REVIEW ARTICLE

# MODERN TRENDS AND PERSPECTIVES OF THE DEVELOPMENT OF ADHESIVE DENTISTRY. INNOVATIVE TECHNIQUES FOR THE APPLICATION OF ADHESIVE SYSTEMS

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## ABSTRACT

**The aim:** To study the latest approaches to optimizing the composition and application protocols of modern adhesive systems, which are used during the restoration of defects in hard dental tissues with restorative materials.

**Materials and methods:** Thirty articles published between January 1, 2020 and February 1, 2023 in the scientific databases PubMed, Scopus, and Google Scholar were selected. The selected scientific works contained the results of laboratory studies, systematic reviews, meta-analyses of the physical and mechanical characteristics of adhesive systems with a modified composition or application protocols different from the instructions of the manufacturing companies.

**Conclusions:** The most promising directions for improving adhesive systems are modifications of the composition and protocols of their use with the aim of deactivating matrix metalloproteinases, improving the structure of the hybrid layer due to the creation of a three-dimensional mesh of collagen fibres with optimal properties, the introduction of antimicrobial agents to slow down the growth of bacterial colonies along the line of the adhesive joint. The available research results of modified adhesive systems are often contradictory, which determines the need to develop standardized test methods to obtain more reliable indicators of their physical, mechanical and biological properties. In some cases, the consequences of non-compliance with the recommendations of the manufacturing companies are a significant deterioration of the characteristics of the hybrid layer, adhesive strength, marginal fit, which, in turn, explains the need for further search for an optimized composition and techniques for applying bonding agents to improve the prognosis of restorative treatment.

**KEY WORDS:** adhesive systems, adhesion to tooth dentin, restorative materials, modified composition, adhesive fixation protocols

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## INTRODUCTION

The adhesive ability of some dental materials to the hard tissues of teeth is of great importance in many fields of modern dentistry, in particular for direct photocomposite restorations, tooth splinting, fixation of orthopaedic and orthodontic structures, etc. [1]. To ensure a long-term and reliable connection of heterogeneous materials and hard tissues of the teeth, adhesive systems (hereafter – AS) have been used for a long time, the development and improvement of which was determined by the desire to invent a material that is optimal in terms of its physical, mechanical and biological characteristics, capable of solving most clinical tasks of dentists.

The cause of a large number of complications in restorative treatment is considered to be imperfect adhesion of restorative materials to the dentin of teeth. The presence of a constant flow of dental fluid in the dentinal tubules, the activation of enzymes that destroy the hybrid layer, the high sensitivity of the adhesive preparation technique to the skills of the operator lead to the occurrence of postoperative sensitivity, secondary caries, pulp inflammation and loss of retention of restorations [2]. The introduction into clinical practice of AS of the VII and VIII generations significantly simplified the restoration of teeth due to the reduction of the number of stages of adhesive preparation, on the other hand, the reliability of such restorations in the long term of operation is considered controversial [3]. In contrast to the latest AS, the "gold standard" in restorative dentistry is called the V generation AS, which are used according to the protocol of etch-and-rinse. These ASs have gained considerable popularity due to the proven high strength of the adhesive bond between restorations and tooth tissues during significant periods of observation. However, the application of such AS using the specified technique often causes postoperative sensitivity and inflammation of the dental pulp [3].

Thus, the existing AS have certain disadvantages, which explains the need to optimize their composition and application protocols. The search and implementation of improved approaches in adhesive dentistry will increase the clinical effectiveness of direct and indirect restorations and improve the prognosis of rehabilitation of patients with lesions of hard dental tissues.

## THE AIM

The aim is to study the latest approaches to optimizing the composition and application protocols of modern adhesive systems, which are used during the restoration of defects in hard dental tissues with restorative materials.

## MATERIALS AND METHODS

Thirty articles published between January 1, 2020 and February 1, 2023 in the scientific databases PubMed, Scopus and Google Scholar were selected for the purpose of the study. The following keywords were used for the search: "adhesive systems", "adhesion to tooth dentin", "restorative materials", "modified composition", "adhesive fixation protocols". The selected works contained the results of laboratory studies, systematic reviews, meta-analyses of the physical and mechanical characteristics of AS with a modified composition or application protocols different from the instructions of the manufacturing companies.

## REVIEW AND DISCUSSION

Several ways of increasing the strength and durability of the adhesive bond for V and VII generation AS are proposed, in particular by changing their application protocols. In a meta-analysis of 68 articles, which reported on the results of laboratory studies of the microtensive strength of dentin samples of extracted teeth with photocomposite materials fixed on their surfaces, it was demonstrated that under identical conditions, the indicators of the samples in which AS was applied with the use of additional manipulations reliably exceed the corresponding indicators of the samples made according to the instructions of the manufacturing companies [4]. For V generation AS, such manipulations were an increase in exposure time ($p<0.001$), the use of electrophoresis ($p<0.001$), application of an additional layer of AS ($p=0.05$), active application of etching gel ($p=0.02$) and adhesive ($p<0.001$). Under the condition of using VII generation AS, the same additional means also improved the adhesive strength: increased application time ($p=0.001$), use of electrophoresis ($p<0.001$), double application of AC ($p<0.001$), active application of the etching gel ($p=0.01$) and adhesive ($p<0.001$). Therefore, by applying simple additional manipulations during adhesive preparation, it is possible to increase the strength of the bond between the photocomposite and tooth dentin in laboratory conditions, which requires further study in clinical studies.

The constant movement of dental fluid through the dentinal tubules in the direction from the pulp to the tooth surface causes difficulties in creating a reliable bond between the restorative material and the dentin during adhesive preparation and contributes to the hydrolytic destruction of the hybrid layer. By means of scanning electron microscopy, it was proved that the effect of iontophoresis on the tooth during the application of AS causes a short pause in the simulated movement of dental fluid, increasing the infiltration of AS in the dentinal tubules, both when applying adhesives using the total etching and self-etching techniques. The maximum depth of the formation of adhesive strands in the dentinal tubules for the control groups of the V and VII generations AS reached the level of 100 μm and 8 μm respectively, while the similar indicators for the same AS with the use of iontophoresis were significantly higher and amounted to 170 μm and 70 μm [5].

In order to increase the physical and mechanical properties of AS and bring them closer to natural human dentin, the addition of nanofiller (in particular, hydroxyapatite crystals) to the AS composition is proposed. When studying indicators of microhardness and quality of polymerization, higher values were obtained precisely in samples formed with the help of modified AS compared to the traditional V generation AS. The paper emphasizes the importance of fixed dimensions of the filler (20x20x50 nm) for creating a biocompatible hybrid layer with a high degree of its integration in dentin and, accordingly, achieving optimal characteristics of AS [6].

Another work proved the effectiveness of using biomimetic nanohydroxyapatite to increase the strength of the bond between the composite and dentin. Dentin samples of extracted teeth, the surface of which was treated with nanohydroxyapatite, after thermocycling demonstrated significantly ($p<0.05$) higher dentin microhardness ($46.44 \pm 1.86$ MPa) and the maximum strength of fixation to the restoration material ($14.41 \pm 1.87$ MPa) in contrast to the same indicators of the control group with the traditional AS application protocol ($38.51 \pm 2.37$ MPa and $7.20 \pm 1.10$ MPa, respectively). Similar results can be explained by the phenomenon of remineralization of dentin due to the formation of calcium and phosphate ion deposits, provided by the presence of nanohydroxyapatite [7].

In a similar way, the mechanical properties of the VII generation AS, modified with a solution of β-tricalcium phosphate of different concentrations, were improved.

In this work, higher indicators of adhesive strength were obtained – 27.75±3.15 MPa and 30.50±3.25 MPa for 5% and 10% solutions of the doped AS, on the other hand, the average strength value for the samples of the control group was found at the level of 24,7±3.64 MPa [8].

Reliable adhesion of restorative materials is ensured primarily by the creation of a hybrid layer on the surface of the prepared dentine, consisting of collagen fibers impregnated with AS. During the operation of restorations, AS gradually lose their properties due to permanent cyclic masticatory load, the catalytic action of dentin enzymes, saliva and bacteria, significant temperature fluctuations. Enzymes released after conditioning of mineralized dentin, in particular matrix metalloproteinases-2, 8 and 9 (hereafter – MMP), activate the degradation of collagen fibres and reduce the quality of the hybrid layer, which in turn reduces the strength of the adhesive bond [3, 9, 10].

To limit the influence of these enzymes, it is proposed to use high-molecular aminosaccharides, for example, chitosan, the compounds of which reduce the activity of MMP, create additional cross-links between collagen fibres, demonstrate odontotropic properties, improve the physical and mechanical characteristics of AS, and have an antimicrobial effect [11, 12]. In a comparative study of the bond strength of V and VII generations AS, used in accordance with the manufacturers' recommendations or with prior application of a 2.5% chitosan solution on the surface of the dentin for 1 minute, it was established that 24 hours after the restoration of hard tissue defects of the extracted tooth samples according to the proposed protocol, the maximum tensile strength values, on average, by 5.77 MPa and 5.87 MPa exceeded the values of the samples produced by the classical techniques of V and VII generations AS, respectively. After 6 months, the same indicators were already 9.06 MPa and 5.33 MPa higher for similar groups of samples [11].

Greater effectiveness of chitosan is proven by the results of a similar study of adhesive strength by the tensile method of samples of intact (group I) and demineralized (group II) dentin. Under the condition of applying the same universal AS for both groups using the self-etching technique and after 6 months of artificial aging, the average strength indicators were 33.39±9.92 MPa and 13.93±5.34 MPa, respectively. At the same time, in the control groups of samples, the above-mentioned indicators were lower and amounted to 32.20±5.85 MPa for intact substrate and 9.74±4.90 MPa for demineralized one [13].

An approach to use the positive properties of chitosan by adding its nanoparticles directly to the AS composition is proposed in order to increase the number of ionic bonds between the chitosan molecules themselves, AS monomers and the collagen network of dentin, which allows creating a strong three-dimensional structure capable of withstanding significant mechanical loads and the influence of the dentin enzymes [14]. It is also possible to introduce chitosan already into the structure of the restorative photocomposite material to obtain a homogeneous mixture. The reliability of the marginal adhesion of the photocomposite to the tooth tissues was studied on the restored samples by recording the depth of penetration of dyes at the dentin-restoration boundary. Thus, it was found that the marginal adhesion of the chitosan-modified photocomposite (the average depth of dye penetration was 0.01204±0.00281 nm for V generation AS and 0.01182±0.00311 nm for VII generation AS) was better, than in samples where defects were restored with the same photocomposite material without additional components (0.01834±0.00181 nm for V generation AS and 0.01294±0.00219 nm for VII generation AS). An important aspect is the non-significant ($p>0.05$) differences between the indicators of the studied and control groups of samples in which self-etching AS was used [12].

Other MMP inhibitors include a 2% solution of chlorhexidine bigluconate (CH), a 17% solution of ethylenediaminetetraacetate (EDTA) and a 2% solution of doxycycline (DO), which are also applied to the surface of the dentin after conditioning and before applying AS [15]. In the study of the strength of the adhesive bond by the shear method with the use of V generation AS, immediately after the production of the samples, the average indicators in the studied and control groups did not differ significantly ($p>0.05$). The value of the average strength for the samples treated with CH was 21.60±5.73 MPa, with EDTA was 19.50±3.44 MPa, with DO was 19.80±3.89 MPa, only with AS was 19.20±2.55 MPa. After 6 months of storage, the strength indicators for all groups of samples, except for those formed with the use of a 2% CH solution, significantly decreased, but did not show significant differences according to the results of statistical analysis – 21.18±5.72 MPa for the CH group, 17.45±3.48 MPa for the EDTA group, 18.30±3.80 MPa for the DO group and 16.44±2.48 MPa for the group of samples using only AS [15].

In a similar work, the effect of applying 2% CH (group I), 10% α-tocopherol (group II) and 1% quartzetin (group III) on the strength of the adhesive bond after 24 hours and 6 months of storage of samples similar to the previous study was studied using a universal AS based on the self-etching protocol. The average indicators of adhesive strength after 24 hours also did not differ significantly ($p>0.05$) and were, on average, 13.27±2.09 MPa, 14.08±3.7 MPa, 13.02±3.22 MPa, 15.77±2.5 MPa in control, I, II and III groups, respectively. At the same time, after 6 months of artificial aging, the same indicator in the samples made using CH was found at the level of 13.11±1.92 MPa, which was significantly ($p<0.05$) higher than the corresponding values of the control, II and III groups – 11.24±2.68 MPa, 7.60±4.08 MPa and 10.12±3.56 MPa [16].

The results of a meta-analysis of 33 scientific works performed between 2002 and 2022 are known, which report on indicators of microtensive strength after 24 hours, 6 and 12 months of artificial aging of samples made using various MMP inhibitors. [17]. According to the authors' conclusions, only the use of 0.2% CH solution reliably increases the strength value, regardless of the generation of AS and the term of artificial aging, while the 2% CH solution did not significantly affect the adhesion parameters.

The opposite approach to creating a reliable hybrid layer is considered to be the effect on the structure of collagen dentin fibers before applying AS. A 3% solution of riboflavin, a 6.5% solution of proanthocyanidin, and a 5% solution of glutaraldehyde are used for this, which cross-link collagen fibres, increase their diameter, prevent collapse, and improve resistance to the action of enzymes, which, in turn, allows you to create a thicker and a more organized hybrid layer [3, 10, 18]. On the other hand, these substances prevent the movement of collagen molecules relative to each other under the influence of mechanical stresses arising in dentin, thus increasing the stiffness of collagen fibres [19]. A meta-analysis of 45 laboratory studies emphasized the positive effect of epigallocatechin-3-gallate, carbodiimide, EDTA, glutaraldehyde, proanthocyanidin, and riboflavin on adhesion strength after 12 months of storage, regardless of the methods of their application and pre-etching of dentin with orthophosphoric acid. At the same time, in certain works included in the meta-analysis, an immediate increase in the shear strength indicators was registered only in those samples in which the dentin surface was treated with proanthocyanidin, in contrast to the control groups of samples with traditional or modified AS application protocols [19].

In another work, on the contrary, the average strength of samples, made with a modified 3% solution of riboflavin AS, was recorded at the level of 10.16±4.19 MPa after 12 months of storage, which was lower than the similar value of the control group – 13.58±3.86 MPa, while the use of riboflavin in the form of a separate aqueous solution, which was applied to the surface of the dentin before the application of AS, made it possible to increase the average index of adhesive strength to 14.73±6.81 MPa [10].

After treatment of the surface of demineralized dentin with a 3% carbodiimide solution, followed by the application of V generation AS, an increase in the average shear strength was recorded from 20.89±1.84 MPa in the control group of samples to 25.73±1.94 MPa in the study group, and after 24 hours of storage from 18.6±2.64 MPa to 24.41±2.92 MPa, respectively [18].

During microtensive tests and scanning electron microscopy of samples of extracted teeth, an increase in tensile strength was determined in those samples on the dentin surface of which a 0.5% (group I) or 1% (group II) solution of phytic acid was applied for 60 seconds before the application of universal AS [20]. Average adhesive strength indicators were 38.37±4.69 MPa (group I) and 35.21±5.41 MPa (group II), which were significantly ($p<0.05$) higher than the strength value of samples made without additional components of adhesive preparation – 18.80+3.68 MPa. Electron microphotographs revealed the organization of a thicker hybrid layer and deeper strands of AS in the samples of groups I and II, which could be explained by deeper demineralization of dentin due to the action of phytic acid. In addition, the application of the specified solution stimulated the formation of cross-links between collagen fibers, prevented their collapse, which generally contributed to a better integration of the monomers of the universal AS to the surface of the dentin [20].

Using confocal laser microscopy, the ability of the new functional monomer N-(3,4-dihydroxyphenethyl)methacrylamide (DMA) to simultaneously form non-covalent bonds with type I dentin collagen fibres and reduce MMP activity was proven [21]. In a comprehensive study, scientists found that applying DMA for one minute to the dentin surface before applying AS increased the adhesive strength and improved the marginal fit of restorations after 10,000 thermocycles in the range from +5$^0$C to +55$^0$C relative to restorations made according to the traditional total etching protocol. Thus, the average tensile strength of samples with DMA was 31.85±8.10 MPa, and that of samples of the control group was 22.63±6.40 MPa. The value of nanoleakage of restorations, calculated as a percentage by computer analysis of microscopy data, was 21.29±4.13% in the studied group, and 50.41±4.82% in the control group [21]. In a meta-analysis of 7 similar laboratory studies, higher mechanical strength, lower solubility, and lower degree of water absorption of AS based on methacrylamides and urushiol were proven compared to traditional methacrylate AS immediately after the production of samples and after 6 months of artificial aging [22].

Zinc compounds also have a simultaneous effect on inhibition of MMP activity and storage of collagen fibres in dentin [23]. In addition, these compounds provide a greater degree of remineralization of dentin along the line of the adhesive joint. In the experiment, the rate of collagen degradation was significantly lower after applying a 3% aqueous solution of zinc oxide to the surface of the dentine, and its value was almost 4 times lower than when using a 2% solution of CH. Electron micrographs of samples formed using the recommended protocol did not reveal signs of porosity and leakage of the hybrid layer [23].

According to scientists, increasing of the number of cross-links between the collagen fibres of dentin and deactivating the MMP only prolongs the service life of restorations, but does not ensure their reliability for a long time, which is explained by the gradual degradation of the hybrid layer. A more effective way to improve the quality of the adhesive bond, according to the conclusions of a meta-analysis of 8 articles, may be deproteinization and destruction of dentin collagen fibres by applying sodium hypochlorite and antioxidants after etching with orthophosphoric acid followed by the application of AS [24]. This treatment of dentin leaves a rough surface with small pits, which provides adhesion similar to that in enamel. In the works included in the meta-analysis, an increase in adhesive strength was demonstrated in samples made using a solution of sodium hypochlorite in concentrations from 5% to 10%, its exposure time from 1 to 2 minutes, V or VII generations AS [24].

A logical way to reduce the probability of the occurrence of secondary caries and, accordingly, to increase the reliability of restorations is to add agents with antimicrobial properties to AS [25-27]. In contact with the surface of such an AS, the permeability of bacterial cell membranes changes, which leads to their destruction. On the basis of a systematic review of the scientific literature on the use of antibacterial drugs in the composition of AS, the authors concluded that the highest efficiency in increasing the strength of the adhesive bond and bactericidal activity in relation to Streptococcus mutans is provided by universal AS modified with quaternary ammonium methacrylate [25]. In the same review, less effective antimicrobial drugs in the structure of AS are described, for example, 2% chlorhexidine, 6% sodium hypochlorite, 0.01% urushiol, dimexide, bezalkonium chloride, etc. Nevertheless, in a parallel study, no significant (p=0.087) difference was recorded in the strength characteristics of AS with ammonium methacrylate and conventional AS of the VII generation. After 24 hours of storage, these indicators were 17.5±2.5 MPa and 12.7±1.6 MPa, and after 3 months of storage in artificial saliva they were 12.3±1.4 MPa and 14.7±2.2 MPa, respectively [26].

The introduction of cetylpyridine hydrochloride into the AS composition allows to reduce the rate of degradation of the adhesive layer and prevent the development of caries around the restorations due to the reduction of esterase activity of oral cavity bacteria [27]. In laboratory conditions, the antibacterial effect of such AS was proven, but in a clinical study, complications in the form of secondary caries occurred even more often than with the use of traditional AS of the VII generation [3]. This can be explained by the unstable rate of release of antibacterial agents and the gradual decrease in their concentration due to chewing movements.

In the study of the growth rate of Streptococcus mutans biofilms on slices of samples prepared using AS doped with titanium dioxide nanoparticles, a stable and long-lasting antimicrobial effect was recorded. After 12 months of sample storage, the number of relative luminescence units (RLU) recorded by the computer analyser was more than three times lower in the samples with modified AS compared to the control group, i.e. 48,000 RLU and 164,000 RLU, respectively [1]. In another work, the values of the adhesive strength of AS with nanoparticles of titanium dioxide (group I of samples), in comparison with the same AS without additional components (group II) were studied. After 3 months, the obtained average values were 12.99±2.53 MPa and 14.87±2.02 MPa for the samples of groups I and II, and after 6 months of storage they were 11.37±1.89 MPa and 14.19±2.24 MPa, respectively [2]. Thus, the modification of AS with antimicrobial nanofillers in laboratory conditions significantly worsened the strength of the adhesive bond of the samples in the short term of the study.

Addition of penicillin V to the AS composition also enhances their antibacterial properties but does not affect the physical and mechanical properties [28]. The maximum adhesive strength for samples made with alloyed AS was, on average, 36.7 MPa±10.9 MPa, and that for samples with ordinary AS was 32.2±7.9 MPa. No significant differences were found in the flexural strength indicators – 21.3±1.6 MPa and 18.7±3.9 MPa, the modulus of elasticity – 492.3±98.4 MPa and 515.1±77.7 MPa, the maximum compressive strength – 65.8±11.3 MPa and 77.5±7.6 MPa, respectively, for the studied and control groups of samples.

Nisin, a food additive used as a preservative, is considered another modifier proposed to increase the antimicrobial activity of AS. In the study of 4 groups of samples: the control group, where the samples were formed using V generation AS, and 3 groups in which nisin was added to AS in concentrations of 1%, 3% and 5%, it was established that the number of colony-forming units (CFU) of Streptococcus mutans was, on average, $0.51x10^{7}$±0.01 CFU, $0.36x10^{7}$±0.03 CFU, $0.34x10^{7}$±0.02 CFU and $0.33x10^{7}$±0.04 CFU, respectively. At the same time, the tensile strength in the same groups was 38.3±2.3 MPa, 35.6±2.1 MPa, 22.3±1.0 MPa, and 27.1±1.6 MPa [29]. Thus, increasing the concentration of nisin to 3% or 5% significantly reduces the adhesive strength of AS, while the use of a 1% solution provides acceptable adhesive strength and pronounced antibacterial properties.

The creation of monomers resistant to all factors of destruction, i.e. hydrolytic degradation, enzymatic cleavage of organic components by esterase of bacteria, saliva, dentin, etc., is considered a promising direction of AS development [22]. At the same time, such monomers, included in the composition of AS, should not reduce their physical and mechanical properties, durability and effectiveness. Dental adhesive doped with a 5% solution of benzyldimethyldodecylammonium chloride is considered one of the examples of such modified AS. Immediately after production, the samples demonstrated a high degree of bacteriostatic and bactericidal action against Streptococcus mutans, maximum and specific tensile strength, hybrid layer thickness, and low cytotoxicity, similar to the classic V generation AS. However, after 10,000 thermocycles in the temperature range from +5$^0$ C to +55$^0$ C, the antimicrobial properties of such AS were lost, while the physical and mechanical properties of the samples remained unchanged [30].

## CONCLUSIONS

During the restoration of defects of hard dental tissues using adhesive technologies, complications related to the imperfection of adhesive systems often arise. To date, the development of adhesive dentistry is taking place in several directions, the most promising of which are modifications of the composition and protocols for the use of adhesive systems with the aim of deactivating matrix metalloproteinases, improving the structure of the hybrid layer due to the creation of a three-dimensional mesh of collagen fibres with optimal properties, the introduction of antimicrobial agents to slow down the growth of Streptococcus mutans colonies along the line of the adhesive joint.

The available results of studies of the characteristics of modified adhesive systems are often contradictory, which determines the need to develop standardized methods of their testing to obtain more reliable indicators of their physical, mechanical and biological properties. In some cases, the consequences of non-compliance with the recommendations of the manufacturing companies are a significant deterioration of the characteristics of the hybrid layer, adhesive strength, marginal fit, which, in turn, explains the need for further search for an optimized composition and techniques for applying bonding agents to improve the prognosis of restorative treatment. There are almost no results of the use of modified compositions and techniques of applying adhesive systems in clinical conditions with long periods of observation, which determines the prospects for future studies.

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