

Enhancing Adhesive Longevity: Two-Year Evaluation of Resveratrol-Integrated Adhesive Agents

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Abstract: Antioxidants may improve the biocompatibility of resin-based materials, while adhesive interface durability is essential for clinical success. This study evaluated the effect of an antioxidant Resveratrol (RES) incorporation on adhesive agents' microtensile bond strength (μ TBS) after 2 years. Five different adhesive agents (G-aenial Bond (GC)/G, Optibond All-in-One (Kerr)/O, Gluma Self Etch (Kulzer)/Gl, Clearfil S3 Bond (Kuraray)/C, and Nova Compo-B Plus (Imicryl)/N) were used. In the experimental groups, 0.5 μ M RES was added. Caries-free human third molars were used for the μ TBS test. Occlusal enamel was removed, and dentin surfaces were abraded with silicon carbide paper to standardize the smear layer. RES was incorporated into adhesives in test groups, and adhesive systems were applied per manufacturers' instructions. A composite build-up was created ($n = 6$). Samples were stored in distilled water for 2 years and stick-shaped specimens were prepared. The μ TBS testing was performed and the failure patterns were evaluated under stereomicroscopic examination. Differences among groups were analyzed using ANOVA and Tukey's multiple comparison test ($p < 0.05$). Adhesive failure was identified as the dominant failure type in every group. Compared to baseline measurements, RES incorporation did not result in a reduction in μ TBS values for any of the tested adhesive agents ($p > 0.05$). The highest μ TBS values after RES addition were recorded in the O and C groups. No significant differences were found between O and C, or among Gl, G, and N; however, the differences between these two subgroups were statistically significant. The incorporation of RES may be used to enhance the biocompatibility of adhesive agents without exerting a negative effect on their bond strength in long-term. Further studies on additional material properties are required.

Keywords: Adhesive agent, antioxidant, resveratrol, microtensile bond strength

1. Introduction

In modern restorative dental practice, adhesive techniques form the basis of most minimally invasive procedures [1]. Adhesive systems must exhibit appropriate physicochemical properties together with favorable biological behavior to ensure predictable clinical performance [2]. Consequently, substantial research has focused on optimizing these characteristics to improve the longevity and reliability of adhesive restorations. A durable union between dentin and the restorative material is fundamental for the longevity and reliability of restorations [3]. Antioxidants incorporated into adhesive formulations have been shown to reduce hydrolytic and free-radical-mediated degradation processes [4], leading to extensive research into various antioxidant compounds. Among these, resveratrol (RES) has attracted attention due to its efficacy even at low concentrations [5].

RES is a naturally occurring polyphenol that has attracted considerable attention because of its potent antioxidant activity. It is predominantly found in grape-derived tissues and several plant-based food

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sources, where it functions as a secondary metabolite involved in defense mechanisms [6]. In addition to its powerful antioxidant properties, RES exhibits a wide range of biological effects. It is notable for its effects in controlling inflammation, preventing the development of cancer, protecting nerve tissue and slowing down the ageing process [7,8]. It also exhibits enhanced biocompatibility by mitigating oxidative stress, limiting the formation of free radicals, and protecting against DNA damage [9]. The addition of RES to adhesive formulations has been shown to markedly reduce cytotoxic effects and provide genoprotective benefits for fibroblasts, thereby enhancing the overall biocompatibility of these materials [9].

The durability of the resin–dentin interface is compromised when the depth of adhesive monomer penetration does not correspond to the level of collagen demineralization [10,11]. Under these conditions, collagen fibrils located at the base of the hybrid layer become susceptible to enzymatic degradation over time [12]. Such progressive breakdown of the hybrid layer promotes microleakage and nanoleakage, thereby increasing the risk of secondary caries and ultimately contributing to the clinical failure of the restoration [13]. RES has been reported to suppress the activity of matrix metalloproteinases (MMPs), particularly members of the MMP family such as MMP-2 and MMP-9 [14,15]. In addition, it inhibits glycolytic acid production and glucosyltransferase activity in *Streptococcus mutans* thereby providing potential protective effects against cariogenic biofilms [16].

The impact of RES on adhesive performance may vary depending on the formulation of the adhesive system. The antioxidant addition should enhance the biocompatibility of the material without compromising its mechanical or adhesive properties to ensure reliable clinical outcomes. Assessment of bonding effectiveness is commonly performed using tensile-based testing methods, which provide valuable information regarding the mechanical integrity and durability of adhesive interfaces [17].

Our previous investigation demonstrated that incorporating 0.5 μM RES into dentin adhesive systems did not compromise short-term μTBS values, indicating that RES may enhance the biological profile of adhesive formulations without adversely affecting their immediate adhesive performance [18]. However, short-term outcomes alone are insufficient to predict the clinical reliability of adhesive interfaces, as degradation processes primarily manifest over extended periods. Therefore, comprehensive long-term assessments are required to better approximate the material's clinical behavior.

Although previous findings have demonstrated that RES-containing adhesive systems may improve dentin bond durability and exhibit antibiofilm potential [19], available evidence regarding their long-term adhesive performance after prolonged aging remains limited, particularly among different one-step self-etch adhesive formulations. Since the long-term stability of the adhesive interface is directly associated with restoration survival and secondary caries prevention [20], further long-term investigations are clinically relevant to determine whether RES incorporation can provide sustainable adhesive stability under extended aging conditions.

This study evaluated the impact of RES addition on the μTBS of five commercially available one-step self-etch adhesives after two years of water aging. It was hypothesized that the inclusion of RES would preserve the bonding performance of the adhesive systems and would not result in a significant reduction in bond strength following long-term storage.

2. Materials and methods

2.1. Microtensile bond strength (μTBS) testing

The study was approved by the Ege University Human Ethics Committee (Approval No. 16-10.1/1), and written informed consent was obtained from all participants enrolled in the study prior to tooth extraction. This study utilized caries-free human third molars, which were first disinfected in 0.1% thymol solution and subsequently preserved in distilled water until the preparation of specimens. The roots were separated 2 mm apical to the cemento–enamel junction (CEJ), after which the occlusal enamel was removed 2 mm coronal to the CEJ using a low-speed, water-cooled diamond saw (Isomet; Buehler, Lake Bluff, IL, USA) to expose flat mid-coronal dentin. Following complete removal of the

pulpal tissue, the dentin surfaces were finished with 600-grit silicon carbide (SiC) abrasive paper under continuous water irrigation for 60 s to create a standardized smear layer. The prepared teeth were randomly distributed into ten experimental groups ($n = 6$), in accordance with established protocols for microtensile bond strength testing [21,22].

Five one-step self-etch adhesives—G-aenial Bond (GC)/G, Optibond All-in-One (Kerr)/O, Gluma Self Etch (Kulzer)/GI, Clearfil S3 Bond (Kuraray)/C, and Nova Compo-B Plus (Imicryl)/N—were evaluated with (+) and without (−) RES incorporation. Based on previous findings demonstrating enhanced fibroblast viability at 0.5 μM RES [9], this concentration was selected for the experimental groups. RES (Sigma-Aldrich, Saint Louis, USA) was added directly to the adhesive bottle immediately before application and homogenized by gentle agitation to prevent antioxidant degradation. According to the manufacturers' guidelines, all adhesive materials were applied and subsequently photoactivated for 20 s using an LED curing unit (Elipar Freelight, 3M ESPE, St. Paul, MN, USA).

The composite resin (Filtek Z250; 3M ESPE, St. Paul, MN, USA) was incrementally placed onto each bonded surface in two 2-mm-thick layers. Each increment was light-cured for 20 s according to the manufacturer's recommendations. Subsequently, the specimens were stored in distilled water at 37°C for a period of two years. Following the aging procedure, each tooth was sectioned perpendicular to the adhesive interface using a diamond saw to obtain beam-shaped specimens ($1.00 \pm 0.003 \times 1.00 \pm 0.003 \text{ mm}^2$). Peripheral beams containing enamel were excluded; twenty central beams from each group were randomly selected for microtensile testing ($n = 20$).

The beams were attached to the testing jig with cyanoacrylate adhesive and subsequently tested in tension at a crosshead speed of 1.0 mm/min using a microtensile testing system (Microtensile Tester, BISCO Inc., Schaumburg, IL, USA). Following fracture, the exact cross-sectional dimensions of each specimen were determined with a digital caliper, and μTBS values were computed and expressed in MPa. Values obtained from beams originating from the same tooth were averaged and treated as a single experimental unit for statistical analysis, in accordance with μTBS testing guidelines. Fracture surfaces were evaluated with a stereomicroscope (LG-P52, Olympus, Tokyo, Japan) at $\times 50$ magnification and categorized into adhesive, cohesive within dentin, cohesive within resin, or mixed failure types. The assessments and testing procedures were performed in a blinded fashion by another investigator using pre-assigned group codes. The design of the study is presented in Figure 1.

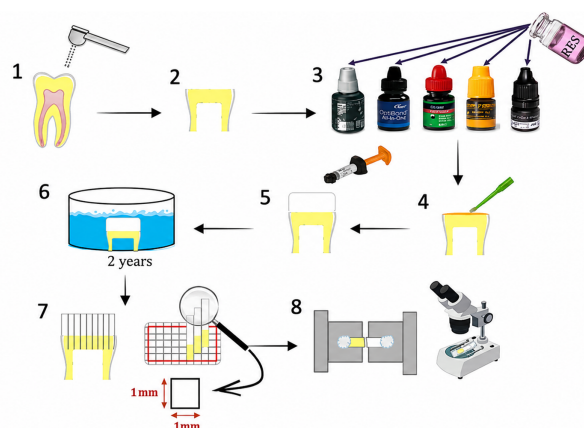


Figure 1. Workflow of RES-modified adhesives and long-term μTBS testing: (1,2) preparation of caries-free human third molar specimens; (3) preparation of five adhesive systems with or without 0.5 μM resveratrol (RES); (4) adhesive application and polymerization; (5) incremental composite resin build-up; (6) storage in distilled water for two years; (7) preparation of $1 \times 1 \text{ mm}^2$ beam specimens; and (8) microtensile bond strength testing followed by stereomicroscopic failure mode analysis.

2.2. Statistical analysis

Statistical analysis was carried out using GraphPad Prism software (version 5.0; GraphPad Software, La Jolla, CA, USA). Data are presented as mean $\pm$ standard deviation (SD). The Shapiro–Wilk test was used to assess normality, whereas Bartlett’s test was applied to evaluate the equality of variances. One-way analysis of variance (one-way ANOVA) was used to determine differences between groups. Pairwise comparisons among groups were subsequently carried out using Tukey’s post-hoc test whenever significant differences were present. The level of statistical significance was set at $\alpha = 0.05$.

3. Results

The mean μ TBS values of all experimental groups are shown in Figure 2. After two years of water aging, adhesive-type failures predominated in all groups, whereas mixed failures were detected only in specimens from the O (+) and O (–) groups. No cohesive failures in dentin or composite were observed (Figure 3).

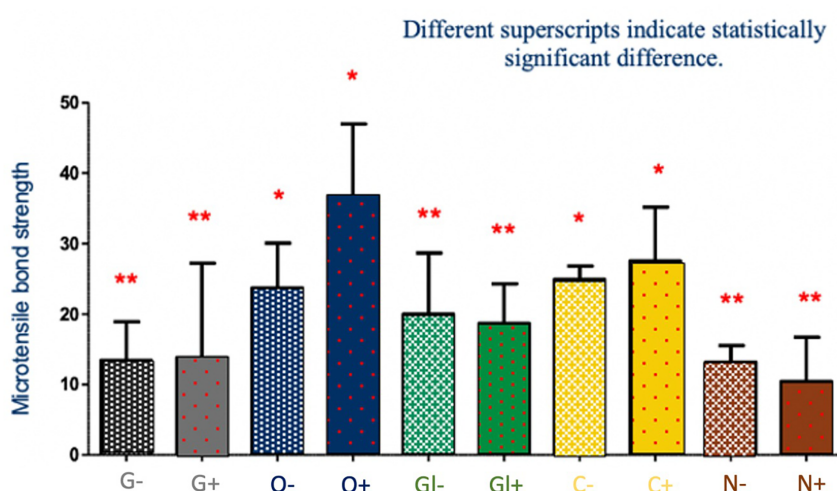


Figure 2. μ TBS values of the adhesive systems with and without RES incorporation after two years of water aging. (G-aenial Bond (GC)/G, Optibond All-in-One (Kerr)/O, Gluma Self Etch (Kulzer)/GI, Clearfil S3 Bond (Kuraray)/C, and Nova Compo-B Plus (Imicryl)/N, +: RES incorporation, –: without RES). (Different superscripts indicate statistically significant differences among the groups. Groups marked with the same symbol (* or **) were not significantly different from each other ($p > 0.05$), whereas groups marked with different symbols (* versus **) showed statistically significant differences ($p < 0.05$))

RES incorporation did not result in a reduction in μ TBS for any of the tested one-step self-etch adhesives when compared with their corresponding control groups. Among the materials evaluated, O (+) exhibited the highest mean bond strength, followed by C (+). Statistical analysis revealed no significant difference between O (+) and C (+) groups ($p > 0.05$).

For the control formulations (–), the μ TBS values of G, GI, and N groups were statistically similar ($p > 0.05$). This pattern was also maintained in the RES-modified versions of these adhesives, with no significant differences detected among their μ TBS means ($p > 0.05$). Within each adhesive system, RES addition caused an increase in μ TBS to varying degrees; however, for G, GI, and N groups, this increase was not statistically significant.

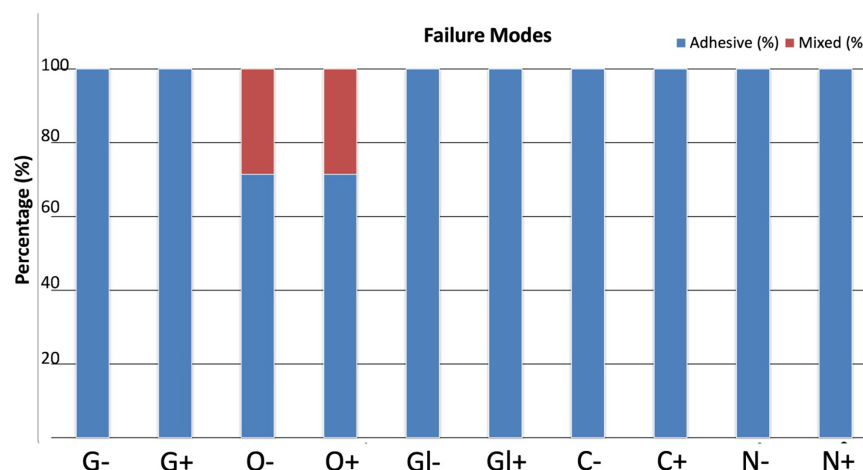


Figure 3. Failure modes of tested groups. (G-aenial Bond (GC)/G, Optibond All-in-One (Kerr)/O, Gluma Self Etch (Kulzer)/GI, Clearfil S3 Bond (Kuraray)/C, and Nova Compo-B Plus (Imicryl)/N, +: RES incorporation, -: without RES)

Comparisons between adhesive systems showed that both O (+/–) and C (+/–) groups demonstrated significantly higher μ TBS values than G, GI, and N groups, regardless of RES incorporation ($p < 0.05$). Conversely, the three lower-performing adhesives (G, GI, and N groups) did not differ significantly from one another ($p > 0.05$).

4. Discussion

Dental materials are in constant contact with the oral environment; therefore, achieving optimal biocompatibility is a fundamental requirement in restorative dentistry. Although a completely biocompatible material is not yet achievable, alternative approaches have been explored to minimize the cytotoxic effects of resin monomers, and antioxidants have emerged as promising candidates in this regard [23]. Importantly, strategies aimed at improving the biological performance of adhesives must not compromise their adhesive capacity.

RES is a naturally occurring polyphenol abundant in grapes, berries and nuts, and is distinguished by its strong antioxidant properties [24,25]. In addition to its antioxidative effects, previous studies have demonstrated its antimicrobial potential. It has been reported that RES exhibits bacteriostatic effects against several Gram-positive species [26], while other investigations have shown that RES-rich *Polygonum cuspidatum* extracts suppress glycolytic acid formation, glucosyltransferase (GLT) activity [27], and various virulence factors of *Streptococcus mutans* [28]. These findings highlight RES as a multifunctional molecule capable of influencing both biological and microbiological pathways relevant to resin–dentin interface degradation.

Polyphenols promote collagen cross-linking and remineralization through their phenolic hydroxyl groups while also inhibiting MMP activity [29–31]. These phenolic hydroxyl groups contribute to the preservation of collagen integrity within the hybrid layer by suppressing MMP-mediated collagen degradation through multiple mechanisms [32]. RES, a naturally occurring polyphenol, may therefore reduce nanoleakage and improve dentin–resin bond strength when applied after contamination by preserving the structural integrity of the dentin–adhesive interface. This effect has been attributed particularly to the inhibition of MMP-9 activity, which enhances the resistance of dentin collagen to enzymatic degradation and promotes collagen cross-linking and stabilization [33].

The varying diffusion properties of adhesive monomers, which play a critical role in the adhesion process, may explain the differing interactions observed between RES and various monomer combinations. Incorporation of RES into adhesive systems has been reported to enhance dentin bond strength and

provide beneficial effects against secondary caries [19]. Furthermore, previous dose–response analyses demonstrated that RES exhibits concentration-dependent biological effects, with higher concentrations showing cytotoxicity, whereas 0.5 μM significantly increased cell viability and provided the maximum protective effect against dentin bonding agent–induced oxidative stress and DNA damage. Therefore, based on its favorable biological profile and protective effects, 0.5 μM RES was selected as the optimal biologically effective concentration for the present study [9].

Although RES did not adversely affect the bond strength of the adhesive interface, degree of conversion, or flexural strength, it significantly improved the antibacterial properties of the adhesive system. In addition, RES contributed to adhesive durability by biologically modifying and stabilizing collagen fibers, promoting collagen cross-linking, reducing nanoleakage formation, and inhibiting MMP activity. Through these mechanisms, RES enhanced the resistance of the hybrid layer to enzymatic and hydrolytic degradation, thereby supporting the long-term stability of the resin–dentin bond [34,35].

The bond strength of adhesive systems is commonly assessed using macro- and micro-tensile or shear testing methods [36]. Among these, the μTBS test is considered the most reliable due to its ability to distribute stresses more homogeneously across the adhesive interface and its sensitivity in detecting subtle differences in bonding performance [37]. For this reason, μTBS testing has become a widely accepted method for evaluating adhesive effectiveness and comparing bonding strategies. Accordingly, μTBS analysis was employed in the present study to determine the effect of RES addition on adhesive durability.

Aging is a critical factor affecting adhesive longevity, and degradation processes may become evident within months or extend over several years. Kitasako et al. reported a significant decline in μTBS from day 3 to day 90 following the placement of a one-step adhesive system *in vivo*, demonstrating the dynamic nature of resin–dentin interface degradation [38]. Similar patterns have been confirmed in multiple studies, showing decreased bond strength after relatively short storage periods [39]. This deterioration is primarily attributed to hydrolytic degradation of resin components and enzymatic breakdown of collagen. Water sorption into the polymer matrix further weakens the interface by reducing mechanical properties and interacting with residual unreacted monomers [11]. Based on findings from comparable aging studies, a 2-year evaluation period was considered appropriate for assessing long-term stability in the present work [40]. Previous studies have demonstrated that the application of different antioxidant agents as primers to the dentin surface prior to adhesive procedures increased bond strength after 10,000 thermal cycles [29,35]. No improvement in microtensile bond strength was observed with antioxidant-modified adhesive systems. Bond strength decreased following 6 months of water storage and subsequently remained unchanged up to the 12-month time point [41]. Another study reported that antioxidant addition enhanced only the immediate bond strength without affecting long-term outcomes [42]. Likewise, the present study found no significant differences in the long-term stability of RES-modified adhesive systems.

Our previous research examined the cytotoxicity of various one-step adhesives using MTT, DCF, 8-OHdG, and Comet assays and demonstrated that RES exerted a protective effect on fibroblasts exposed to adhesive agents [9]. Although these results were promising, long-term biocompatibility and bonding data were necessary to determine whether RES could be incorporated into adhesive formulations without impairing their clinical potential. In the present study, five self-etch, one-step adhesives—G-aenial Bond, Optibond All-in-One, Gluma Self Etch, Clearfil S3 Bond, and Nova Compo-B—were tested with or without 0.5 μM RES. Caries-free third molars were used for μTBS evaluation, and specimens were stored in distilled water for two years. After aging, tensile loading was performed at 1.0 mm/min, and fracture modes were analyzed under stereomicroscopy. Across all groups, adhesive failure was the predominant fracture pattern, consistent with typical outcomes for aged interfaces. RES incorporation did not significantly decrease μTBS in any adhesive system ($p > 0.05$). Optibond All-in-One and Clearfil S3 Bond demonstrated the highest μTBS values following RES addition. While no significant differences were detected between these two adhesives, or among G-aenial Bond, Gluma Self Etch, and

Nova Compo-B, the three lower-performing adhesives formed a statistically distinct group from the two higher-performing ones.

The short-term μ TBS values obtained in previous work [18] indicated that Optibond All-in-One, Clearfil S3 Bond, and Nova Compo-B Plus produced higher bond strengths than G-aenial Bond and Gluma Self Etch, with no difference between the latter two. Importantly, the addition of RES did not reduce μ TBS in any material. After two years of aging, the overall trend remained consistent: adhesive failure dominated, Optibond All-in-One and Clearfil S3 Bond yielded the highest μ TBS values, and G-aenial Bond, Gluma Self Etch, and Nova Compo-B Plus remained statistically similar. No RES-containing formulation exhibited decreased μ TBS. Another study reported that RES application enhanced the adhesive strength of dental adhesives to enamel following bleaching [43]. It has been determined that RES, by inhibiting the activity of MMPs on cleaned dentin surfaces, promotes collagen remineralization and significantly improves bond strength by reducing nanoleakage and substantially increasing the stability of the hybrid layer [19,44].

The improved bonding performance of Clearfil S3 Bond and Nova Compo-B Plus in terms of μ TBS has been associated with 10-MDP, which exhibits a high affinity to hydroxyapatite and contributes to the formation of durable nanolayered interfaces. [18,45]. However, in the present 2-year evaluation, Optibond All-in-One—despite lacking 10-MDP—showed the highest μ TBS, suggesting that factors other than MDP content may influence long-term performance. Polyphenols show chemical compatibility with MDP without compromising the chemical bonding performance of MDP with dentin [44]. Resin chemistry, solvent composition, hydrophilicity, and polymer network stability may all contribute to these outcomes. Antioxidants have been incorporated into adhesive systems to counteract spontaneous polymerization, inhibit free radical degradation, and reduce hydrolysis of resin monomers [4]. Nevertheless, certain limitations cannot be overlooked, as RES is prone to sunlight-induced degradation and oxidation by environmental oxygen [46]. Previous studies have assessed the long-term durability of adhesive–dentin interfaces using collagenase aging and thermocycling [19,47]. However, the most established aging protocol is prolonged water storage [48]. Consistent with this rationale, the present study evaluated the performance of adhesive–dentin bonded specimens (+/–RES) after two years of water storage, and no adverse effects on μ TBS were observed under these conditions. RES demonstrated compatibility with all tested adhesives and did not compromise bonding integrity, reinforcing its potential as a biologically favorable additive for adhesive dentistry. In addition, nanoleakage analysis and SEM-supported failure mode evaluations were not performed, limiting the comprehensive characterization of interfacial microstructural alterations and fracture patterns. Furthermore, physicochemical properties of the adhesive systems after RES incorporation, including viscosity, polymerization behavior, and handling characteristics, were not evaluated. Since the findings were obtained solely under *in vitro* conditions, future studies should investigate the long-term clinical performance of these adhesive systems under more clinically relevant conditions. Future research should explore additional material properties, including polymerization behavior, nanoleakage patterns, enzymatic resistance, and mechanical stability under more clinically relevant conditions. Long-term *in vivo* studies and evaluations using different adhesive categories are also warranted to further substantiate the potential of RES as a functional biomodifier in adhesive dentistry.

5. Conclusion

Within the limitations of this *in vitro* investigation, the incorporation of RES into one-step self-etch adhesive systems did not exert any detrimental effect on their long-term microtensile bond strength after two years of water aging. These findings suggest that RES may be incorporated into adhesive formulations as a promising bioactive additive capable of enhancing the biological profile of adhesive agents without compromising their long-term adhesive performance.

Considering that degradation of the resin–dentin interface is a multifactorial process associated with hydrolytic, enzymatic, and chemical degradation pathways, preservation of adhesive stability

over time is of substantial clinical importance. From a clinical perspective, maintaining long-term adhesive integrity may contribute to reducing restoration failure, restoration replacement frequency, and secondary caries risk, which remain major challenges in adhesive restorative dentistry. Therefore, RES-modified adhesive systems may represent a clinically applicable and translational approach for the development of more durable and biologically enhanced adhesive restorations without altering conventional bonding protocols or increasing clinical complexity.

Nevertheless, the findings of the present study should be interpreted within the limitations of an *in vitro* design. Long-term *in vivo* studies and evaluations using different adhesive categories are also warranted to further substantiate the potential of RES as a functional biomodifier in adhesive dentistry.

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Availability of Data and Materials: The data that support the findings of this study are available from the Corresponding Author upon reasonable request.

Ethics Approval: Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent Informed consent was obtained from all individual participants included in the study.

Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

RES	Resveratrol
μTBS	Microtensile Bond Strength
G	G-Aenial Bond
O	Optibond All-in-One
GI	Gluma Self Etch
C	Clearfil S3 Bond
N	Nova Compo-B Plus

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