

## Adverse Effect of The Application of Chlorhexidine on A Self-Etch Calcium Dependent Adhesive

Roberto Tello Torres, Gustavo Huertas Mogollón, Jason Cáceres Monzon, Paolo Bragagnini Ramos and Carlo André Aguirre Becerra\*

*Equipo de Rehabilitación Oral Adhesiva (Roa), Chiclayo, Peru*

\*Corresponding Author: Carlo André Aguirre Becerra, Equipo de Rehabilitación Oral Adhesiva (Roa), Chiclayo, Peru.

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### Abstract

A bibliographic review of the application of chlorhexidine as a protease inhibitor is presented when self etch adhesive systems are used, in order to determine if this inhibitor has any effect against the bond strength of the adhesive system used in dentine.

In the light of the investigations it has been concluded that chlorhexidine in percentages of 2% or more could interfere with the chemical reaction of a self-etch calcium-dependent adhesive, since both chlorhexidine and calcium released from the dentin in the adhesive process will have affinity for the phosphate of the adhesive, being able to interfere in this way in the correct union.

It has also been reported that percentages of up to 1% of chlorhexidine, did not present interference in the adhesive process.

**Keywords:** Chlorhexidine; Calcium; Dentine

### Introduction

The longevity of dentine adhesion has been studied for many years, however there are extrinsic factors such as the susceptibility of contemporary adhesives to water sorption, oral fluids, polymerization, resin leaching and intrinsic degradation mechanisms such as enzyme activation such as metalloproteinases (MMP) that lead to a degradation of the hybrid layer and the collagen matrix [1].

The activity of metalloproteinases could be controlled by the action of protease inhibitors, which could be beneficial for the preservation of the hybrid layer. This has been demonstrated in several *in vivo* and *in vitro* studies, in which chlorhexidine was applied, known to have an inhibitory effect on broad spectrum MMPs and which significantly improved the integrity of the hybrid layer formed by a simplified etch and rinse adhesive. However, there are few reports of whether chlorhexidine can be used with self etch adhesives to preserve adhesion to dentin. Confirming that chlorhexidine can be used with self etch adhesives would be the first step to ensure that the use of chlorhexidine in self etch adhesives would not impair immediate bond strength to dentin [2].

Reason why the purpose of the following literature review is to determine if the application of chlorhexidine has any effect against the bond strength of self etch adhesive systems.

### Development of the text

In the last 50 years the adhesive systems have evolved in a staggered way, today we find self etch systems, which do not need an acid attack step separately, since these contain acidic monomers that simultaneously condition and primer the dental substrate [3].

Consequently, this approach is easier to use (fewer steps, less application time) and less sensitivity in the technique, resulting in reliable clinical performance. Another important clinical benefit of self etch adhesives is the absence or lower incidence of postoperative sensitivity on the part of patients compared to when using etch and rinse adhesives, this is largely due to their lower aggressiveness against dentin in comparison with phosphoric acid, and the more superficial interaction it has with dentin leaving a large part of the dentinal tubules clogged with smear layer [3,4].

The morphological characteristics of the adhesive tooth interface produced by a self-etch depend to a large extent on the interaction of the functional monomers with the dental substrate and the pH of the solution of the adhesive system since the real depth in which the self-etching adhesives interact in dentin it differs from a few hundred nanometers like the self-etch ultra mild with pH 2.5 considered as a nano interaction. An interaction depth of around 1 micron is achieved with self etch mild adhesives with a pH of 2; a depth of interaction between 1 and 2 microns is achieved with the self-etch adhesive of intermediate strength, with a pH between 1 and 2. And a depth of interaction of several microns is obtained with a strong self etch with a pH of 1. Only with strong self etch adhesives are the typical resin tags in dentine formed, while it is barely formed with the self-etch mild and ultra mild adhesives [3].

### Mechanism of action of the adhesive system self etch calcium dependent

The fundamental mechanisms of adhesion to dentine are based essentially on micromechanical and ion exchange processes. In the first, the minerals of the dental hard tissue are removed and replaced by resinous monomers which, upon polymerization, generate a micromechanical bond in the created porosities, this process which it is called hybridization in dentin, it involves the infiltration and subsequent polymerization of the resinous monomers in the created surfaces, based mainly on diffusion [3,5,6].

While micromechanical retention is a prerequisite for good adhesion (within clinical circumstances) the potential benefit of the chemical interaction between the functional monomer of the adhesive system and the dental substrate has generated great attention, and this treats in that the functional monomer (with phosphate content, in this case 10 MDP) interacts with the tissues based on hydroxyapatite of the dentine generating decalcification and the subsequent release of the calcium ion. In addition, the functional monomer itself will release phosphate and hydroxide generating an electrically neutral surface. The phosphate released by the functional monomer when presenting negative electric charge will be compatible with the calcium released from the hydroxyapatite of the dentine with a positive electric charge, forming a stable salt and providing adhesion [3-5,7,8].

### Degradation of the hybrid layer

Despite these mechanisms of action, there are intrinsic factors that are related to the same tooth and to the matrix of metalloproteinases that will generate the disintegration of the hybrid layer [2,9,10].

These MMPs are a group of 23 enzymes capable of completely degrading the components of the extracellular matrix, and in human dentin we find collagenase (MMP 8), gelatinases (MMP 2 and 9) and enamelysin (MMP 20) [2,9,10].

It has been shown that simplified etch and rinse adhesives and less aggressive versions of self etch are capable of releasing and activating endogenous MMPs during adhesion to dentin, and that they are believed to be responsible for collagen degradation and disintegration of the hybrid layer [9,11].

The activity of metalloproteinases could be suppressed by the action of protease inhibitors, which could be beneficial for the preservation of the hybrid layer. This has been demonstrated in several in vivo and in vitro studies, in which chlorhexidine was applied, known to have an inhibitory effect on broad spectrum MMPs and which significantly improved the integrity of the hybrid layer formed by a simplified etch and rinse adhesive [2].

However, several studies of the application of chlorhexidine at 2% and self-etch adhesive systems have reported as results that the dissociation of chlorhexidine and its cationic characteristic with positive electronic charge could interfere with the adhesion mechanism of self etch adhesive systems to dentin, and this is because since chlorhexidine is an element with positive electronic charge, it will have affinity with the phosphate with negative electronic charge released from the same functional monomer of the adhesive system, thus reducing the binding capacity of this phosphate with the calcium released from the decalcification of hydroxyapatite from the dentin and interfering with the immediate bond resistance, which will be diminished (See Table 1) [11-14].

Study	CHX application	Bond Strength test	Concentration of CHX	Type of Storage Medium	Duration of Storage	Bond Strength Reduction (%)
Carrilho., <i>et al.</i> 2007	Pretreatment Solution	$\mu$ TBS test	2% CHX	Artificial Saliva	6 Months	23.4% (CHX) 45.3% (Control)
Campos., <i>et al.</i> 2008	Pretreatment Solution	$\mu$ TBS test	0.2%, 2% CHX	Distilled Water and thermocycling Artificial Saliva	6 Months	30.1% (0.2% CHX) 24.3% (2% CHX) 42.3% (control)
Komori., <i>et al.</i> 2009	Pretreatment Solution	$\mu$ TBS test	2% CHX	Artificial Saliva	6 Months	22.7%(2% CH X) 46.2% (control)
Zhou., <i>et al.</i> 2009	Incorporated into adhesive Composition	$\mu$ TBS test	0.05%, 0.1%, 0.5%, 1% CHX	0.9% NaCl 0.02% Sodium azide	6 Months	28.8% (0.05% CHX) 0.7% (0.1% CHX) 5.9% (0.5% CHX) 2.9% (1% CHX) 18.7% (control)
Stanislawczuk., <i>et al.</i> 2009	Pretreatment Solution	$\mu$ TBS test	2% CHX	Distilled Water	6 Months	0% (2% CHX) 29.3% (control)
Loguercio., <i>et al.</i> 2009	Pretreatment Solution	$\mu$ TBS test	0.002%, 0.02%, 0.2%, 2%, 4% CHX	Distilled Water	6 Months	11.6% (0.002% CHX) 9.6% (0.02% CHX) 11.3% (0.2% CHX) 10.5% (2% CHX) 14.3% (4% CHX)
Breschi., <i>et al.</i> 2010	Pretreatment Solution	$\mu$ TBS test	0.2%, 2% CHX	Artificial Saliva	6/12 Months	14.7%/25.8% (0.2% CHX) 12.6%/24.4% (2% CHX) 30.6%/59.2% (control)
De Munck., <i>et al.</i> 2010	Pretreatment Solution	$\mu$ TBS test	0.05% CHX	Distilled Water	6/12 Months	36.4%/68.7 (0.05% CHX) 38.6%/49.7% (control)
Ricci., <i>et al.</i> 2010b	Pretreatment Solution	$\mu$ TBS test	2% CHX	Oral Function	12 Months	26.3%(2% CHX) 43.9% (control)
Mantro., <i>et al.</i> 2012	Pretreatment Solution	$\mu$ TBS test	0.5%, 2% CHX	Artificial Saliva	12 Months	34.5% (0.5% CHX) 21.4% (2% CHX) 59.8% (control)
Sacramento., <i>et al.</i> 2012	Pretreatment Solution	$\mu$ TBS test	2% CHX	Distilled Water	6/12 Months	77.8%/84.9% (2% CHX) 81%/91.1% (control)
Yiu., <i>et al.</i> 2012	Incorporated into adhesive Composition	$\mu$ TBS test	2% CHX	Artificial Saliva	12 Months	18.6% (2% CHX) 42% (2% CHX)
Ali., <i>et al.</i> 2013	Pretreatment Solution	$\mu$ TBS test	2% CHX	Artificial Saliva	6 Months	13.7% (2% CHX) 36.5% (control)
Sabatini 2013	Incorporated into adhesive Composition	$\mu$ TBS test	0.2%, 2% CHX	Distilled Water	6 Months	0% (0.2% CHX) 0% (2% CHX) 0% (control)
Francisconi., <i>et al.</i> 2015	Pretreatment Solution	$\mu$ TBS test	0.004%, 2% CHX	Deionized Water	6/12 Months	35.2%/61.2% (0.004% CHX) 15.9%/67.8% (2% CHX) 40.2%/78.2% (control)
Montagner., <i>et al.</i> 2015	Pretreatment Solution	$\mu$ TBS test	2% CHX	Distilled Water	18 Months	20.5% (2% CHX) 44.5% (control)
Zheng., <i>et al.</i> 2015	Pretreatment Solution	$\mu$ TBS test	2% CHX	Artificial Saliva	9 Months	0% (2% CH X) 26.2% (control)

**Table 1:** Data from the studies included in a systematic review.

CHX: Chlorhexidine;  $\mu$ TBS: Microtensile Bond Strength; SBS: Shear Bond Strength.

However, the application of chlorhexidine in percentages lower than 2%, that is 0.03%, 0.05%, 0.5%, 1%, has been reported not to present adverse effects in the immediate bond resistance in dentin. Several studies have shown that in percentages as low as 0.03% chlorhexidine has an adequate effect on metalloproteinases, so there would be no justification for using it at a higher percentage, especially if the adhesive system used is a self-etch [2,15].

### Conclusions

Therefore, it can be concluded that Chlorhexidine in very low percentages as 0.03% is effective as an antibacterial and as an inhibitor of metalloproteases, which is why there would be no reason to use it at 2%, whose adverse effect has already been evidenced.

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