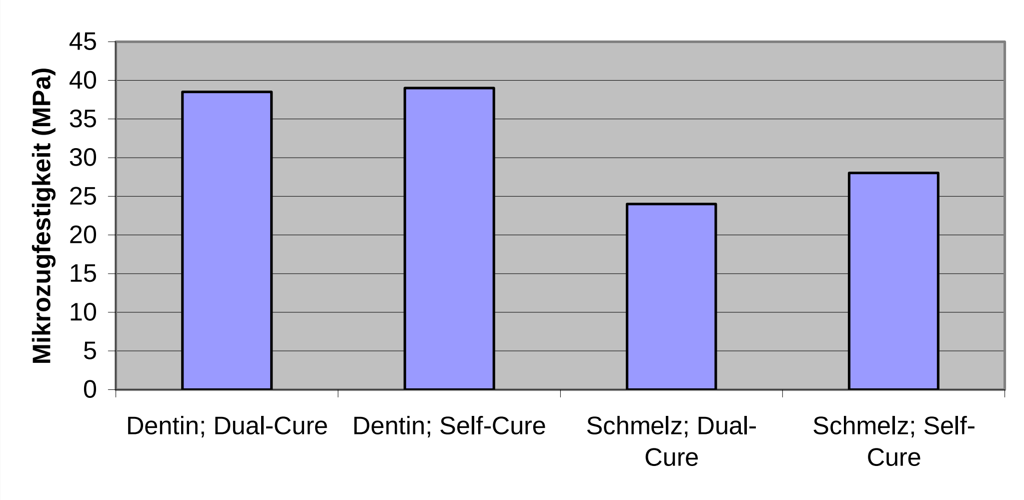
Tensile bond strength tests are increasingly used to examine dental adhesives. Many investigators use what are known as microtensile strength tests.



Microtensile bond strength values of AdheSE compared with those of competitive products. Unless otherwise mentioned, Z 100 was used as the composite. Data from competitors have been examined under identical conditions. Source: *De Munck J et al*, Microtensile bond strengths of one- and two-step self-etch adhesives to bur-cut enamel and dentin. American Journal of Dentistry, in press.

Head of study: Prof Dr Bart van Meerbeek, Katholike Universiteit Leuven, Belgium

In another test, the application of AdheSE Activator was investigated.

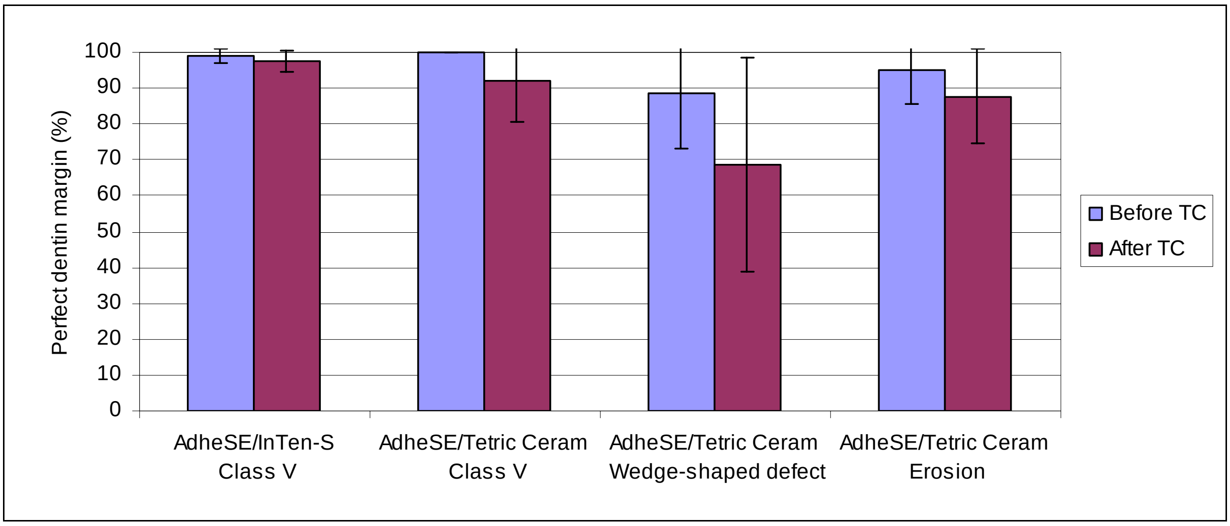


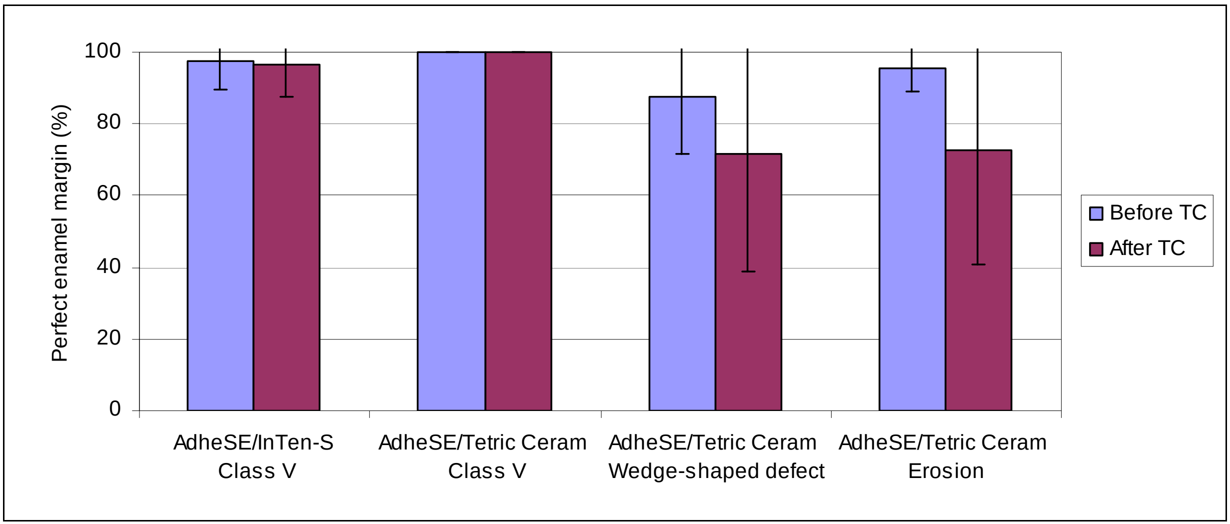
Microtensile strength tests were conducted at the University of Minneapolis by Prof. Perdigao. The specimens were stored in warm water at 37 °C for 24 hours before tensile stress was applied. The same tensile strength is recorded for both purely self-curing and dual-curing specimens.

3.4 Quality of margins

3.4.1 Tightness of the margins

Examinations of the tightness of the margins are conducted in the laboratory to establish the quality that restorations can achieve in clinical situations. For this purpose, either Class V or Class II restorations are placed in extracted teeth. The quality of the margins is examined by taking impressions. In addition, the samples may be subjected to temperature cycling. Masticatory functions are simulated by cyclic mechanical loading.





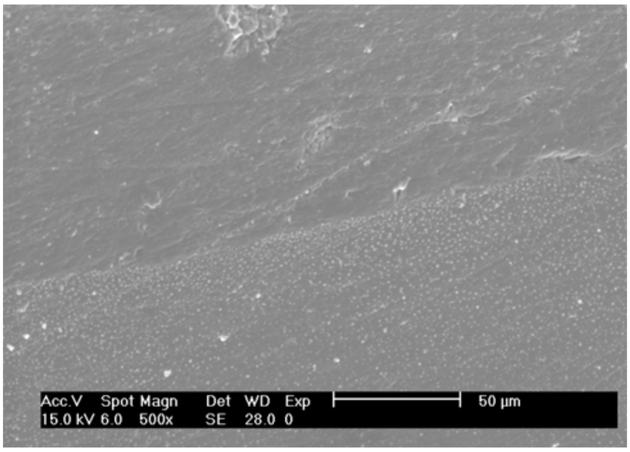
Artificial Class V cavities were restored with AdheSE and either InTen-S or Tetric Ceram. The cavities were prepared in such a way as to allow both dentin and enamel to be cut with a diamond bur. In the third test group, extracted teeth with natural wedge-shaped lesions and in the fourth group, teeth with cervical erosions were employed without further mechanical preparation. Instead, wedge-shaped lesions and erosions were only cleaned with a polishing paste to remove plaque and pellicle layers. The results show that all the test groups achieved excellent marginal quality in dentin as well as enamel before temperature cycling (TC). In the Class V restorations, 2000 temperature cycles between 5 and 55 °C did not lead to a significant deterioration of the marginal quality. A slight decrease in the quality of the margin was noted after temperature cycling of wedge-shaped lesions and erosions.

Head of study: Dr Uwe Blunck, Charité, Berlin, Germany.

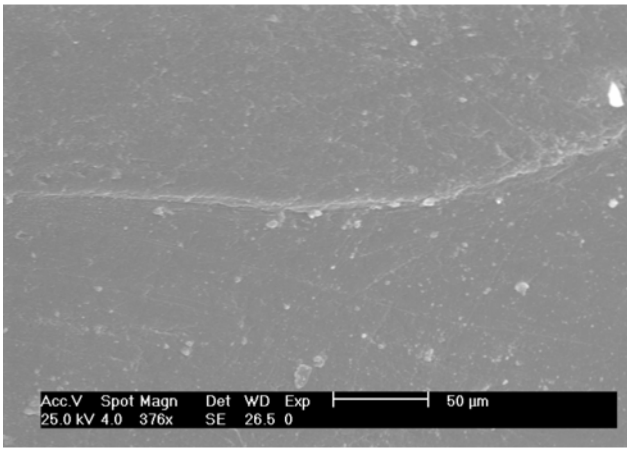
3.4.2 SEM pictures

The quality of the margin between the tooth structure and a composite bonded with AdheSE has been documented by scanning electron micrographs. Class IV cavities were treated with the restorative composite called Artemis. AdheSE was used as the adhesive. The following images show that the immaculate interface between the dentin and the composite remains virtually unchanged after 1,200,000 cycles in the chewing simulator and the subsequent 3000 temperature cycles between 5 and 50 °C.

Investigation: Prof Dr I Krejci, University of Geneva, Switzerland



(AdheSE & anterior composite) before loading in dentin: Excellent marginal adaptation.



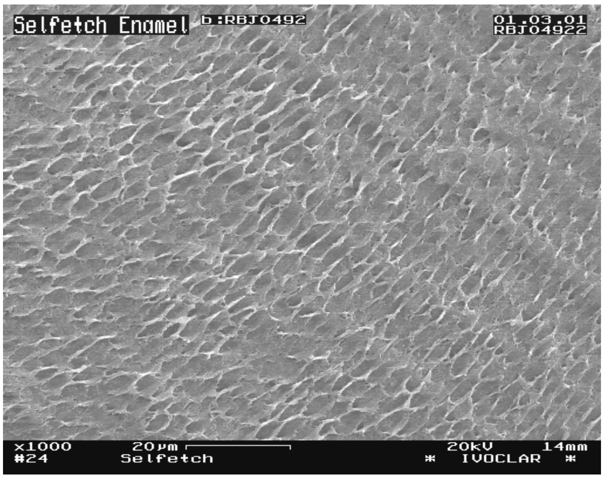
(AdheSE & anterior composite) after loading in dentin: Almost perfect marginal adaptation.

Investigation: Prof Dr I Krejci, University of Geneva, Switzerland

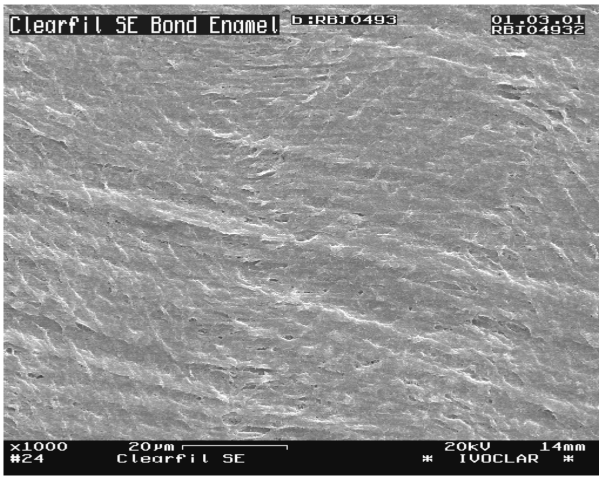
3.5 Morphological examinations

Morphological examinations show the structures of the transition between the tooth structure and the restorative material. Electron microscope images obtained during the examination of AdheSE are shown below.

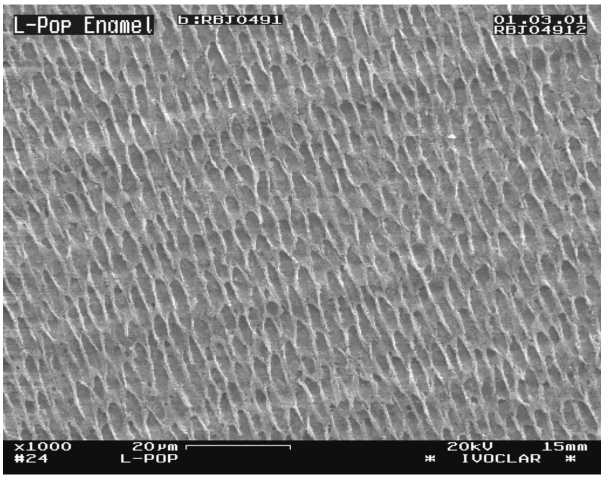
Enamel etching pattern



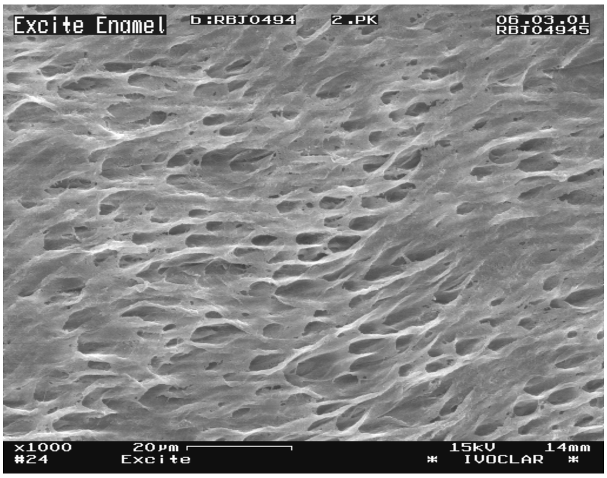
Enamel etching pattern of AdheSE Primer



Enamel etching pattern of Clearfil SE Bond



Enamel etching pattern of Prompt-L-Pop

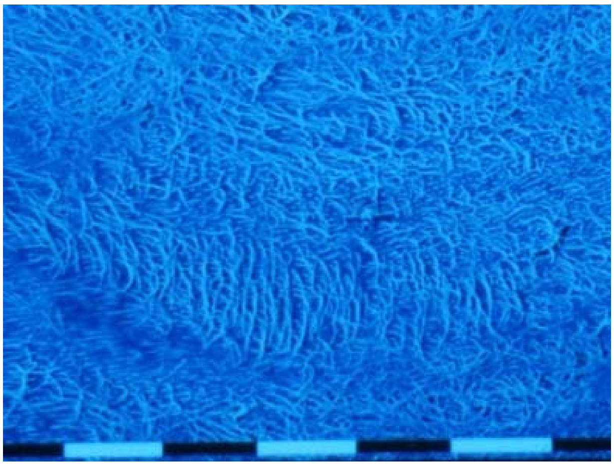


Enamel etching pattern of Total Etch (Excite)

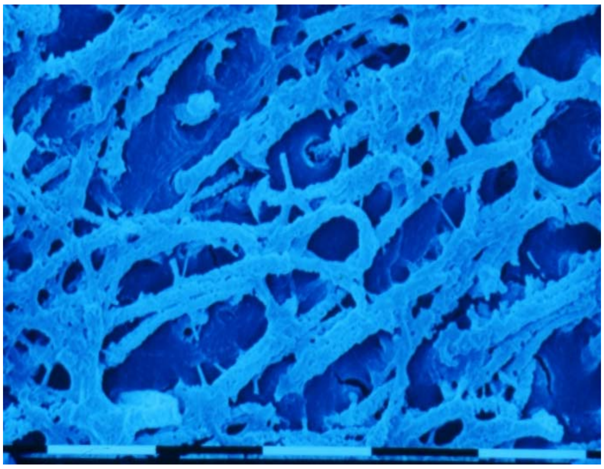
In order to ensure enamel bonding, the primer must be acidic enough to expose the retentive pattern of prisms of dental enamel. The above electron micrographs show that AdheSE Primer can achieve a pronounced etching pattern on ground enamel, although it is not as pronounced as that achieved with phosphoric acid etching (Total Etch).

Investigation: R&D Ivoclar Vivadent, Schaan, Liechtenstein.

Resin tags



Scanning electron microscopic image of a Class V restoration with AdheSE and Tetric Flow (scale unit 0.1 mm). AdheSE has homogenously formed resin tags throughout the entire restorative surface.



Magnification from right (scale unit 10 µm). Resin tags of about 20-µm length with lateral branches are visible.

After obtaining the informed consent of the patients, Class V restorations were fabricated with AdheSE and Tetric Flow for anterior teeth that could not be saved for periodontal reasons. One week later the teeth were extracted. Subsequently, the tooth structure was dissolved with phosphoric acid (36%) and sodium hypochlorite (2%). Then, the remaining restoration was vapour-plated with gold and examined by scanning electron microscopy.

Head of study: Prof Dr Marco Ferrari, University of Siena, Italy

4. Clinical investigations (*in vivo*)

AdheSE has been the subject of clinical studies at various European and American universities. A summary of the studies is provided below.

4.1 Internal clinical investigations of AdheSE

Head of study:	Dr Arnd Peschke, R&D, Ivoclar-Vivadent AG, Bendererstr 2, 9494 Schaan, Liechtenstein
Objective:	Obtain clinical data on the use of AdheSE in Class I – IV cavities
Study design:	Class I and II restorations: Fifteen posterior restorations were placed using Tetric Ceram and 15 using Artemis, Class III and IV: 30 anterior restorations using Artemis
Result:	AdheSE is very easy to handle and considerably facilitates clinical treatment procedures. After 6 months none of the restorations showed any undesired side effects that could be traced to the material, such as irritation of the gingiva.

4.2 Comparison of a new self-etching adhesive for the treatment of Class I and II cavities with the established Excite dentin adhesive used in the total etch technique in combination with the composite Tetric Ceram Heavy Body

Head of study: Prof Dr H G Schaller, Zentrum für Zahn-, Mund- und Kieferheilkunde, Poliklinik für Zahnerhaltung und Paradontologie, Grosse Steinstr 19, 06097 Halle/S, Germany

Objective: Determine the suitability of AdheSE in combination with Tetric Ceram HB composite for restoring occlusal stress-bearing Class I and II cavities in a clinical investigation

Study design: One hundred cavities in 50 patients were restored. Twenty-seven of the cavities were classified as Class I and 72 as Class II. All the restored teeth were vital.

Results: Five cases of postoperative sensitivity (3 Excite, 2 AdheSE) were recorded.

After one year no failures, no problems resulting from secondary caries and no visible marginal discolouration were observed.

4.3 Clinical investigation of AdheSE and Excite for the restoration of cervical defects

Head of study: Dr Uwe Blunck, Charité, Medizinische Fakultät der Humboldt-Universität, Augustenburger Platz 1, 13353 Berlin, Germany

Objective: Determine the effectiveness of the AdheSE and Excite adhesive systems for the restoration of cervical defects.

Study design: Sixty teeth were restored in 30 patients: split mouth design.

Results: After 18 months, a retention loss rate of 6.9 % was recorded for AdheSE. Thus, AdheSE meets the ADA standards. Postoperative sensitivity was not established. A statistical evaluation with the Chi squared test did not reveal any statistically significant difference with regard to marginal behaviour and appearance of the restoration if either of the adhesive systems were used.

4.4 Clinically controlled investigation of the Artemis restorative material in combination with AdheSE

Head of study: Prof Dr K Merte, Poliklinik für Konservierende Zahnheilkunde und Parodontologie, Universität Leipzig, Härtelstr 16-18, 04107 Leipzig, Germany

Objective: Evaluate the AdheSE and Artemis system for the restoration of posterior teeth using a mouldable material (Class I and II cavities)

Study design: Forty-nine restorations were placed in 27 patients, of which 18 were Class I cavities and 31 Class II cavities. All the teeth were vital.

Results: After 18 months, a cumulative error rate of 6.4 % was recorded with regard to marginal quality and secondary caries.

4.5 Clinical evaluation of the AdheSE System in Class V cervical abrasions

Head of study: Prof Dr Gerard Kugel, Department of Restorative Dentistry, Tufts University, 1 Kneeland St, Boston, MA 02111, USA

Objective: Evaluate the behaviour of the recently developed AdheSE on dentin and enamel surfaces in cervical abrasions.

Study design: Fifty restorations were placed in 30 patients

Results: The 18-month report is available: No postoperative sensitivities, retention loss rate of 6.9%. Hence, AdheSE meets the ADA standards.

4.6. Evaluation of anterior dental porcelain veneers using a self-etch bonding system

Head of study: Dr. Marcos Vargas, University of Iowa, Iowa City, USA

Objective: Investigate the survival rate of IPS Empress Esthetic veneers. Compare the cementation with the self-etching AdheSE DC (and Appeal) and a total etch system (Syntac Classic / Appeal).

Study design: 40 veneers

Results: The clinical study started in July 2004.

4.7 Ceramic inlays with AdheSE Activator / Variolink II versus Excite DSC / Variolink II

Head of study: Prof. Dr. G. Arnetzl, University of Graz, 8010 Graz, Austria

Objective: Clinically compare the handling and occurrence of postoperative sensitivity with total etch and self-etch applications in indirect restorative therapy.

Study design: 30 inlays or onlays

Results: Study start May 2004; no serious problems or complications have been reported so far.

4.8 Initial clinical experience with two versions of the "SE Activator" for the cementation of ceramic inlays

Head of study: Dr. A. Peschke, clinic, Ivoclar Vivadent AG

Objective: Investigate the clinical behaviour of AdheSE DC as regards handling and occurrence of postoperative sensitivity. Evaluate the marginal quality.

Study design: 10 inlays in 6 patients

Results: Average observation period 8 months. No postoperative sensitivity has been reported (despite the fact that no relining material has been used, even with cavity margins near the pulp).

5. Biocompatibility

5.1 Composition

Primer: phosphonic acid acrylate, bis-acrylamide, water, initiators and stabilizers

Bond: dimethacrylates, hydroxyethyl methacrylate, highly dispersed silicon dioxide, initiators and stabilizers

5.2 General considerations

The bonding component contains only monomers, initiators and stabilizers, which are ubiquitously used in dental resin-based materials. Therefore, it can be considered to be safe for use for the indicated purpose on the basis of the current knowledge. The self-etch primer contains phosphonic acid acrylate which is already employed in the total etch adhesive Excite. Additionally, the new cross-linking monomer bis-acrylamide is used in the AdheSE Primer. Therefore, this toxicological evaluation emphasizes the toxicity of the new primer component.

5.3 Cytotoxicity

XTT cytotoxicity data are available for bis-acrylamide in L929 cells. The data are given (listed?) in Table 1 in comparison with other established monomers. The results show that bis-acrylamide and phosponic acid acrylate exhibit low cytotoxicity in comparison with the most frequently employed monomers Bis-GMA and triethylene glycol dimethacrylate.

Component	**XTT_{50}**	**Cell line**	**Ref**
Bis-acrylamide	880 µg/ml	L929	1
Urethane dimethacrylate	600 µg/ml	L929	2
Phosphonic acid acrylate	60 µg/ml	L929	3
Triethylene glycol dimethacrylate	25 µg/ml	L929	2
Bis-GMA	25 µg/ml	L929	2

Table 1: XTT cytotoxicity data of selected monomers in L929 cells.

5.4 Mutagenicity of AdheSE Primer

Ames tests

Phosphonic acid acrylate was found to be negative in the *Salmonella typhimurium* reverse mutation assay [4]. Bis-acrylamide is negative in this test system as well [5]. Therefore, the components of the AdheSE Primer are not mutagenic in the *Salmonella typhimurium* reverse mutation assay.

Mouse micronucleus test

5 µL of AdheSE Primer were injected subcutaneously in mice. No mutagenicity was found in the rodent bone marrow micronucleus assay [6].

Mouse lymphoma test

AdheSE Primer and AdheSE Bond were mixed in a 1:1 ratio and polymerized to solid test specimens. Extracts of these specimens were tested for mutagenicity with the mouse lymphoma mutagenicity assay. In this test system under the experimental conditions AdheSE was found to be non-mutagenic [7].

According to these results, AdheSE poses no genotoxic risk.

5.5 Irritation

The irritation potential of AdheSE Primer and AdheSE Bond has been evaluated with the HET-CAM Test. Thereby, the test solution is placed onto the chorionallantoic membrane of hen’s eggs. The occurrence of vascular injury or coagulation is the basis for employing this technique as an indication of the potential of a chemical to damage mucous membranes. AdheSE Primer and AdheSE Bond exhibited a similar irritation score as the clinically used dentin adhesives Syntac Single-Component, Syntac Sprint, Systemp.desensitizer and Prompt L-Pop [8]. Hence, the results of AdheSE Primer and AdheSE Bond are comparable with established products, which are in clinical use without problems.

5.6 Application specific considerations

When the AdheSE Primer is used correctly, approximately 20 µL are applied on a tooth. Diffusion through dentin tubules into the pulp is possible, but it was found that HEMA is diluted approximately 6000 fold before it reaches the pulp [9]. One can assume that AdheSE Primer will be diluted in the same order of magnitude prior to reaching the pulp. Additionally, most monomers in the primer will be immobilized upon polymerization, which will further reduce the amount that could reach the pulp. If a drop (20 µL) of AdheSE Primer is spilled in the mouth, it will immediately be diluted in approximately 2 ml of saliva. These considerations show first, that only minute quantities of material can get into contact with human tissues, and second, that the AdheSE components are immediately diluted upon exposure with the mucosa or during diffusion into dentinal tubules. This further reduces the toxicological risk of the product.

5.7 Conclusions

The data presented show that the toxic properties of AdheSE Primer and AdheSE Bond are similar to those of other dentin adhesives that are in successful clinical use. Attention has to be paid to the irritant properties, which require careful handling and application. Especially, contact with eyes and skin has to be prevented, because AdheSE Primer is highly acidic. The safety precautions are specified in the Instructions for Use.

Literature on toxicology

[1] Cytotoxicity assay in vitro: Evaluation of materials for medical devices (XTT-Test) RCC Project 686401. December 2000.

[2] In vitro cytotoxicity assay: evaluation of materials for medical devices (XTT-test) with five monomers. RCC Project 652768, May 1997.

[3] Cytotoxicity assay in vitro: Evaluation of materials for medical devices (XTT-Test) with MA 154 flüssig. RCC Project 620902, October 1998.

[4] Salmonella typhimurium reverse mutation assay. RCC-CCR Report 620904, October 1998.

[5] Salmonella typhimurium reverse mutation assay. RCC-CCR Report 686402, March 2001.

[6] Toxikon Final Report: 01-0867-G1. Rodent bone marrow micronucleus assay-ISO. April 2001.

[7] Toxikon Final Report: 01-3678-G1. Mouse lymphoma mutagenesis assay-ISO. September 2001.

[8] HET-CAM test with Syntac Single-Component, Syntac Sprint, Excite, Excite DSC, Systemp.desensitizer, Self Etch Primer V, Self Etch Bonding V, Self Etch Primer S, and Prompt L-Pop. NIOM Test Report no. 008/01, June 2001.

[9] Bouillaguet S, Wataha JC, Hanks CT, Ciucci B, Holz J (1996). In vitro cytotoxicity and dentin permeability of HEMA. J. Endodont. 22:244-248.

6. References

Folwaczny M, Mehl A, Kunzelmann KH, Hickel R (2000). Tooth colored restorations of class V lesions using four different materials - five year results. J. Dent. Res. 79:361.

Frankenberger R, Kraemer N, Petschelt A (2000). Technique sensitivity of dentin bonding: Effect of application mistakes on bond strength and marginal adaption. Operative Dent. 25:324-330.

Gwinnett AJ (1992). Moist versus dry dentin: its effect on shearbondstrength. Am J Dent 5:127-129.

Leinfelder K (1996). A conservative approach to placing posterior composite resin restorations. J Am Dent Assoc 127:743-748.

Mazer R, Cury C, Teixeira L, Leinfelder K (1994). Influence of Maleic acid on the retention of abfracted lesion restorations. J. Dent. Res. 73:275.

Moszner N, Zeuner F, Rumphorst A, Salz U, Rheinberger V (2001). Hydrolysestabile Phosphonsäuremonomere als Dentinhaftvermittler. Dental Praxis 0:105-112.

Pröbster L, Ulmer HJ, Engel E (1996). Four-year survival rate study of Empress restorations. DGZPW 0:59.

Schroeder HE (1991). Oral Structural Biiology New York: Thieme.

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