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Chlorhexidine and the Degradation of the Hybrid Layer – Narrative Review

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Abstract

Introduction: The clinical lifespan of the restoration is based on the resistance that the hybrid layer structure performs to degradation that is influenced by several local factors, with short-term or long-term action effects on the tooth. **Methods**: The purpose of this study includes the presentation of published data on the advantages and disadvantages of the use of one of the most advertised dentinal solutions, chlorhexidine, in the resistance of hybrid layers to structural degradation. The way in which the adhesive resin is connected to the acidified dentin structure depends on the physical or chemical factors of this connection between two structures with very different characteristics. The study is of review type, using key words and their combination on the PubMed electronic search pages. **Results**: Chlorhexidine is known for its inhibitory properties against activated dentinal metalloproteinases, a consequence of the acidification process, the stage of the protocol for the realization of dentinal restorations realized with composite. Thus, this surface area is directly proportional to its size versus the duration of clinical use of dental composite restoration. Microretention is realized between acidified dentin or enamel and extensions of adhesive resin against preprepared spaces, dentinal tubules. **Conclusion**: During the acidification process, precursor to the placement of the adhesive resin layer, metalloproteinases of dental origin are also activated, enzymes that are responsible for degradation of the hybrid layer. These enzymes have their expressed activity depending on the presence of $Zn2+$ or $Ca2+$ ions. There are several ways of inhibiting these enzymes and there are several ways of inhibiting the degradation process of the hybrid layer.

KEYWORDS
Hybrid layer; Chlorhexidine; Degradation; Metalloproteinases; Adhesive resin layer

1 | INTRODUCTION

The support of composite as a dental restorative material, to the prepared dentine structure as surrounding walls of the carious cavity, is based on the ability to connect by means of microretention. Microscopically, microretention is encountered at the level of the

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hybrid layer, which in its component structure includes not only adhesive resin but also acidified dentin structures with its clinical advantages and disadvantages.[1-3] The hybrid layer is now a structure whose construction has been fixed in many microscopic photographs of the cross-sections of the area where the composite filling has been applied. In its composition, the hybrid layer contains the decalcified structure of the tooth and the photopolymerized structure of the adhesive resin.[4,5] From this definition comes the conclusion that the hybrid layer is obtained from the union of two elements with different states, that is, the structure of the tooth, which is hard and solidified, and the structure of the resin, which changes from a fluid state to a hardened structure. Seen from this point of view, it is understood that the hardened structure of the part of the tooth has its microscopic morphology, presented with dimples and grooves or tubules which do not have the same structure.[2,5-10] This is because the tooth where the composite restoration will be placed will be prepared with burs for accurate contouring according to the shape-sketch and Black's principles, but even then it will be acidified where the dentinal tubules will be emptied of their contents, will be emptied from dentinal fluid to give way to penetration of adhesive solution. [4,11-13] The adhesive resin, on the other hand, contains not only fluids but also resistance in the process of penetration on the acidified surfaces of the preparation. It is this fluid substance which, when photopolymerized, can even exert attractive forces against the abrasive structures where it has been attached.[14-18] It is the bond then when it is photopolymerized, can even exert attractive forces against the prepared structures of the tooth where it has been attached. The application of acid to the structure of the dentin affects the drying of the dentinal tubules where Thomson's fiber floats, an extension of the odontoblast to which the dentinal tubule belongs.[4,8,12,19-25] But when acidification is applied, the drying process occurs at dentinal fluid; leaving these tubes as empty spaces in the shape of beehives, ready for the penetration of the bond. After the introduction of the adhesive resin and its hardening, this layer with acidified tubular dentin and hardened resin as a result of photopolymerization is called a hybrid layer.[26-32] On the other hand, the hybrid layer is also used as the notion of sealing the dentinal tubules, since if this connection is done correctly, the dentinal tubules are blocked at their exits, preventing any possible flow of residual fluid or introduction of liquid substances between the resin. and acidified dentin, with the aim of creating a bond with a resistance effect between the composite and the restored tooth.[2,33-40]

The study is oriented around the collection of already published data on the effect of chlorhexidine on inhibiting the degradation of the hybrid layer. The application of this solution either simply in the composition, or as part of the primer, draws attention to the fact that chlorhexidine solution is used in different concentrations and with different treatment purposes. This is the element that draws attention to the ups and downs in the appearance of the advantages and disadvantages of applying this solution.[4,8,12,16,27,41-44]

2 | METHOD

We performed an electronic search in PubMed using the keywords "chlorhexidine", "hybrid layers", and "degradation", combining them with boolean operator. The study covers 20 years, with publications published in PubMed describing the use of chlorhexidine and its effect on the suppression of endogenous metalloproteinase enzymes in dentin.[40-57] We chose the inclusion and exclusion criteria for the analysis after reviewing the abstracts and publications gathered thus far. The study only looked at studies that directly investigated how CHX affects the inhibition of endogenous MMPs in mineral-depleted dentin. Exclusion criteria included studies that employed CHX to diagnose cavities prior to the completion of the preparation procedure. We excluded the term from the research based on the following criteria. At this stage, 25 articles were selected as part of the basic articles included in the study.

- Studies on the use of CHX to disinfect carious lesion sites prior to preparation.
- Studies focused on the involvement of MMPs in caries development.
- Studies investigating other approaches or solutions for limiting hybrid layer deterioration that do not rely

on MMP inhibition.

A total of 32 articles were selected, of which 7 articles were not taken for further evaluation as they did not meet 1 or some of the following criteria:

- articles analyzing the application of a new antibacterial monomer, such as dimethylaminododecyl methacrylate (1 article),
- articles that analyzed the application of adhesive resin layers with an inhibitory effect on the degradation of the dentinal matrix by promoting resin-dentin interlayer stability (1 article),
- articles analyzing the application of another type of MMP inhibitor – galardin, EDTA, polyvinylphosphoric acid, quaternary ammonium methacrylate (4 articles),
- articles analyzing the application of chlorhexidine in the disinfection of carious lesion areas before preparation (1 article).

3 | RESULTS

The results of processing the collected data are presented according to the tables below.The trend of articles on the application of chlorhexidine to acidified layers of dentin is presented in Table 1, accompanied by data according to the intervals of publication years.

TABLE 1 Selected articles according to the years of publication, to show the trend of scientific research in this field*

Year of Publication* Article Type	2001–2007	2008–2014	2015–2022	Total
In vitro**	1 (4%)	7 (28%)	7 (28%)	15 (60%)
In vivo***	3 (12%)	-	1 (4%)	4 (16%)
Review	-	4 (16%)	2 (8%)	6 (24%)
Total	**4 (16%)**	**11 (44%)**	**10 (40%)**	**25 (100%)**

**The electronic search was carried out for the years 2001–2022, divided in 7-year time intervals, except for the last interval.*
***In vitro experiments were performed on human extracted teeth, usually extracted third molars or temporary molars were used.*
****In vivo studies have evaluated the longevity effect of composite restorations on teeth in oral cavities with Black Class I and II preparations.*

TABLE 2 Selected articles according to the years of publication, to show the trend of scientific research in this field

Year of Publication	2001–2007	2008–2014	2015–2022
In vitro	1 (4%)	7 (28%)	7 (28%)
In vivo	3 (12%)	-	1 (4%)
Review	-	4 (16%)	2 (8%)
Total	**4 (16%)**	**11 (44%)**	**10 (40%)**

TABLE 3 Summary of the effects of chlorhexidine on the hybrid layer, which also affects how the success of the application of this solution is evaluated.

Type of article* Method of assessment	In vitro	In vivo	Review	Total
Bonding strength	4 (16%)	2 (8%)	3 (12%)	9 (36%)
Degradati of HL	5 (20%)	1 (4%)	1 (4%)	7 (28%)
Inhibition of MMP	5 (20%)	-	1 (4%)	6 (24%)
Collagen network	1 (4%)	1 (4%)	1 (4%)	3 (12%)
Total	**15 (60%)**	**4 (16%)**	**6 (24%)**	**25 (100%)**

TABLE 4 Occurrence of positive or negative effects of chlorhexidine in the hybrid layer.

Effect type Method of assessment	Negative effects	Positive effects	Total
Bonding strength	2 (8%)	7 (28%)	9 (36%)
Degradation of HL	7 (28%)	-	7 (28%)
Inhibition of MMP	1 (4%)	5 (20%)	6 (24%)
Collagen network	-	3 (12%)	3 (12%)
Total	**10 (40%)**	**15 (60%)**	**25 (100%)**

TABLE 5 The method of evaluating the effect of chlorhexidine on the hybrid layer depending on the years of publication.

Year of Publication* Method of assessment	2001–2007	2008–2014	2015–2022	Total
Bonding strength	1 (4%)	3 (12%)	5 (20%)	9 (36%)
Degradation of HL	2 (8%)	4 (16%)	1 (4%)	7 (28%)
Inhibition of MMP	-	3 (12%)	3 (12%)	6 (24%)
Collagen network	1 (4%)	1 (4%)	1 (4%)	3 (12%)
Total	**4 (16%)**	**11 (44%)**	**10 (40%)**	**25 (100%)**

TABLE 6 Time-based evaluation of CHX on the hybrid layer.

Evaluation element Evaluation time	Bonding strength	Degradation of HL	Inhibition of MMP	Collagen network	Total
1 month	1 (4%)	-	-	-	1 (4%)
4 months	1 (4%)	-	1 (4%)	-	2 (8%)
6 months	1 (4%)	3 (12%)	-	-	4 (16%)
9 months	-	1 (4%)	-	-	1 (4%)
12 months–1 year	1 (4%)	1 (4%)	-	1 (4%)	3 (12%)
14 months	-	1 (4%)	-	-	1 (4%)
18 months	-	1 (4%)	-	-	1 (4%)
24 months-2 years	1 (4%)	-	-	-	1 (4%)
36 months	1 (4%)	-	-	-	1 (4%)
10 years	-	-	1 (4%)	-	1 (4%)
Total	**6 (24%)**	**7 (28%)**	**2 (8%)**	**1 (4%)**	**16 (64%)**

TABLE 7 This table shows in quantitative terms how the effect of CHX is evaluated, depending on its concentration, on the action it performs in the hybrid layer.

% of CHX Method of assessment	0.2%	2%	Total
Bonding strength	2 (8%)	3 (12%)	5 (20%)
Degradation of HL	-	1 (4%)	1 (4%)
Inhibition of MMP	2 (8%)	1 (4%)	3 (12%)
Collagen network	-	-	-
Total	**4 (16%)**	**4 (16%)**	**8 (32%)**

TABLE 8 This table summarizes the data on the selected articles regarding the way CHX acts depending on whether the action is related to the type of bonding systems or the penetrating ability of the resin.

Evaluation element Method of assessment	Types of bonding systems	Resin infiltration	Total
Bonding strength	3 (12%)	-	3 (12%)
Degradation of HL	-	1 (4%)	1 (4%)
Inhibition of MMP	-	-	-
Collagen network	-	3 (12%)	3 (12%)
Total	**3 (12%)**	**4 (16%)**	**7 (26%)**

4 | DISCUSSION

Various studies show that the bond between the composite layer and dentin degrades over time due to the action of MMPs on collagen fibrils left unprotected after acidification. The longevity of a composite filling is highly dependent on the measures taken to minimize this effect.[26] In vitro studies have shown that if CHX is applied with the goal of inhibiting activated MMPs, the CHX remains in the hybrid layer for up to 10 years after clinical application. In fact, this is based on only one study, hinting that perhaps more research is required in this field.[27] When CHX is analyzed by comparing it with cross-linking agents, one study states that the latter have a higher ease of application than CHX.[28] This fact can also be mentioned as a negative element of the application of CHX. A positive element of the application of CHX is the strength of the bond, which according to a study[29], has no difference at the time of application. However, this bond increases its strength over time and with the age of the composite restoration, compared to teeth and restorations where CHX has not been applied. The way of applying CHX depends on the concentration; according to a study[30], it requires 60 seconds of application for CHX with a concentration of 0.2%. According to another study[31], it is emphasized that increasing the concentration of CHX does not necessarily increase the strength of the bond.

Despite the different types of bonding systems, one study[32] emphasizes that the best-controlled way to apply CHX is after acidification with phosphoric acid, followed by rinsing with water and applying 2% CHX for 30 seconds. This data is also supported by another literature source[49], which states that the effect of CHX on bonding systems with self-acidification has no value in inhibiting MMPs. Another study[54] suggests that the CHX effect is achieved after 10 minutes of application—a duration impossible to achieve clinically. Regardless of how CHX is applied, one study[36] shows that in teeth treated with CHX, the structure of the hybrid layer is more regular in the combination of resin with dentinal tubules. These data contradict the findings of another study[37], which states that the application of CHX does not increase the bond strength but rather keeps it stable, compared to teeth without CHX application. Contrary to recent studies, one report[41] states that proanthocyanidins or grape extract have better effects in inhibiting MMPs than CHX. This finding is supported by another source[53], which states that the effect of 2% CHX is 79.8%, while that of proanthocyanidins is 87.6%, as assessed by the colometric system. CHX should be considered for future applications in systems that allow gradual release.[45]

CHX is evaluated across years of publication, showing the growing interest of scientific research on this topic. For the years 2001–2007, most articles (16%) are of the *in vitro* type, a pattern that becomes even more pronounced at 44% during 2008–2014. Meanwhile, during 2015–2022, *in vivo* studies rise to 45%. However, studies with experimental *in vivo* designs are either missing or few in number. When analyzing how CHX works, 36% of the articles assess bond strength, 28% assess inhibition of the degradation of the hybrid layer, 24% assess inhibition of MMPs, and 12% assess the structure of the collagen network. According to *in vitro* studies, the degradation of the hybrid layer and inhibition of MMPs are more commonly evaluated, each using different instruments and methods.

According to data in Table 4, CHX has negative effects estimated at 40% and positive effects at 60%, regardless of the mode of action. These effects are presented at the highest value of 28%, tied to bonding strength. This suggests that CHX is not the definitive key to completely or safely inhibiting the degradation of the hybrid layer. Studies show varying time frames for evaluating the effect of CHX. This variability demonstrates CHX's relevance but does not provide definitive data on the duration of its effects. Depending on the concentration of CHX applied. Table 7 shows that the effects of CHX are not related to its concentration, whether 0.2% or 2% (both estimated to have an effect of 16%). The types of bonding systems have attracted attention, with 12% analyzing their influence and 16% focusing on the effect on resin infiltration [Table 8]. This reflects a trend in the development of different bonding systems and related marketing activities in this field.

5 | CONCLUSION

In vivo studies analyzing the effect of CHX on the hybrid layer should be more in number, as they are actually lacking regardless of the annual periods under analysis.CHX increases the strength of the bonding as it affects the inhibition of MMPs preventing the degradation of the hybrid layer and creating collagen structures suitable for the penetration of the bonding resin. The best application of CHX is in the case of the bonding system with acidification and bonding in stages, in concentrations of 0.2 or 2%, but emphasizing that the increase in the % of CHX will not increase the value of its clinical effect. Regardless of the method of application or the mechanism of action of CHX, the negative effects are minimally more reduced than the positive effects of CHX.More data is required in this area.The duration of the positive effect in time periods is from 1 month to 10 years, given that this should be analyzed further. The application or not of CHX in the future will affect the production method of the bonding systems or the type of resins with an impact on increasing the penetration ability.

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Conflict of interest

The authors have no conflicts of interest to declare.

Supporting Information

Additional supporting information may be found at the journal's website.

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