

Methacryloyloxydodecylpyridinium Bromide (Mdpb)-Containing Dental Adhesives: A Narrative Review

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Background:

Secondary caries remains one of the leading causes of failure of resin-based restorations. Conventional adhesive systems provide reliable bonding but generally lack intrinsic antibacterial activity. Methacryloyloxydodecylpyridinium bromide (MDPB) has emerged as a promising antibacterial monomer for incorporation into dental adhesives.

Objective:

This review aims to summarize the current evidence regarding the chemical characteristics, antibacterial mechanism, bonding performance, aging resistance, and clinical outcomes of MDPB-containing adhesive systems.

Methods:

The available literature on MDPB-containing dental adhesives was critically reviewed, with emphasis on antibacterial activity, bond strength, artificial aging, and clinical performance.

Results:

Current evidence indicates that MDPB provides long-lasting antibacterial activity through a contact-killing mechanism while preserving the mechanical and bonding properties of adhesive systems. Laboratory studies consistently demonstrate inhibition of *Streptococcus mutans*, reduced biofilm formation, satisfactory bond strength, and acceptable durability after artificial aging. Clinical studies have also reported favorable retention and marginal adaptation, although evidence supporting superior long-term prevention of secondary caries remains limited.

Conclusion:

MDPB is a promising bioactive antibacterial monomer that enhances the biological performance of dental adhesive systems without compromising adhesive efficacy. Nevertheless, additional well-designed randomized clinical trials with extended follow-up periods are required to confirm its long-term clinical effectiveness and caries-preventive potential.

Introduction

With its increased aesthetic properties and conservative approach, dental resin composite has become the material of choice for direct restorations. However, retaining these resin-based restorations is hindered by restorative failure, and in clinical practice, it is known that secondary caries accounts for a major reason to replace these restorations. Secondary caries develop at the interface between the tooth and the restoration when bacteria invade, form biofilms, and leak between the tooth and the restoration, leading to restoration failure.¹

Among oral bacteria, *Streptococcus mutans* is considered the main cariogenic bacteria because of its carbohydrate metabolism, development of biofilm and ability to attach to tooth surface. The acid generated by these bacteria can cause the demineralization of tooth structure surrounding restorations, increasing the likelihood and risk of recurrent caries and subsequent failure of the restoration.²

Traditional dental adhesives are mainly aimed at providing micromechanical bonding and retention with dental substrates and have limited or no intrinsic antibacterial activity. Recurrent caries may occur from bacteria trapped under restorations and/or from microorganisms that penetrate over time. This has led to a vast amount of research into the development of antibacterial adhesive systems that have the ability to inhibit bacterial growth without adversely affecting the adhesive properties. The addition of antibacterial properties to dental adhesives is a new and exciting strategy for improving the longevity of the restoration and reducing the likelihood of secondary caries.¹

1. Development of Dental Resin Adhesives

There have been many minor advances and innovations in dental resin adhesives, which are vital to modern restorative dentistry. The history of these materials is a history of the changing demands of clinical practice, and of the development of dental materials science.

2. Current Generations of Dental Adhesives

Since the late 1950s, there has been a significant expansion in the clinical applications of adhesive system materials. An investigation of agents capable of bonding resins to dental structures was commenced. The initial endeavor to create an adhesive technique for bonding acrylic resins to dental structures was undertaken by Dr. Hagger, a Swiss chemist employed by DeTrey/Amalgamated Dental Company.³ In 1951, he created the initial dental adhesive product named "Sevriton Cavity Seal." This bonding agent contained adhesive glycerophosphoric acid dimethacrylate (GPDM).² In 1952, a study by Mclean and Kramer indicated that the "Sevriton Cavity Seal" substance, which contains glycerolphosphoric acid dimethacrylate (GPDM),⁴ Later, in 1955, Dr. Michael Buonocore, recognized as the pioneer of 'Adhesive Dentistry,' introduced the concept of acid-etched enhanced adhesion after noting that certain automobile manufacturers employed phosphoric acid to treat metal surfaces for improved primer adhesion.⁵ He followed by implementing this concept to improve resin adhesion to enamel surfaces and, in his pioneering research, applied 85% phosphoric acid.⁶ In 1965, Bowen attempted to resolve this issue via N-phenylglycine and glycidyl methacrylate, referred to as NPG-GMA. It is a bifunctional chemical or coupling agent. This indicates that one end of the molecule bonds to dentin while the other polymerizes with composite resin. The bond strengths of these initial systems ranged from 1 to 3 megapascals. The clinical

outcomes associated with these systems were inadequate. This formed what is known as first-generation adhesives.^{7 8}

These systems focused primarily on bonding dental materials, such as resins, to enamel. The composition consisted of an acidic primer, usually phosphoric acid, to etch the enamel surface, followed by an adhesive resin to bond the material. The bonding mechanism relied on mechanical bonding via acid etching, which opened enamel pores, allowing the resin to penetrate and form a mechanical lock. However, these systems were only moderately effective on dentin, and the bond strength was relatively weak. The durability of the bond was also a concern, as it was more susceptible to degradation over time, especially in the moist environment of the oral cavity.⁸ As a result, the first-generation systems laid the foundation for later, more advanced adhesive systems that improved bonding strength and durability. Later generations of adhesive materials from the second generation onwards included improvements to the dual bonding to enamel and dentin, and improvements in ease of use to enhance their clinical performance..

The second generation of adhesives were introduced as an improvement over the first generation in the late 1970s. The aim to improve bond strength and durability was achieved using these adhesives by incorporating chemical bonding mechanisms into these compounds so that they interact with the tooth structure. The main focus was on achieving adhesion by maintaining and bonding the smear layer instead of eliminating it. Usually the bonding process includes etching the enamel with phosphoric acid and then applying a bonding primer that is formulated to improve dentin bonding. More effective than the 1st generation systems, which mainly targeted enamel, this makes it more effective.⁹ There were still some restrictions that applied to that, such as the possibility of some sensitivity after surgery, and the fact that it can degrade over time, particularly when exposed to moisture.

The 1980s saw an important shift in the knowledge and understanding of dentin's histological and physiological properties, which revolutionized adhesive dentistry. Based on these insights, new dentin bonding agents were developed, which could infiltrate the collagen matrix well, and stable, durable bonds were formed.⁹

One of the breakthroughs during this time was the development of the hybrid layer that was discovered by Nakabayashi and his team in 1982, a milestone in the history of dental adhesives. This small zone of interface between dentin and resin was a new mechanism that included both the micromechanical interlocking and chemical interaction. At the same time, third generation adhesive systems developed to address the pitfalls of previous systems, especially for low adhesion to the smear layer and lack of long term performance. They were the first systems to intentionally use chemical bonding as well as micromechanical retention, paving the way for more successful and long-lasting adhesive restorations.^{10 11}

The hybrid layer is a newly identified interface area between adhesive resin and dentin, which is created at the microscopic level, and is a crucial step in the evolution of adhesive dentistry, as defined by Nakabayashi et al. (1982).⁸ They noted that when phosphoric acid is applied to dentin and then the dentin is infiltrated with resin, a distinctive intermingling of demineralized collagen fibers and resin takes place. This zone is called the hybrid layer and plays an important role in the development of a good bond between the resin material and dentin substrate.¹²

The hybrid layer provides good bond performance by micromechanical interlocking, resulting in significantly improved bond strength and durability. The characterization has enhanced our understanding of the complex nature of dentin bonding, which is more complex than enamel bonding because of dentin's higher organic composition and inherent moisture. For any procedure involving dentin, the successful creation of the hybrid layer is believed to be key to long lasting, clinically effective adhesion.¹³

The fourth generation, developed in the 1980s-1990s, was a revolution in adhesive dentistry with the introduction of the concept of the total-etch and the first dentin-duplication concept (the hybrid layer). Because of their high bond strength, durability and good clinical performance, these adhesives are often referred to as the "gold standard."¹⁴

The Total etch process conditions both enamel and dentin with phosphoric acid which provides consistent etching of both surfaces, and ensures proper bonding. This approach is regarded as the "gold standard" and consists of three steps: an etchant, a primer, and a bonding agent. The technique-sensitive etching is very effective, but takes 15–20 seconds, after which the dentin is rinsed and left moist to ensure the collagen doesn't collapse. Hydrophilic primers aid in resin infiltration and hybrid layer formation.¹⁵

The complexity of the previous generation's use led to the development of the fifth generation in the early 1990s. This was a major leap in dental adhesive technology, as it streamlined the fourth generation process. These adhesives were also referred to as "one-bottle total-etch systems," and were actually a combination of the primer and adhesive, which reduced the time and complexity of application while maintaining good bond strength.⁶ The formulation usually consisted of a mixture of hydrophilic and hydrophobic monomers, solvents (ethanol or acetone) and photoinitiators all in one solution. The integration into a single bottle was conceived to minimise the variability in the application process and to minimise technique dependent errors. Acid etching the surfaces with 35-37% phosphoric acid, the primer and bonding agent were mixed together for application at the same time. This method prevented the damage to collagen, and reduced postoperative sensitivity.¹⁵

Self-etching sixth generation adhesives were introduced in the late 1990s as a solution to the problems encountered with total-etch adhesives including moisture sensitivity, technique sensitivity, and post-operative complications. These adhesives simplify the process, as they combine the priming, etching, and bonding steps in fewer steps, for greater clinical reliability. Besides, they are less sensitive to dentin hydration levels. Their formulation has been advanced, with the inclusion of functional monomers like methacryloyloxydecyl dihydrogen phosphate (MDP), which increases the chemical affinity to hydroxyapatite, which strengthens the hybrid layer and bond strength. But because they have relatively high pH, they may not be effective enough to etch the enamel; therefore, selective enamel etching is recommended.^{16 17}

Between 1999 and 2005, 7th generation dental adhesives simplified the process of bonding in restorative dentistry, etchant, primer and bonds all in one step. This streamlined technique diminished errors and postoperative problems. These are all beneficial in general practice as they reduce the risk of over-drying and save time, and are demineralizing, as they acidify enamel and dentin.¹⁸

Seventh generation adhesives became popular because of their ease of use and quick and easy application. They use a single formulation that simultaneously etches, primes and bonds, thereby saving clinical time and decreasing the chance of technique-related failures.¹⁹ Their

characteristics make them particularly well suited for minimally invasive procedures, paediatric dentistry and patients with limited cooperation.⁸

Although they are very convenient from a clinical standpoint, there are significant drawbacks in these systems. They use acidic monomers that demineralize and infiltrate the tooth structure at the same time, however, these monomers are highly acidic and over time will undergo hydrolysis and chemical degradation.²⁰

In addition, water sorption of 7th generation self-etching adhesive is higher when compared to previous generation self-etching primers. This property may reduce resin penetration, lead to voids and have a negative effect on long-term bond integrity.²¹ They show these disadvantages in their performance. The first adhesive system to perform as a 7th generation adhesive has been found to have the lowest bond strength over time.¹⁸ Their reported shear bond strength ranges from 19.80 to 30.30 MPa.¹⁶ To meet such challenges, current research efforts aim at the improvement of their chemical composition, aiming to optimize the ratio of monomers to solvents and to find new monomers with better bond strength and durability.²²

In the 2010s "universal" (also called 8th generation) dental adhesives became multi-purpose systems that would work with a variety of bonding protocols, such as self-etch (SE), etch-and-rinse (ER), and selective enamel etching.⁸ The properties of these adhesives ensure they bond to an extensive array of substrates, both enamel and dentin as well as a variety of restorative materials, regardless of how the adhesive is applied. The chosen technique, however, affects clinical performance: in the SE (etch and prime) mode the etching and priming operations are performed simultaneously, while in the ER (etch and rinse) mode a separate phosphoric acid etching step is required with rinsing and the application of the adhesive.²³

Eight generation adhesives provide superior binding to enamel, dentin, and to difficult substrates like zirconia and metal. They allow no postoperative irritations because they eliminate rinsing and drying steps and employ advanced monomers for stronger and more durable bonding. In dental clinics, it is recommended to use 8 generation adhesives, due to the fact that it is easy to use, reliable and adaptable for any clinical situation.²⁴

One of the important developments in this generation was the use of functional monomers, including 10-MDP, which can bind to calcium in the tooth structure, thus ensuring a long-lasting bond. This bond has been first reported in 2004 by Yoshida et al. by means of X-ray photoelectron spectroscopy (XPS)³¹. 10-MDP also has some mild etching properties which help to maintain tooth structure while increasing the chemical adhesion. In addition, many universal adhesives contain silane that allow better chemical bonding with silicon-based ceramics and resin composite, thus being suitable for direct and indirect restorations.²⁵

These features of these systems result in better bond strength, moisture resistance and decreased dependence on technique.²⁰ In 2010, Voco America introduced Voco Futura bond DC, a commercial eighth generation adhesive that contains nanosize fillers to help improve the bonding performance by promoting better infiltration of the monomer and creation of a hybrid layer, resulting in a longer shelf life.²³ The shear bond strengths of these adhesives reported range from 22.10 to 37.10 MPa, suggesting enhanced mechanical properties compared to previous generations.²⁶

The biocompatibility of general adhesives is lowest among the adhesive systems, hence is good for clinical use.^{27 28} Furthermore, Rosa et al. performed a systematic review and meta-analysis in 2015 that found that when using a mild universal adhesive, bond integrity and long-term performance were significantly improved with selective enamel etching. It was also found, however, that the application of phosphoric acid on dentin prior to the application of adhesive did not increase bond strength but it did increase the risk for post-operative sensitivity.^{20 29} The aim of continuous research is to optimize the formulations of universal adhesives, with the use of optimized solvents and photoinitiators to enhance the polymerization efficiency and technique sensitivity.²²

3. From Total-Etch to Self-Etch Adhesive Systems

A significant shift in dentistry from total-etch to self-etch adhesive systems has occurred in the field of bond strength improvement. New generations of adhesives are specifically developed to fulfill the evolving demands and problems of clinical practice, continuing innovations in adhesive technology.

Total-Etch Systems: These systems (fourth and fifth generation) are based on the acid-etch method developed by Buonocore and use phosphoric acid to both enamel and dentin followed by bonding agent application. The bond strength for these systems is usually between 20 and 30 MPa, which provides adequate bond strength, though requires some fine tuning to avoid postoperative sensitivity and other issues. These work well, but total-etch systems are more susceptible to interference from contaminants such as blood and saliva that can compromise bond strength.^{16 30}

Self-Etch Systems: Sixth, seventh and eighth generation adhesives are self-etch, meaning that the etching and priming functions are combined in one product. The bond strength is usually in the range of 18 to 35 MPa, which is also advantageous because of the low technique sensitivity and risk for postoperative discomfort. Two-step self-etch adhesive have demonstrated greater shear bond strength when compared to total-etch and multimode adhesives. However, in certain cases, especially when total-etch is used to bond to calcium silicate cements, it may be possible to achieve higher bond strength.³¹

The focus of each generation of dental cements has been to increase bonding strength and make application easier. The fourth and fifth generations (total-etch systems) were used mainly for the purpose of maximum bond strength but were more sensitive to the application variables and needed more precise techniques. The sixth through eighth generations (self-etch systems) were designed to be easier to use and more consistent in performance, which sometimes led to a slightly lower but more predictable bond. New developments like universal adhesives seek to combine the benefits of both, to be effective as either total-etch or self-etch adhesives, but with greater strength in a range of clinical scenarios.^{32 8}

4. Evolution of Antibacterial Dental Adhesives

The main purpose of conventional dental adhesives was to establish strong micromechanical and chemical bonds between the restorative materials and dental tissues. While there have been some improvements in binding strength and sealing, these glues generally do not have a natural antimicrobial property. Therefore, the residual microorganisms that remain after cavity preparation, along with bacteria entering through the gaps at the

margins of the cavity, can contribute to the formation of biofilms and the development of secondary caries. To overcome these limitations, antibacterial compounds have been added to the adhesive system to not only inhibit bacterial proliferation at the tooth–restoration interface, but also retain the bonding ability of the adhesive. Several antibacterial agents have been studied in recent decades, such as chlorhexidine, silver nanoparticles, zinc oxide nanoparticles, quaternary ammonium compounds and bioactive molecules. Based on the action of the antibacterial systems, antibacterial dental adhesives can be classified into two general types: releasing antibacterial systems and immobilized antibacterial systems.³³

5. Releasing Antibacterial Agents

Releasing antibacterial systems work by releasing active agents to the environment over time. These include chlorhexidine, the ions of silver and the fluoride-releasing materials. These agents have an initial antibacterial effect but their effectiveness can wane over time as the agents release the compounds. Furthermore, if released continuously, the mechanical properties of the adhesive can deteriorate and the porosity of the material can be increased.¹

6. Immobilized Antibacterial Agents

Immobilized antibacterial systems are composed of antibacterial compounds which are covalently bound and are not mobile after the polymerization process. Their antibacterial effect is mainly through contact inhibition or contact lethality on the bacteria that adhere to the material surface. In dentistry, the most extensively studied immobilized antibacterial agents are the quaternary ammonium compounds, such as 12-methacryloyloxydodecylpyridinium bromide (MDPB). Unlike release systems, immobilized drugs can provide long-lasting antibacterial activity with minimal degradation of drug materials.³⁴

7. . MDPB (12-Methacryloyloxydodecylpyridinium Bromide)

I. Chemical Characteristics

Methacryloyloxydodecylpyridinium bromide (MDPB) is a polymerizable antibacterial monomer, which is a member of quaternary ammonium compounds. It was a specially developed product to be incorporated into dental adhesive systems to give intrinsic antibacterial activity without adverse effect on the adhesive properties. Structurally, MDPB comprises a methacrylate moiety that enables copolymerization with resin monomers and a pyridinium bromide group that confers antimicrobial activity. These functional groups are attached to each other with a hydrophobic alkyl chain, allowing interaction with the bacterial membranes. After the light curing, MDPB is covalently incorporated into the crosslinked resin matrix, thus remaining trapped within the adhesive layer without losing the antibacterial properties. This polymer bound configuration offers sustained antimicrobial effect while reducing the loss of active components, as compared to traditional antimicrobial products with gradual release. MDPB adhesives therefore can help to decrease bacterial colonization at the resin/dentin interface and to prevent secondary caries.³⁵

II. Antibacterial Mechanism and Biological Benefits

Most of the antibacterial effect of MDPB is thought to be due to its quaternary ammonium group. The electrostatic attraction between the cationic surface of MDPB and negatively charged bacterial membranes leads to disruption of membranes, leakage of intracellular compounds and eventual death of the bacteria. The mechanism of action of MDPB is contact killing, as it does not release antimicrobial agents after polymerisation. It has been demonstrated to work against multiple oral microorganisms, including the key pathogen in dental caries and biofilm *Streptococcus mutans*. MDPB has been shown to possess antibacterial activity and inhibitory activity against matrix metalloproteinases (MMPs) and cysteine cathepsins which break down collagen in the hybrid layer. MDPB may have a beneficial effect on enhancing the long-term stability of the resin–dentin bond and on increasing the durability of restorations by inhibiting enzymatic activity. Moreover, its fixed state may decrease the risk of bacterial resistance and have satisfactory biocompatibility.^{1 36}

III. Incorporation into Contemporary Adhesive Systems

MDPB has been used in many current self-etch adhesives, often in conjunction with functional monomers like 10-MDP and fluoride releasing monomers. These bioactive components provide several therapeutic benefits such as hydroxyapatite chemical interaction, anti-bacterial properties, and remineralizing properties towards adjacent dental tissues. Importantly, available evidence suggests that incorporation of MDPB does not adversely affect bond strength or mechanical performance of adhesive materials. Instead, it may improve the biological integrity of the adhesive interface by limiting bacterial penetration and reducing enzymatic degradation. Therefore, MDPB-containing adhesives may be particularly beneficial in high-caries-risk patients, in minimally invasive restorative procedures, and in deep dentin restorations, where effective bacterial control is essential.³⁷

IV. Experimental Evidence on MDPB-Containing Adhesives

Accumulating evidence from laboratory and clinical investigations supports the beneficial effects of MDPB incorporation into adhesive systems. Belmar et al.³⁷ reported that an adhesive containing MDPB and reactive fillers exhibited bond strength comparable to conventional systems when applied to eroded dentin, while demonstrating improved interfacial stability after aging. An increase in elastic modulus overtime further suggested enhanced durability of the adhesive interface. Likewise, Saiprasert et al.³⁸ demonstrated that quaternary ammonium methacrylamide monomers exhibit potent antibacterial activity, as well as improved hydrolytic stability and mechanical performance compared with conventional methacrylate-based materials. Hashimoto et al.³⁹ reported that incorporating MDPB significantly improved antibacterial activity and preserved the durability of the resin–dentin bond by stabilizing the hybrid layer and inhibiting enzymatic degradation. Collectively, these findings highlight MDPB's potential as a bioactive component to enhance the longevity and clinical performance of adhesive restorations.

V. Bond Strength Performance of MDPB-Containing Adhesives

Consequently, using antimicrobial agents in dental adhesives has been associated with the concerns of their effect on bonding and mechanical properties. Ideally, the antibacterial adhesive should be able to give a persistent antimicrobial effect whilst still adhering to the

dental surface. Several investigations have demonstrated that adhesion bond strength is not compromised when methacryloyloxydodecylpyridinium bromide (MDPB) is added to adhesive formulation and may improve the durability of the adhesive bond.⁴⁰

The micro-shear bond strength (μ SBS) and micro-tensile bond strength (μ TBS) are commonly used to assess the bond strength of resin-based materials. These methods provide valuable information regarding the integrity and durability of resin-tooth bond under different ageing conditions. Many studies demonstrate that bond strength obtained with adhesives that contain MDPB is comparable to that of conventional adhesive systems both immediately after bonding and after storage. The long binding ability is due to the anti-bacterial activity of MDPB and its inhibitory activity against collagen-degrading enzymes including matrix metalloproteinases (MMPs) and cysteine cathepsins, all known to play a role in hybrid layer degradation.⁴¹

MDPB has been tested with respect to the efficacy of bonding with enamel and dentin substrate. MDP-containing adhesives have been shown to have good bond strength in enamel while not compromising resin penetration or resin polymerization. MDPB when incorporated into dentin could contribute to the interfacial stability by decreasing the activity of bacteria and the degradation of collagen fibrils exposed in the dentin. This may affect the longevity of restoration in deep dentin restorations, where there is a residual dentinal permeability and dentinal permeability may also be much higher, leading to the increased presence of germs and affecting the restoration's longevity.⁴²

Comparative studies have shown that adhesives containing MDPB can be as effective as, or slightly superior to, conventional adhesives that do not contain any antibacterials. Moreover, functional monomers such as 10-MDP can improve the properties of MDPB-containing adhesives in terms of chemical bond with hydroxyapatite and long-term activity of the antimicrobial effect. The synergistic effects of these components keep the resin–dentin interface intact and may enhance the longevity of adhesive restorations. However, further clinical research in the long-term is warranted to demonstrate the durability of these devices in intraoral applications.^{41 37}.

VI. Antibacterial Efficacy Against Oral Pathogens

One of the main advantages of the use of MDPB in adhesive is its ability to provide antibacterial characteristics at the tooth restoration interface. Biofilm formation and bacterial colonization play an important role in the development of secondary caries, therefore an antibacterial adhesive is proposed as a method to improve the longevity of restorative treatments.¹

S. mutans is a well studied bacterium among oral bacteria because of its well established association with the onset and progression of dental caries. This bacterium is able to attach to tooth surface, organize into structured biofilms and generate organic acid that can lead to demineralization of dental hard tissues. Therefore, the inhibition of the growth of *S. mutans* is considered an important goal when creating antibacterial adhesive systems.⁴³

Several in vitro studies have shown that adhesives that contain MDPB have shown significant antibacterial activity against *S. mutans*. The positively charged quaternary ammonium group of MDPB binds to negatively charged membranes of the bacteria and causes the disruption of these membranes resulting in bacterial death. Since the MDPB is immobilized

in the polymerized resin matrix this is being demonstrated to exert its antibacterial effect mainly by a contact killing mechanism rather than by the release of antimicrobial chemicals.⁴⁴

MDPB also has been shown to affect biofilm development and maturation, as well as reduce bacterial viability. Since biofilms are known to be more resistant to antimicrobial treatment than planktonic bacteria, preventing the formation of the biofilm at the adhesive contact may be of major importance in decreasing the penetration of the biofilm and recurrent caries. Aging processes, salivary proteins, and the thickness of the biofilm on the surface of the material may affect the antibacterial activity of MDPB.

The antibacterial activity of MDPB-containing adhesive has been tested by different laboratory methods. The viability of bacteria is usually determined after exposure to the substance(s) being investigated using colony forming unit (CFU) enumeration. The agar diffusion test is commonly used to evaluate the zones of inhibition around the antibacterial drugs, but in immobilized system like MDPB the antibacterial component will not diffuse into surrounding medium, so the effectiveness of the agar diffusion test may be reduced. In addition, live/dead staining procedures in conjunction with fluorescence microscopy allow the visualization of bacterial cells in the biofilm state both alive and dead on the surface of materials, providing valuable information about the survival and structure of the biofilm. The antibacterial effect of MDPB containing adhesive systems has been proven repeatedly with these test methods in bacterial efficacy studies against cariogenic microorganisms.⁴⁵

VII. Durability and Aging Resistance of MDPB-Containing Adhesives

The success of adhesive restorations in the long term depends not only on the bond strength of the initial cementation, but also on the resistance to degradation in oral conditions. Over time this adhesive interface is constantly subjected to moisture, temperature changes, enzyme activity and bacterial colonization which can compromise bond stability. Therefore, it is essential to determine the durability and ageing properties of antibacterial adhesives to predict their lifelong therapeutic efficacy.⁴²

There are many techniques available for artificial aging with a major focus on imitating the oral environment and determining the strength of adhesive systems. Of these, water storage is probably one of the most commonly used types of aging. If the water exposure is prolonged, hydrolytic degradation of the resin components, plasticization of the polymer matrix and degradation of the hybrid layer can occur. Despite these difficulties, a number of studies have demonstrated that MDPB-based adhesives have acceptable bond strength after water storage, demonstrating acceptable hydrolytic degradation resistance.^{46 42}

Thermocycling is a prevalent method of aging which mimics thermal stresses that occur during the intake of hot and cold foods and drinks. Microleakage and reduction in bond strength can be caused by repeated thermal changes, which cause expansion/contraction strains at the tooth-restoration interface. There is some evidence that adhesives containing MDPB can bond satisfactorily following thermocycling, but this may depend on the adhesive formulation and duration of the thermocycling.⁴⁷

Artificial saliva has been used for storage to better simulate the chemical complexity of the oral cavity. In the aging of artificial saliva, the cumulative effects of moisture, ions and salivary constituents on adhesive stability can be evaluated. Previous studies have demonstrated that the antibacterial activity of MDPB-containing adhesives and their bonding properties were retained for long-term storage in artificial saliva, which are quite satisfactory. However, there is still limited long-term experience and additional studies are required to demonstrate their clinical longevity.⁴⁸

The durability of the hybrid layer is a critical determinant of the longevity of restoration. Degradation of exposed collagen fibrils by matrix metalloproteinases (MMPs) and cysteine cathepsins is recognized as one of the primary mechanisms responsible for deterioration of the resin–dentin bond. By reducing bacterial colonization at the adhesive interface, MDPB-containing adhesives may contribute to preserving the integrity of the hybrid layer and improving long-term bond stability. Nevertheless, further studies are required to clarify whether MDPB directly modulates the activity of endogenous dentinal enzymes.⁴⁹

8. Clinical Studies and Long-Term Outcomes

Although *in vitro* studies have shown antibacterial properties and good bonding performance of MDPB-containing adhesives, these merits need to be validated in a clinical setting to ensure long-term success in the oral cavity. Clinical investigations are essential in providing valuable insight into the success of the adhesive restoration in an intricate set of oral challenges: masticatory forces, thermal cycling, saliva and microbial activity.⁵⁰ There have been many clinical studies on the effectiveness of MDPB-containing adhesive systems over an extended period of observation. Several parameters that are evaluated in this type of research include retention, marginal adaptability, postoperative sensitivity, and secondary caries. Through research, MDPB-based adhesives have proven to be equally or in some cases better therapeutic performance than conventional adhesive systems..⁵⁰

One of the main parameters used to assess long term clinical success of adhesive restorations is retention rate. Currently, there are sufficient clinical data to show that when MDPB is used in adhesion systems, they provide acceptable bond strength during follow-up and their performance is similar to that of traditional adhesive systems. This good retention has been attributed to the bonding stability and ability of the materials to maintain the integrity of the resin/dentin adhesion under functional oral conditions.⁵¹

Another important parameter which affects the longevity of adhesive restorations is marginal adaptation. Marginal integrity failure can allow bacteria to penetrate, lead to microleakage and ultimately result in failure. During the 5 year period, acceptable marginal adaptation has been reported in clinical studies with restorations that were bonded with MDPB containing adhesives. With the antibacterial activity of MDPB, there are indications that it could assist in reducing bacterial colonization at the margin of the restoration, but at this time there is not enough clinical evidence to draw a direct connection between MDPB's antibacterial activity and increased marginal integrity. Further long-term randomized clinical studies are needed for a better understanding of the clinical advantages of adhesive systems containing MDPB.⁵¹

MDPB has great clinical potential for secondary caries prevention. The use of MDPP

adhesives could help reduce the proliferation of bacteria within the bond between the restoration and the tooth structure, which can reduce the risk of reoccurrence of carious lesions, a major reason for replacement of restorations. However, there is a limited amount of direct clinical data available from which to conclude that there is a reduction in secondary caries when using MDPB, and further long term randomized clinical trials are required to substantiate these protection claims. ¹

Although the potential for MDPB-containing adhesive systems has been demonstrated in many short-term clinical studies, there are relatively few long-term clinical studies to support it. Further research with more participants and longer follow-up periods is necessary to give more solid data on long-term clinical effectiveness and caries prevention. ⁵²

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