REVIEW ARTICLE

Influence of Human and Bacterial Enzymes on Resin Restorations: A Review

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Abstract

Background: Esthetic satisfaction has been a prime concern for patients. This has led to a surge in the development of esthetic restorations and dental composites in the field of restorative dentistry over the past decade. Resins are the most preferred restorative material. However, their failure rate was observed to be high.

Aim: This review is aimed for clinician, discussing the influence of human and bacterial enzymes on resin restorations.

Review results: Composite restoration failure is multifactorial with an interplay of mechanical functions such as masticatory forces and abrasion with biological factors such as host modulated and bacterial enzymes. Salivary esterases and bacterial esterases act on the ester-link bond of resin restoration to form byproducts of methacrylic acid and Bis-hydroxy-propoxy-phenyl-propane. Salivary enzymes form microgaps between the resin–tooth interface and provide a suitable environment for bacterial growth. Bacteria colonize the resin–tooth interface to weaken the resin bond strength. The presence of bacteria draws neutrophils into the hybrid layer. The activation and degranulation of neutrophils leads to enzyme secretions that act on bacteria. However, this can also have adverse effects on resin restoration. Acids prompt the activation of matrix metalloproteinases (MMPs). Proteinases secreted by MMPs uncoil the collagen fibrils of the dentin matrix and degrade tooth structure. The salivary esterases, bacterial esterases, neutrophils, and MMPs work synergistically to degrade dental resin material, resin–tooth interface, and dentin. This causes failure of dental resin restorations and secondary caries formation.

Conclusion: Biological degradation of resin restorations is inevitable irrespective of the material and techniques used. Salivary esterases such as cholesterol esterase and pseudocholinesterase and cariogenic bacterial esterase can degrade dental resin, weakening the hybrid layer at the resin–tooth interface, affecting the bond strength, and causing failure. Ester-free resin and incorporation of antimicrobial materials, esterase, and MMP inhibitors are strategies that could ameliorate degradation of the restoration.

Keywords: Bacterial esterases, Biodegradation, Composite resin, Matrix metalloproteinases, Methacrylic acid, Neutrophils, Salivary esterases.

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Introduction

Dental caries lesions are managed by mechanically removing demineralized lesions using cavity preparation techniques and restoring using suitable filling material.[1] Most commonly used restorative materials are amalgam,[2] resin-based restorative materials,[3] and glass ionomer cement.[4] Amalgams have fallen out of favor in the recent decade, despite being a low-cost material and possessing high strength. This is mainly due to esthetic concerns, the need for mechanical retention, and concerns regarding mercury toxicity.[5] Glass ionomer cement cannot be used for anterior restorations due to its mechanical properties.[6] Dental resin composites remain the most commonly preferred restorative material for both anterior and posterior restorations.[7,8]

The resin composite material consists of four main components: polymeric resin matrix, filler particles, coupling agent, photoinitiator, and inhibitor.[9] Polymer resin matrices are the building blocks of the composite restoration. It consists of monomers coupled by esters into the polymer matrix. The most commonly available resin monomers are bisphenol-glycidyl-dimethacrylate (BisGMA), triethylene glycol dimethacrylate (TEGMA), urethane dimethacrylate (UDMA), and bisphenol A polyethylene glycol diether dimethacrylate (BisEMA).[10,11] Polymer matrix fillers are added to improve flow, strength, and microhardness. Silica, quartz, and ceramic are the common filler materials used.[12,13] A coupling agent is used to improve the bonding between hydrophilic dentin and hydrophobic resin.[14] Silanes are the most commonly used coupling agents.[15] The initiator and inhibiter are added to the mode of curing—either self-cure or light-cure composite resin.[16]

A smear layer is formed on the cavity walls after cavity preparation. This layer is removed by a procedure called acid etching.[17] 37%

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phosphoric acid is the most commonly used etchant in dentistry.[18] Acid etching removes the smear layer and opens the dentin collagen tubules which form microresin tags on the teeth surface postbonding procedure.[19] Acid etching is of two types: self-etch technique and total-etch technique.[20] In the self-etch technique, acid etchant and monomer are present in the same system and applied on the teeth surface to form a hybrid layer.[21] In the total-etch technique, an acid etchant is applied first and then cleaned from the surface after which a primer layer is applied on top of the etched surface to establish a hybrid layer. Composite is placed on the prepared tooth surface and cured either using visible light or chemically.[22]

Composite materials are available in various types, and material selection is done based on the type of restoration and teeth involved. They are divided into the posterior composite, anterior composite, and pit and fissure sealants based on the area of application on teeth. Based on filler particle, it is classified into a macro-filled composite (10–25 µm), micro-filled composite (0.03–0.5 µm), and hybrid composite (0.1–3 µm).[23] Composite restorations are proved to be better long-term restorative material; however, the failure rate is observed with class II and large molar restorations compared to premolar restorations.[24] Advantages of composite restorations being high fracture-resistant, esthetically pleasing, minimally invasive procedure, less toxic, and easy to repair. Secondary caries, technique sensitivity, high cost, polymerization shrinkage, and marginal leakage are some of the disadvantages.[25]

Composite restorations are observed to have a high failure rate when compared to amalgam.[25] Failure of resin restorations can be categorized into mechanical factors and biological factors. Mechanical degradation occurs mainly due to masticatory forces leading to surface wear and eversion of composite, exposing the inner matrix leading to weakening and failure of the restoration. Elution of the composite monomers in the saliva also leads to degradation. Polymerization shrinkage occurring during curing lends to bacterial accumulation, leading to future failure of the restoration.[26,27]

Human saliva is composed of enzymes secreted from various sources like salivary glands, oral microbiome, oral tissues, and ingested substances.[28] Amylase, esterase, hyaluronidase, lipase, maltase, carbonic anhydrase, and proteolytic are commonly present in the human saliva.[29–31] Research on the role of salivary and bacterial enzymes on biodegradation of dental resin implied that enzymes lead to weakening and premature failure of dental resin restorations.[32–34]

Salivary esterases and bacterial esters have an effect on the ester links of polymerized resin leading to dissolution and softening of the composite resin. Salivary enzymes activity on the resin–teeth interface eventually results in microleakage and bacterial growth. The bacterial enzymes act on resin restorations causing a reduction in the bond strength. Matrix metalloproteinases (MMPs) present in the dentinal tubules is activated by acid etching. MMPs exert collagenolytic activity on collagen fibrils leading to failure of the restoration. Neutrophils from the gingival sulcus secrete esterases and can impact the longevity of the restoration.[35,36]

Biodegradation of dental resin restorations is caused by esterase enzyme secreted by human saliva and bacteria, MMPs, and neutrophils. The activity of enzymes on resin restoration causes failure of restoration by decreasing its bond strength, and this has impacted the longevity of the restoration and thus should have thorough knowledge on the impact of enzymes on the resin restorations. This paper summarizes the impact of host-modulated enzymes and bacterial enzymes on dental resin restorations with a note on prevention and recent material developments.

Enzyme Activity on Degradation of Resin Restoration

Biodegradation and failure of dental resin restorations by enzymes are categorized into material degradation, resin–tooth interface degradation, and tooth demineralization and discussed below.

Hydrolysis of Composite Resin

Esterases are the most common enzymes associated with composite resin in the oral cavity. Esterase enzyme hydrolyzes composite resin and adhesives into its by-products. It acts on the unprotected ester group linkages of methacrylate present in the resin monomer and polymerized composite matrix. Esterase hydrolyses of composite differ based on the material used. BisGMA was hydrolyzed into Bis-hydroxy-propoxy-phenyl-propane (Bis-HPPP) and methacrylic acid (MA). Triethylene glycol dimethacrylate (TEGDMA) was hydrolyzed into triethylene glycol methacrylate (TEG). BisEMA was hydrolyzed into ethoxylated bisphenol A.[37]

Degradation of Resin–Tooth Interface

The resin–tooth interface is prone to degradation. Salivary esterases act on the polymerized composite. Initially, salivary esterases react with unreacted and partially reacted ester substrates and later on permeate to react with the bulk matrix. Hydrolysis of ester-link composite leads to composite degradation and propagation of marginal gaps over time.[38] Marginal gaps lead to microleakage around the restoration and provide a favorable environment for bacterial colonization and formation of a cariogenic bacterial biofilm resulting in restoration failure and secondary caries.[39] Bacterial colonization in the hybrid layer activates neutrophils from the gingival sulcus. Neutrophils secrete enzymes to act on the bacteria which may affect the resin–tooth interface leading to degradation and restoration failure.[40] Enzymes released from saliva, bacteria, and neutrophils synergistically act on resin and resin–tooth interface, enhancing resin–tooth interface degradation and failure of resin restoration.[37]

Demineralization of Tooth Material

Cavity preparation and removal of demineralizing teeth structure lead to exposure of dentinal tubules. Dentinal tubules consist of various collagen degrading substrates, and these become active postetching. Matrix metalloproteinases MMPs present in the dentin is the main reason for the degradation of teeth structure.[41,42] MMP8 acts as collagenase and hydrolyzes dentin collagen by unwinding the collagen fibrils of the alpha chain.[43] MMP2 and MMP9 act as a gelatinase and alter the morphology of the dentin collagen.[44,45] The activity of MMP2, MM8, and MMP9 on tooth structure decreases the fracture toughness and bond strength in the hybrid layer and might lead to secondary caries formation.[46]

Biodegradation of dental resin occurred mainly due to esterase activity on the ester link of resin monomer and enzyme activity on dentin collagen fibrils and resin–tooth interface. This leads to a decrease in bond strength and failure of resin restoration.

Host-modulated Enzymes

The impact of enzymes produced by the human body against composite resin is far-reaching and are broadly classified under the following headings:

- Enzymes secreted by salivary glands:
  - Cholesterol esterase (CE)
  - Cholinesterase
    - Acetylcholinesterase
    - Pseudocholinesterase (PCE)
- Enzymes secreted by innate immunity:
  - MMP
  - Neutrophils

Impact of Salivary Enzymes on Dental Resins

Human saliva is an amalgamation of water, electrolytes, enzymes, antimicrobial agents, and other organic and inorganic substances. Esterase and other enzymes present in the saliva hydrolyze composite resin, and this leads to biodegradation of composite resin and release MA as a by-product. Biodegradation decreases the strength of dental resin, increases the wear of the composite,[47] and softens the resin matrix.[32]

Cholesterol Esterase

Cholesterol Esterase is the dominant esterase in the saliva.[48] It acts on the ester links of dental resin and catalyzes the hydrolysis of long-chain fatty acid esters of cholesterol.[49] CE activity on BisGMA dental resin showed an elevated release of Bis-HPPP and TEGDMA compared to controls. Santerre et al. conducted a study on biodegradation of three commercially available composite resins using CE. Biodegradation was assessed using three methods: weight loss, surface microhardness, and liquid chromatography. The increase in the release of degrading materials is noted by liquid chromatography. Surface degradation and decrease in the microhardness of both BisGMA and TEGDMA are confirmed by the activity of CE.[50]

Cholinesterases

In human saliva, two types of ChE are present: acetylcholinesterase and PCE.[51] These esterases highly act on hydrolyses of choline esters than other esters.[52] Hydrolysis of dental resin mainly involves PCE.

Pseudocholinesterase

Pseudocholinesterase catalyzes resin degradation by hydrolyzing low-molecular-weight choline esters in the dental resin. The higher molecular weight of PCE leads to early esterase activity.

Research done by Finer and Santerre on the application of CE and PCE on BisGMA and TEGDMA reveals that CE and PCE have a hydrolyzing effect on synthetic dental resin leading to degradation of composite resin. Liquid chromatography analyzed the presence of degraded products, and this confirmed that esterase levels present in the human saliva can degrade composite resin. Usage of specific esterase inhibitor phenylmethylsulfonyl fluoride observed a change in the amount of degrading activity compared to the control group.[53]

Cholesterol Esterase action resulted in an eight-fold increase in Bis-HPPP and a two-fold increase of MA posthydrolyzing BisGMA compared to PCE.[33] CEs have a higher ability to hydrolyze BisGMA, and PCE has a higher affinity to hydrolyze TEGDMA.[54]

Babak et al. assessed the degrading effects and strength of the resin–dentin interface of composite resin. In this study, the composite adhesive specimens are incubated in phosphate-buffered saline or human-derived salivary esterase (HDSE) for up to 180 days. The specimen incubated in the HDSE group showed elevated Bis-HPPP, confirming the hydrolyzing activity of salivary esterases on composite. Fracture toughness measured by universal testing machine presented decreased integrity of resin–dentin interface in HDSE group.[55]

Impact of MMPs on Dental Resins

MMPs are zinc- and calcium-dependent enzymes present in the dentin. There are 23 types of MMPs present in the human body. They can be briefly classified into collagenases, gelatinases, matrilysins, and stromelysins. Esterases and proteases produced by MMPs have a degrading effect on components of the extracellular matrix. Collagenases and gelatinases can degrade collagen from the dentin matrix.[56,57] Gelatinases MMP2, MMP9,[58] collagenase MMP8,[43] and stromelysin MMP3 were proved to have a degrading effect on collagen fibrils.[59]

Dentin collagen fibrils are made of rigid triple helix structure, and MMPs act on the helical structure and defragment it into one-fourth and three-fourth fragments. MMP1 and MMP3 act on the binding site in collagen and uncoil the collagen fibers leading to degradation of collagen.[42,60] Telopeptidase enzyme of MMP2 and MMP9 acts on the telopeptide of type I collagen and creates space for collagenase leading to the uncoiling of collagen fibrils and was suggested to degrade dentin and bone matrix.[61,62] Cysteine cathepsins activate MMPs by exposing the binding site for MMPs and degrading the collagen.[63]

The bond strength of resin restorations is mainly contributed by the resin–dentin interface present in the hybrid layer. Improper application of adhesive resin post–acid etching leads to exposure of dentin collagen fibers. MMPs are present in the dentinal tubules as inactive proenzymes are activated by the low pH environment created by acid etching.[64] MMPs activity leads to an increase in the gelatinolytic activity on dentin collagen fibers.[65] This leads to the uncoiling of collagen fibrils present in the dentin tubules leading to breakage of the bond between resin matrix and dentin. Thus, the degeneration of the hybrid layer leads to a weak resin–dentin interface and failure of the restoration. These enzymes might also act on resin composite and degrade the restoration.[66]

Mazzoni et al. conducted a study on gelatinolytic hybrid layer degradation by the localized activity of MMPs using *in situ* zymography and functional enzymes activity test. *In situ* zymography proved that gelatinolytic activity and hydrolysis of resin restoration are possible post–acid etching and adhesive applications in the hybrid layer. Functional enzymatic activity assay detected the increase in MMP2 and MMP9 following acid etching. This study confirmed the intense increase in MMP activity with acid etching and adhesive resin application.[67]

The application of proteinase inhibitors and chlorhexidine postbonding procedure has demonstrated the impact of MMPs and cysteine cathepsins on collagen degradation in the hybrid layer. Reduced activity of MMPs was noted post–proteinase inhibitor application.[68]

Impact of Neutrophils on Dental Resins

Neutrophils are a part of the innate immune system. The gingival sulcus is the main source of neutrophils in the oral cavity,[69] especially

in diseased conditions such as gingivitis and periodontitis.[70] Neutrophils presence around the teeth, restoration, and the resin–tooth interface is inevitable.[71] Proteolytic and esterase enzymes present in the neutrophils can damage the restoration.[72,73]

Gitalis et al. studied the enzymatic activity of neutrophils on dental resin adhesives. Resin adhesives are incubated with and without neutrophils and measured for resin degradation activity, MMP activity, and dentin degradation activity. After 48 hrs of incubation, the specimens incubated with neutrophils observed the increased presence of Bis-HPPP, generic MMP2, MMP8, MMP9, and hydroxyproline. This study confirmed the degradation activity of neutrophils on a dental adhesive, rein–dentin interface, and dentin leading to secondary caries or premature failure of the restoration.[74]

Enzyme Activity of Neutrophils

Neutrophils present in the saliva may contribute some amount of resin degradation.[74] Neutrophils become pro-inflammatory and secrete enzymes in contact with foreign bodies. Phorbol myristate acetate, formylmethionine-leucyl-phenylalanine, and lipopolysaccharides are known to induce neutrophils for degranulation and formation of a neutrophil extracellular trap.[75] These enzymes act on microorganisms and can also cause collateral damage to teeth and restorations. Neutrophils showed CE-like activity when cleaved with nitrophenyl esters under intraoral degradative conditions. This enzyme significantly hydrolyzed BisGMA into Bis-HPPP under a 48-hour observation.

Cathepsin G, a serine protease present in neutrophils, is released during degranulation. Serine proteases present in saliva and bacteria can hydrolyze methacrylate resin monomer.[46] Salivary, bacterial, and neutrophil serine proteases bear a striking similarity in that they contribute to resin degradation.[40]

During degranulation, myeloperoxidase and hypochlorous acid are released which plays a key role in the degradation of resin composite. Hypochlorous acid acts on the ester links and hydrolyzes BisGMA into Bis-HPPP. Myeloperoxidase acts on Bis-HPPP in the presence of water resulting in a vinyl ether bond and later cleaved to form a byproduct, bisphenol A.[40]

In neutrophils, specific granules contain MM8 and MMP9, and gelatinase granules contain MMP9. MMP8 collagenase activity can fragment dentin, and MMP9 gelatinase can further degrade dentin. Cathepsin G and neutrophil gelatinase–associated lipocalin indirectly trigger MMP8 and MMP9 leading to degradation of tooth material and resin–tooth material interface.[40,74]

Neutrophils Activity on Composite

Under controlled conditions in a laboratory study, increased Bis-HPPP was noticed with neutrophils compared to the control group implying the accelerated degradation of composite with neutrophils. In the first 48 hours, accelerated degradation occurs when neutrophils act on unreacted and partially reacted BisGMA molecules. Post 48 hours, Bis-HPPP release decreases. The amount of degradation was material-based, with self-etching showing less degradation compared to total etch. In self-etch material, hydrophobic BisGMA and acids are present which prevents hydrolysis.[40,74]

Neutrophils Activity on Dentin

The organic matrix of dentin is primarily composed of hydroxyproline type I collagen. Hydroxyproline release from dentin is correlated with its degradation. Neutrophils significantly increased hydroxyproline release compared to the control media suggesting degradation of dentin collagen. Qualitative evidence with scanning electron microscopy confirms the degradation of the dentin under neutrophil incubation. The presence of neutrophils in the dentinal tubules suggests a path into dentin for degradation.[40,74]

Neutrophils Activity on the Resin–Tooth Interface

In aged composite restorations, a marginal gap was formed between resin and tooth interface leading to interfacial biofilm formation.[76] Neutrophils follow the bacteria to enter the marginal gap and secrete enzymes to eliminate bacteria that might act on the resin–teeth interface leading to restoration failure and secondary caries formation.[40,74]

Bacterial Enzymes

The acid activity of cariogenic bacteria on a tooth's surface leads to dental caries. Cariogenic bacteria secrete enzymes along with acids which can degrade resin composites and their adhesives. *Streptococcus mutans*, *Lactobacillus acidophilus*, *Streptococcus sobrinus*, and *Enterococcus faecalis* are some of the most common bacteria causing dental caries. These bacteria are often present on the biofilm adhering to the surface of the resin composite.[77–79]

S. mutans secretes esterase enzymes that have a hydrolytic degradation effect on cured composite resin and its adhesives leading to failure of restoration and secondary caries.[80] Growth of these bacterial biofilms on the surface of composite restoration leads to surface degradation.[81] Enzymes of *S. mutans* have the highest esterase activity contributing to surface degradation and degradation of the resin–tooth interface. Microleakage around the restoration and in the hybrid layer creates a suitable environment for bacterial biofilm formation.[76] Lysis of *S. mutans* in the biofilm releases intercellular components, and these enzymes act on the resin–tooth interface and resin restoration leading to degradation.[82] They act on resin surface and resin–teeth interface and reduce the life span of restoration.[83]

Huang et al. studied the activity of cariogenic bacteria *S. mutans* on both BisGMA and TEGDMA in neutral and acidic pH. Enzymatic assays confirmed increased esterase hydrolysis activity with BisGMA compared to TEGDMA in both neutral and acidic pH. It secreted lactic acid by reacting with carbohydrates and creating an acidic intraoral environment initiating caries. The degradation effect of these bacterial enzymes on composite did not present with significant changes following the alteration in pH level.[84] *S. mutans* activity on self-etch composite released a high amount of Bis-HPPP compared to total-etch and conventional composite resin. Self-etch composite is hydrophilic and increases water sorption, increasing the susceptibility of ester bonds to undergo hydrolysis.[85,86]

Muna et al. assessed the esterase-like enzyme activity of *E. faecalis* on self-etch and total-etch dental resin adhesive. Liquid chromatography analysis confirmed the presence of Bis-HPPP, thus proving the esterase-like enzyme activity and hydrolysis of the resin–tooth interface and degrade resin restorations. It secretes minimal PCH-like esterase and higher CH-like esterase similar to *S. mutans*. The protease collagenase enzyme secreted by *E. faecalis* has a mild effect on dental resin, resin–tooth interface, and hybrid layer. Scanning electron microscopy study revealed surface degradation of dental resin incubated with *E. faecalis* compared to control. Increased release of Bis-HPPP was presented when *E. faecalis* was incubated with conventional and total-etch resin compared to self-etch resin.[87]

Lactobacillus casei is the most common bacteria associated with advanced caries and possess an esterase-like enzyme activity.[88]

Sree Vidya et al. incubated dental resin cement in the bacterial suspensions of *L. casei* and *E. faecalis* and assessed for bacterial esterase activity. Bacterial esterase activity assay showed esterase-like activity in both bacteria, and increased Bis-HPPP is evident in all the samples. This decreased the microhardness of resin due to the degradation activity of the esterase-like enzyme on resin cement.[89] Dual cure resin cement shows better resistance against degradation compared to conventional resin cement.

Prevention of Enzymatic Degradation of Dental Resin

Modified Ester Group Dental Resin

Salivary and bacterial enzymes act on ester links of composite leading to degradation of the resin. To overcome the disadvantage of high ester links in composite, low ester-link composite was formulated. There is evidence of greater adherence of *S. mutans* to the surface of the high ester-link group. To prevent composite degradation, low ester composite should be preferred over high ester-link composite.[90]

MMP Inhibitors

Chlorhexidine has a potential anti-MMP2, anti-MMP8, and anti-MMP9 activity.[91] Postetching application of chlorhexidine inhibits the activity of MMPs and cathepsins. Thus, chlorhexidine can be used to prevent MMP hydrolase activity, protect the hybrid layer from degradation, and improve the bond strength of resin restoration.[92]

Antimicrobial-releasing Resins

Incorporation of antimicrobial material into dental resin can prevent bacterial biofilm formation on resin restorations to improve bond strength restoration and prevent secondary caries. Chlorhexidine was incorporated into composite resin for sustained release of up to 10 years. Studies show that 50% of the material loss was observed in the initial few days followed by a diminished low release from the resin matrix. Surface degradation was observed due to elution of the chlorhexidine and thus was not suggested for clinical use.[93]

Mussel adhesive proteins (MAPs) are polyphenolic proteins present in marine mussels to help for underwater adhesion.[94] 3,4-dihydroxyphenylalanine (DOPA) present in MAP have catechol groups that possess hydrogen bonding and metal-ligand capabilities and was found to be water impervious adhesive used on bone and teeth.[95] The catechol group of DOPA in MAP helps to inhibit bacterial collagenase activity. MAPs competitively binding to chelated calcium ions are necessary for bacterial collagenase activity. A covalent bond was formed between the catechol group and amino group of collagen fibers. This enhances resistance to degradation by bacterial collagenases.[96] Application of MAP primer on dentin collagen matrix enhanced bacterial collagenase resistance and improved bond strength. Thus, this can be used to prevent bacterial enzymatic degradation of resin–tooth interface.[97]

Previous literature on the degradation of dental resins is confined to *in vitro* studies with little *in vivo* research. The degradation of dental resin is a multifactorial process and occurs over a period of time. A majority of studies were carried out over relatively short periods and do not reflect on long-term outcomes. Research in simulated oral environments may not hold completely true in actual clinical practice. Further long-term research on the composite degradation by the host proteome and the effects of the components of the restoration on the human body is necessary to drive forward innovation in restorative materials. Future investigation should focus on the impact of digestive enzymes, and diet should be done on the longevity of restorations.

Conclusion

Biological degradation of resin restorations is inevitable irrespective of the material and techniques used. Salivary esterases such as CE and PCE and cariogenic bacterial esterase break the ester links of polymer and monomer matrix into by-products MA and Bis-HPPP leading to degradation of dental resin. MMPs present in the dentinal tubule are activated by acid etching, and uncoiling of triple-helical collagen fibril was done by the proteinase activity of MMP2, MMP8, and MMP9. This leads to the weakening of the hybrid layer at the resin–tooth interface, affecting the bond strength and causing failure. Neutrophils exert enzyme activity of both esterases and MMPs. Salivary and bacterial esterases, MMPs, and neutrophils have an impact on the degradation of dental resin, resin–tooth interface, and dentin. Ester-free resin and incorporation of antimicrobial materials, esterase, and MMP inhibitors are strategies that could ameliorate degradation of the restoration.

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