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IP Indian Journal of Conservative and Endodontics

Journal homepage: https://www.ijce.in/

Review Article

Comparative evaluation of the effect of various antioxidants on the shear bond strength of the composite resin to the bleached enamel: A systematic review and metaanalysis

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Abstract

In order to assess and compare the impact of different antioxidants on the shear bond strength of composite resin to bleached enamel, this study aimed to do a systematic review of the literature and meta-analysis. Bleaching is considered as the conservative and less invasive option for treating discolored tooth. The shear bond strength of composite resin to bleached enamel may be negatively impacted by bleaching byproducts. From January 2017 to July 2023, two reviewers separately searched the Cochrane, PubMed, and Google Scholar databases for relevant material using MeSH words, text words, and Boolean operators.. evaluation of the risk of bias for in vitro research conducted using the Quality Assessment Tool for In Vitro Studies (QUIN Tool). RevMan 5.4 was used to apply the meta-analyses using the random effects model (RevMan 5.4, The Nordic Cochrane Centre, Copenhagen). A Q test was used to evaluate heterogeneity, and I^2 statistics were used to quantify it. Out of the 60 studies that were initially recovered, eight were chosen for a systematic review, and eight of those were able to be included in the meta-analysis. With a normalized mean difference of 6.05 (95% CI = 4.97 to 7.12; Z value = 10.99), grape seed extract had the highest shear bond strength values of all ten antioxidants.

Antioxidant therapy is thought to be a suitable way to increase the shear bond strength of bleached teeth. Among all the antioxidants grape seed extract is the most effective antioxidant in restoring the composite resin's shear bond strength to bleached enamel.

Keywords: Antioxidants, Shear bond strength, Bleaching

Received: 25-01-2025; **Accepted:** 26-02-2025; **Available Online**: 31-03-2025

1. Introduction

Tooth discolouration may arise from both internal and external sources. Conventionally, these discolorations can be managed with a veneer or crown; more cautiously, whitening is an option. Because of its proven effectiveness and patient appeal, tooth whitening is a common dental procedure.[1] High-concentration sodium perborate, carbamide, or hydrogen peroxide solutions can be used to bleach non-vital teeth. These solutions are typically deposited and left in the pulp chamber for a few weeks, with occasional adjustments made throughout the anticipated.[2] Following intracoronal bleaching, a composite resin restoration is needed to cover the cavity. This helps to minimize root canal failure by preventing germs from recontaminating the tooth. Since post-whitening methods frequently contain peroxide and residues inside the dentin tubule, which might degrade composite resin adhesion and exacerbate microleakage, it is not recommended to restore the tooth right away after bleaching. By preventing vinyl radical composite resin from spreading, these molecules will result in the early termination of the polymer chain. Furthermore, they will produce polymers with so little mechanical strength that the bonding strength weakens, resulting in microleakage and poor adhesion.[3]

One of the negative consequences of bleaching is that it might weaken the shear connection between composite resin restorations and the tooth surface.[4] Oxygen, a

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http://doi.org/10.18231/j.ijce.2025.003

breakdown product of hydrogen peroxide, reduces bond strength after bleaching because it interferes with resin entry into the dentinal tubules and hinders resin polymerization.[5]

Delaying the composite restorations for 1-3 weeks was recommended to overcome this problem. However, restorative operations cannot be carried out right after bleaching due to this waiting period. After bleaching, a number of techniques have been put up to restore the weakened connection, including:

1. Removal of superficial layer of enamel
2. Treatment with alcohol before the restoration
3. Use of adhesives containing organic solvents
4. Application of antioxidant agents

Antioxidants are frequently applied because they reverse the damaged bonding and restore the bleached surface's altered redox potential. They are advised before bonding so that the bonding process can start right away for the clinician.[5] Antioxidant treatment before bonding operations appears to successfully replace the delay of restorations or orthodontic bracket cementation. Following the bleaching treatments, antioxidant treatments such sodium ascorbate, green tea, aloe vera, tocopherol, and sodium bicarbonate have shown promising efficacy in reversing the transitory negative effects of teeth whitening and avoiding the need to delay restorations.[6]

In order to clarify the relative efficacy of various antioxidants in boosting the shear bond strength of composite resin to bleached enamel, this systematic review attempts to thoroughly assess the body of available literature.

2. Materials and Methods

2.1. Protocol and registration

The PROSPERO International Prospective Register of Systematic Reviews, maintained by the National Institute for Health Research, has registered the current systematic review (registration number: CRD42023431088). The Cochrane Collaboration's guidelines for systematic reviews were followed in the conduct of this review.

2.2. Literature search

From January 1, 2017, to July 31, 2023, a thorough search was conducted in Medline using resources such as PubMed, Scopus, Web of Science, and Google Scholar.

Table 1 summarizes the search phrases and words utilized. Major endodontic journals were also searched for in-press papers that could not be located in databases. We manually searched the reference sections of every article that was included to find any more that weren't found using the aforementioned techniques. The English-language articles were taken into account.

For PUBMED, the following search limits were set.
Filter: Title/Abstract
Publication date: 1-1-2017 to 31-07-2023
Language: English

2.3. Eligibility criteria

Based on the components of the PICOS inquiry, the following search strategy was defined using the controlled vocabulary (MeSH terms) and free terms:

1. Population (P): Extracted non- carious human permanent teeth bleached with peroxides.
2. Intervention (I): Application of anti-oxidants to the bleached enamel surfaces of extracted non carious human permanent teeth before bonding.
3. Comparison (C): Bleached enamel where anti-oxidants are not applied prior to bonding.
4. Outcome (O): The composite resin's shear bond strength to the bleached enamel.
5. Study design (S): Invitro studies

The inclusion and exclusion criteria listed in **Table 2** were used to choose the studies:

2.4. Data collection process

A standardized form in Microsoft Office Excel 2013 (Microsoft Corporation, Redmond, WA, USA) was used to extract the data. The titles and abstracts of every document were evaluated independently by two review authors. **Table 3** presents an analysis of the features of the included research. All of the research that might be pertinent were found in full. They were chosen for thorough investigation if they seemed to fit the inclusion criteria or if the title and abstract included insufficient information to allow for a definitive judgment. Two review authors evaluated the full-text papers separately and twice.

A standardized form in Microsoft Office Excel 2013 (Microsoft Corporation, Redmond, WA, USA) was used to extract the data. The titles and abstracts of every document were evaluated independently by two review authors.

Table 3 presents an analysis of the features of the included research. All of the research that might be pertinent were found in full. Those that seemed to fit the requirements for inclusion or for which the abstract and title had insufficient information to clearly A third reviewer or discussion and consensus were used to settle any disputes about the listed studies' eligibility. Only papers that met all the requirements for admission were accepted, including in vitro studies assessing the composite resin's shear bond strength to bleached enamel conducted on extracted human permanent teeth.

2.5. Assessment of risk of bias

The selected studies' quality was individually appraised using the Quality Assessment Tool For In Vitro Studies (QUIN Tool), which considered the following twelve different criteria: clearly stated aims/objectives, detailed explanation of sample size calculation, detailed explanation of sampling technique, details of the comparison group, detailed explanation of methodology, operator details, randomization, method of measurement of outcome, outcome assessor details, blinding, statistical analysis, and presentation of result.

2.6. Meta-analysis

Meta-analyses were conducted using the random effects model and RevMan 5.4 (The Nordic Cochrane Centre, Copenhagen). Heterogeneity was measured using a Q test and quantified using I^2 statistics. Data on mean and standard deviation were acquired from selected research. The effect of antioxidant treatment on composite shear bond strength to bleached enamel was thought to be the most significant outcome.

3. Results

3.1. Search strategy

Figure 1 depicts a flowchart of the PRISMA Statement-based study selection process. The electronic screening of PubMed and Google Scholar yielded 60 articles. After deleting duplicates, we evaluated 35 full-text papers based on their titles and abstracts for this study. A total of 19 items were reviewed for eligibility, and 11 of them were excluded due to the following reasons:

1. Unbleached control group was taken in 8 studies
2. Tensile bond strength was assessed as outcome in one study
3. Antioxidants were applied on bovine teeth in one study
4. One study evaluated the shear bond strength between orthodontic brackets and enamel.

Hence total 8 articles were included for qualitative analysis

3.2 Risk of bias in individual studies

The above table summarizes the risk of bias for the considered studies. (**Table 4**). Except for one study conducted by Moharram et al, which revealed a low risk of bias, all of the included studies presented with a moderate risk of bias. All of the studies specified their aims and objectives, but only one of them included the estimation of sample size. All studies provided enough details about the comparison group as well as an explanation of the methodology. None of the studies provided information about the outcome assessors. In six investigations, the results were appropriately presented, and the statistical analysis was adequately documented.

3.3. Meta-analysis

In studies including more than one anti-oxidant, all relevant experimental intervention groups from the study were pooled into one group. Similarly, in studies with more than one control (no anti-oxidant) group, all relevant control groups of the study effects model were applied, or else ($I2 \leq 50\%$), a fixed effects model was used to combine into a single group, as suggested in the Cochrane Handbook [Ref]. If the test demonstrated significant heterogeneity ($I2>50\%$), a random effects model was employed. Otherwise, if $I2 \leq 50\%$, a fixed effects model was utilized.Antioxidants considerably increased bond strength compared to control groups (**Figure 2**A) ($p<0.00001$). The meta-analysis included twelve comparisons from eight trials. Separate analyses were done for each of the antioxidants used in many studies, including sodium ascorbate, pomegranate extract, grape seed extract, and green tea extract (**Figure 2**B, C, D, and E). The funnel plot to analyze publication bias for compressive strength revealed a higher potential of publication bias since the papers included had an uneven distribution (**Figure 2**F).

Table 1: Search strategy in pubmed database

S.No.	Category	Keywords
1	Population	Extracted non- carious teeth [MeSH] OR extracted sound teeth [MeSH] AND bleached OR bleaching OR Tooth Bleaching[Mesh]
2	Intervention	Antioxidants [MeSH] OR antioxidant[MeSH] OR natural Antioxidants [MeSH] OR synthetic Antioxidants [MeSH] AND dental enamel [MeSH] AND before bonding [MeSH] OR prior bonding [MeSH] composite resin[MeSH] OR adhesive resin[MeSH]
3	Comparison	Bleached enamel [MeSH] OR Bleached teeth[MeSH] AND no antioxidant[MeSH] OR no antioxidants[MeSH] before bonding [MeSH] OR prior bonding [MeSH]
4	Outcome	Shear bond strength [MeSH] OR Micro shear Bond strength [MeSH].
5		1 AND 2 AND 3 AND 4

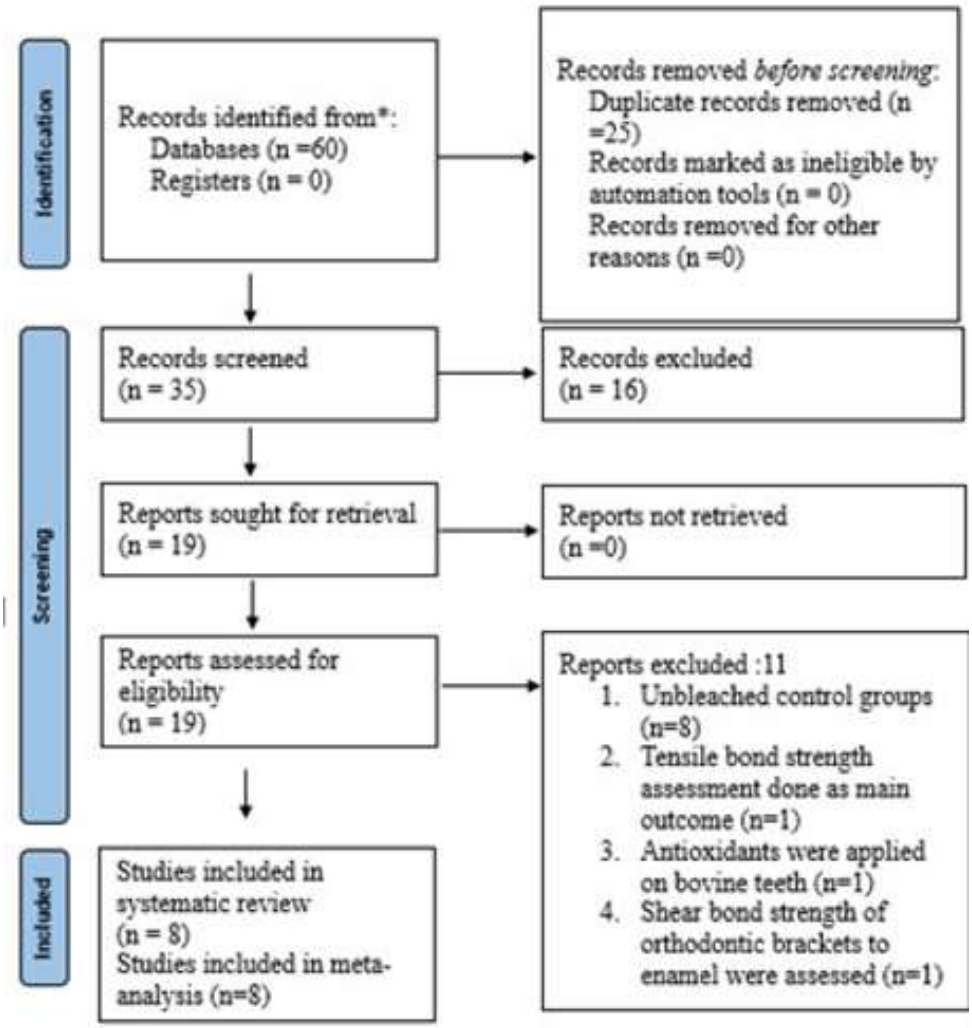

Figure 1: Flow diagram for study identification

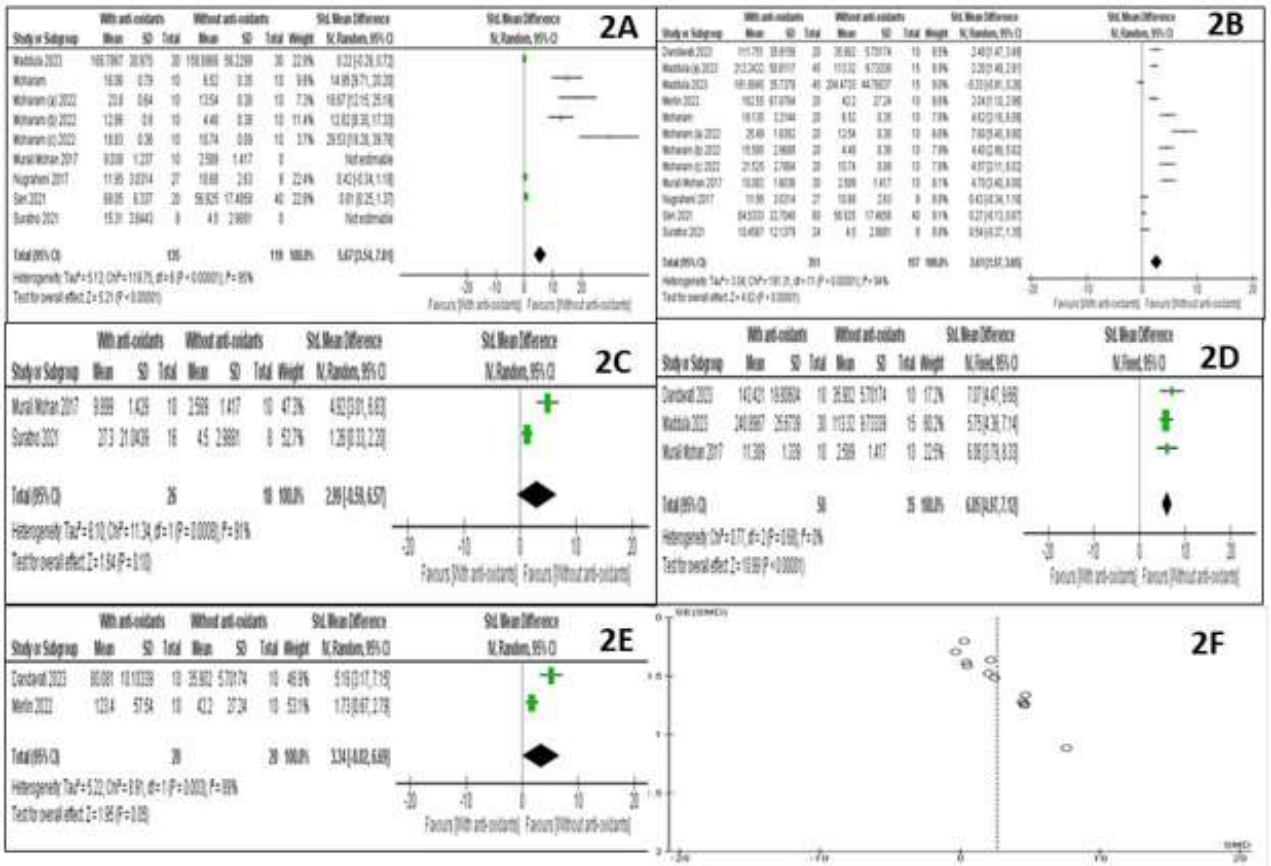

Figure 2: A: Comparison of overall shear bond strength among the study groups with and without antioxidants; **B:** Comparison of shear bond strength among the study groups with and without sodium ascorbate antioxidant; **C:** Comparison of shear bond strength among the study groups with and without pomegranate extract antioxidant; **D:** Comparison of shear bond strength among the study groups with and without grape seed extract antioxidant; **E:** Comparison of shear bond strength among the study groups with and without green tea extract antioxidant; **F:** Assessment of publication bias for shear bond strength

Table 2: Selection criteria for the studies

Inclusion criteria	Exclusion criteria
Invitro studies.	Reviews, editorial letters, case reports, case series & randomized and nonrandomized clinical trials.
Studies that evaluated the effect of the use of at least one antioxidant (natural or synthetic) on the shear bond strength of composite resin to bleached enamel.	Studies which evaluated tensile, and micro-tensile bond tests and experimental group in which antioxidants are not applied.
Only studies conducted from January 2017 to July 2023 are included.	Studies conducted before January 2017 and after July 2023
Allows the selection of English journal articles.	Articles published in languages other than English
Studied done only on extracted human teeth were included.	Studies done on bovine teeth
Studies where Control group involves the bleached enamel where anti-oxidants are not applied prior to bonding.	Studies where Control group involves the unbleached enamel were excluded.

Table 3: Data extraction table

S.No.	Author of study	Year and Study design	Study sample	Bleaching agent	Antioxidants	type of restoration		Results
1	Tunjung Nugraheni and colleagues	2017 Invitro study	9	35% H2O2	0.025 ml of 35% sodium Ascorbate.	**Bonding agent**	**Composite resin**	Application frequency of 35% sodium ascorbate effect on shear bond strength of composite resin restoration in bleached dentin by 35% H2O2.
						bonding agent (Tetric N-Bond Universal, Ivoclar Vivadent)	Composite resin restoration (Z 350, 3M Espe, USA).	
2	Murali Mohan T and colleagues	2017 Invitro study	40	30% H2O2	10% Sodium ascorbate 10% Pomegranate peel extract 10% Grape seed	bonding agent (Adper single bond, 3M ESPE, USA)	Composite resin (Filtek Z 100, 3M ESPE, USA,	Among the antioxidants, 10% Grape seed extract application after bleaching showed better bond strength.
3	Pooja sen et al	2021 Invitro study	100.	35% H2O2	Beta-carotene gel Sodium Ascorbate solution Alpha-tocoferol gel	Meta P & Bond	Composite resin (3M Filtek Z250XT Composite Syringe)	The mean shear bond strength values of Sodium Ascorbate solution showed significantly high bond strengths than Betacarotene gel and 5 Alpha-tocoferol gel.
4	Indes Rosmalisa Suratno et al and colleagues	2021 Invitro study	32	40% of H2O2	5% pomegranate extract gel 10% pomegranate extract gel 10% ascorbic acid extract gel	_	Nano hybrid composite resin	The pomegranate gel extract as an antioxidant increased the shear bond strength of the composite resin restoration after the 40% hydrogen peroxide bleaching application.
5	Merlin Ann Joseph and colleagues	2022 Invitro study	30.	40% H2O2	2% Olive leaf extract 2% green tea extract	_	The self-adhesive composite resin (Dyad Flow Self	Shear Bond Strength for the 2% grean tea Extract group was higher than

							Adhesive Composite, Kerr)	the olive leaf extract and control group.
6	Lamiaa M. Moharam and colleagues	2022 Invitro study	60	White smile Power Whitining	10% açai berry extract 10% sodium ascorbate prepared gels	experimental etch and rinse (ER) adhesive and a commercial ER adhesive (Solobond M)]	nanohybrid resin composite	Açai berry extract is a powerful antioxidant agent, that has the potential to instantly restore the bleached enamel depleted SBS. The commercial adhesive has successfully restored the depleted SBS of the bleached enamel than the tested experimental adhesive.
7	Durga Charishma et al and colleagues	2023 Invitro study	120	35% H2O2	10% sodium ascorbate 5% grape seed extract 5% pine bark extract).	Single Bond Universal Adhesive	Composite resin (Fltek Z 250 XT USA)	All the antioxidants' immediate application could reverse compromised bond strength. Among them, 5% grape seed extract shows the highest increase in shear bond strength.
8	Divyashree D Dandavati et al and colleagues	2023 Invitro study	60	40% H2O2	6.5% proanthocyanidin 5% green tea extract		Incremental composite build up using Teflon mold	Application of antioxidants on bleached enamel reversed the compromised bond strength of composite restoration. The application of proanthocyanidin proved superior followed by green tea extract.

Table 4: Risk of bias assessment table

Criteria	Dandavati 2023	Maddula 2023	Merlin 2022	Moharam 2022	Murali Mohan 2017	Nugrahen i 2017	Sen 2021	Suratno 2021
Clearly stated aims/objectives	2	2	2	2	2	2	2	2
Detailed explanation of sample size calculation	0	0	0	2	0	0	0	0
Detailed explanation of the sampling technique	NA	NA	NA	NA	NA	NA	NA	NA
Details of comparison group	2	2	2	2	2	2	2	2
Detailed explanation of methodology	2	2	2	2	2	2	2	2
Operator details	0	0	0	0	0	0	0	0
Randomization	NA	NA	NA	NA	NA	NA	NA	NA
Method of measurement of outcome	2	2	2	2	2	2	2	2
Outcome assessor details	0	0	0	0	0	0	0	0
Blinding	2	2	2	2	2	2	2	2
Statistical analysis	1	2	2	2	2	1	2	2
Presentation of results	2	2	2	2	2	2	2	2
Total Score	13	14	14	16	14	13	14	14
Total Score (in %)	65	70	70	80	70	65	70	70

4. Discussion

The purpose of this systematic review and meta-analysis is to assess and compare the effect of various antioxidants on the shear bond strength of composite resin to bleached enamel. According to the statistical analysis, when compared to the control group, applying antioxidant agents prior to adhesive repair considerably increased the shear binding strength of composite resin to bleached enamel.

According to the quality evaluation about the available research, all the studies included presented with a moderate risk of bias[1,3,4,5,6,8,9] except for one study done by Moharram et al,[7] which demonstrated a low risk of bias.

The examined literature contained numerous in vitro research, including two systematic reviews. One systematic review was published in 2017; the other in 2021. The inclusion criteria for the former are less stringent, and no quantitative analysis was conducted. Furthermore, it excludes numerous newly published research because it was published in 2017.[11] The later study, published in 2021, solely looked at the influence of natural antioxidants on the shear bond strength of composite resin to bleached enamel[12] and, according to the quality evaluation of the available studies, none had a low risk of bias, compromising the quality of the data obtained by this systematic review. As a result, it was convenient to undertake a current review and quantitative analysis of the available information on the topic.

Among all the 8 studies included in this systematic review and meta-analysis 7 studies used varying concentrations of hydrogen peroxide were used as bleaching agent and one study by lamia et al used White smile whitening power as bleaching agent. The diversity seen among the bleaching treatments may have an influence on the antioxidant therapy findings; consequently, a uniform bleaching technique should be established for additional investigations on this topic, in order to minimize this potential bias. All the studies showed heterogenicity in sample size taken, storage condition, concentrations and time of applications of antioxidants type of restoration placed and the crosshead speed of universal testing machine. Despite heterogeneity, all ten antioxidants studied in this systematic review and meta-analysis improved the shear bond strength of composite resin to bleached enamel.

Bleaching, as described by the American Dental Association, entails using an oxidative chemical to change the material's light-absorbing and/or light-reflecting properties, improving its value (whiteness).[13] Extracoronal whitening is the most popular, effective, and conservative treatment for stained teeth.[17] Bleaching agents can affect the chemical composition of teeth, lowering calcium and phosphate levels in enamel and dentin.[10] Antioxidants enable free-radical polymerization of adhesives to proceed without early termination, resulting in reversal of the impaired bonding.[11] Metanalysis was done on all ten antioxidant compounds included in this study, including sodium ascorbate, pomegranate extract, grape seed extract, and green tea extract, which were used in more than one study. Additional antioxidants were found but not metaanalyzed because they were all reported in a single study.

Sodium Ascorbate, a sodium salt of ascorbic acid, is a powerful antioxidant that extinguishes responsive free radicals in organic systems.[14] Tunjung Nugraheni et al found that if teeth were bleached with 35% H2O2 and then treated with 35% sodium ascorbate multiple times, the shear bond strength of composite resin increased. This study used sodium ascorbate in gel form for increased ease and control of application.[3] Because SA is hydro soluble and biocompatible, it can be used orally and in the food business widely. Furthermore, there is proof that SA has no detrimental effects on dentin metalloproteinase.[2] According to material safety assessments, sodium ascorbate poses a larger health risk than oligomeric proanthocyanidins.[18]

Green tea catechins (GTCs) are the primary antioxidative components, consisting of four major epicatechin (EC) derivatives: EC (6.4%), epigallocatechin (19%), EC gallate (ECG - 13.6%), and EGC gallate (EGCG - 59%). Green tea contains EGCG, the most active and abundant catechin. This water-soluble and nontoxic chemical has the capacity to kill free radicals.[16] Green tea polyphenols' hydroxyl groups, which aid in the binding and neutralization of free radicals, are directly related to their antioxidant properties. According to previous research, utilizing 2% green tea extract as an in-office procedure to repair bleached enamel's lost shear bond strength is a viable option.[6]

Pomegranate peel extract has been proven to effectively remove free radicals and reduce oxidative stress by donating hydrogen atoms, preventing chain reactions that convert superoxide to hydrogen superoxide. The high antioxidant activity of pomegranate extract is due to the strength of the extracted component. One of the components in the extract are tannin compounds; for example, punicalagin, which is categorized as a ellagitannin and is a donor of antioxidant activity in pomegranate extract gel compared to other constituents.[5]

Grape seed extract is composed of oligomeric proanthocyanidin (OPC) in the form of monomeric

phenolic chemicals such as catechin, epicatechin, epicatechin 3 0 gallate, and free flavanol monomer. They possess free radical scavenging and antioxidant properties.[15] OPCs have been widely used in medicine to treat a variety of vascular diseases.[19] Proanthocyanidin-rich foods include grape seed extract, cocoa beans, pine bark extract, cranberries, lemon tree bark, and hazelnut tree leaves. OPCs possess antiviral, antibacterial, anticarcinogenic, anti-inflammatory, and antiallergenic properties. When 6.5% grape seed extract was applied immediately afterwards, Nair et al. (2018) discovered that the bond strength reverted, outperforming other antioxidants.[9]

Proanthocyanidin stabilizes and promotes the crosslinking of Type I collagen fibrils through proline hydroxylation, increasing dentin's mechanical characteristics.[10] The success of PACs can be related to their specificity to free radicals, as well as the availability of several donating sites that entrap superoxide radicals, hence increasing the proanthocyanidins' scavenging potential.[2] When material safety data were investigated, oligomeric proanthocyanidins showed no mutagenic effects.[1]

To summarize, the findings of this systematic review and meta-analysis may be clinically relevant because, despite a lack of clinical evidence, the benefits of using certain antioxidants prior to post-bleaching immediate adhesive restorations were confirmed by available in vitro data. Among the four antioxidants subjected to meta-analysis, grape seed extract (z = 10.99) outperformed sodium ascorbate (z = 5.21), green tea (z = 1.95), and pomegranate extract (z = 1.64). As a result, in the current meta-analysis, grape seed extract was found to be more effective in restoring the shear bond strength of composite resin to bleached enamel.

5. Limitations

This systematic review and meta-analysis includes investigations conducted in vitro. To get a clinically significant conclusion, randomized controlled trials must be carried out. The use of multiple antioxidants at varying doses and application durations may induce bias due to heterogeneity in molecular structure and antioxidant activity. More standardized in vitro research with low risk of bias, as well as clinical trials should be done in this approach.

6. Conclusion

According to the findings of this systematic review and meta-analysis, applying all antioxidants after bleaching, regardless of type, form, concentration, or duration of application, can improve shear bond strength. Antioxidant therapy is therefore considered an appropriate approach for enhancing the Shear bond strength of bleached teeth. The level of Shear bond strength following antioxidant treatments may vary depending on the type of antioxidants utilized. In the current meta-analysis, grape seed extract is found to be more efficient in restoring the shear bond strength of composite resin to bleached enamel.

7. Source of Funding

None.

8. Conflict of Interest

None.

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Cite this article: Salman A, Warhadpande MM, Dakshindas D, Rathod YV. Comparative evaluation of the effect of various antioxidants on the shear bond strength of the composite resin to the bleached enamel: A systematic review and metaanalysis. *IP Indian J Conserv Endod*. 2025;10(1):9–19.