REVIEW ARTICLE

Antibacterial Properties and Shear Bond Strength of Titanium Dioxide Nanoparticles Incorporated into an Orthodontic Adhesive: A Systematic Review

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Abstract

Objective: The present review was conducted to test whether the addition of titanium dioxide (TiO_2) nanoparticles (NPs) within orthodontic bracket adhesives would alter their properties and assess their antimicrobial activity against cariogenic microorganisms in addition to noteworthy mechanical properties.

Materials and methods: Using predetermined inclusion criteria, an electronic search was conducted using Dissertations and Thesis Global, the Web of Science, Cochrane, Scopus, and Medline/PubMed. Specific terms were utilized while searching the database.

Results: Only seven of the 10 included studies assessed shear bond strength (SBS). The mean SBS among the control group varied from 9.43 ± 3.03 MPa to 34.4 ± 6.7 MPa in the included studies, while in the experimental group, it varied from 6.33 ± 1.51 MPa to 25.05 ± 0.5 MPa. Antibacterial activity was assessed in five of the 10 included studies using TiO_2 NPs, which could easily diffuse through bacterial media to form the growth inhibition zone.

Conclusion: Antibacterial NPs added to orthodontic adhesives at a concentration of 1–5 wt% inhibit bacterial growth and have no effect on bond strength.

Keywords: Antibacterial, Nanoparticles, Orthodontic adhesive, Shear bond strength, *Streptococcus mutans*.

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Introduction

Fixed appliance therapy in orthodontics is the most conventional method for the treatment of dental malocclusions.[1] On the contrary, orthodontic appliances cause plaque retentive sites due to their attachments that affect the oral hygiene status of the individual with subsequent increases in oral bacteria during orthodontic therapy. As a result, the risk of adverse effects such as caries, gingival inflammation, and white spot lesions (WSLs) is increased.[2]

WSLs, or enamel decalcification, are most typically seen around the brackets of central and lateral incisors. WSLs are pale, and opaque with significant loss of minerals, increasing the porosity of the enamel and giving it a chalky white appearance that affects the teeth's esthetic appeal.[3] *Streptococcus mutans* (*S. mutans*) is an anaerobic gram-positive bacterium that plays a vital role in enamel decalcification and progression of dental caries. These lesions form as a result of poor oral hygiene and an increased load of *S. mutants* and other microbes, resulting in low pH, thereby intensifying various lesions.[4]

To limit the progression of WSLs, a variety of techniques have been implemented. WSLs are difficult to treat since they have a multifactorial etiology. However, maintaining good oral hygiene is the first line of preventive measure to limit these lesions. Other approaches include fluoride products, casein phosphopeptide-amorphous calcium phosphate (CPP-ACP), probiotics, and polyols.[5] Numerous antibacterial agents have been introduced into the adhesive cements, to treat WSLs. Fluoride is the most common additive agent, with products such as mouthwashes, gels, toothpaste, varnishes, bonding agents, and elastomers for the prevention of WSLs.[6] Although fluoride-containing agents are initially effective, the rate of ion release diminishes over time, and there is a higher failure rate because the addition of fluoride to bonding cement influences their mechanical properties.[7,8]

Nanotechnology has recently gained popularity in dentistry due to its larger surface area and active interaction with bacterial cell walls. Some of the nanoparticles (NPs) that can be used as antibacterial agents to coat brackets or as an additive to cement and adhesives to reduce demineralization are titanium dioxide (TiO_2), silver, gold, silica, copper, and zinc oxide.[9] The highly reactive nature of NPs stems, their ability to bind to tissue proteins, increases the permeability of the cell wall and nuclear envelope, eventually resulting in cell lysis. TiO_2 is the material of choice for the researchers due to its color compatibility, biostability, and chemical stability. Additionally, the photocatalytic reaction forms

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and continuously releases hydroxyl radicals and superoxide ions, which can decompose organic compounds.[10,11]

Researchers are working on a variety of antibacterial NPs to prevent WSLs.[12] To date, the systematic review focusing primarily on the shear bond strength (SBS) and antibacterial properties of TiO_2 NPs incorporated into bracket adhesives for effective and early prevention of WSLs are lacking in the literature. The current systematic review was carried out to determine whether the adhesives containing TiO_2-NPs are superior to conventional adhesives in contexts of SBS and antibacterial properties.

Materials and Methods

Protocol

The present review followed the PRISMA guidelines (preferred reporting items for systematic review) to ensure the diligence and clarity of this review.[13]

PICOS Format

In PICOS format, the following was defined as the main research question—orthodontic adhesives are in the population (P); antibacterial properties of NPs are in the intervention (I), SBS of modified orthodontic adhesives containing TiO_2 NPs are in comparison (C) on bacterial inhibition zone, as well as SBS is in outcome (O); experimental studies were included under section study (S).

The primary goal was to determine the antibacterial action of TiO_2-NPs containing adhesive in preventing WSLs, while the secondary goal was to determine SBS.

Eligibility Criteria

The inclusion criteria listed below are: (1) *in vitro* trials; (2) studies determining the antibacterial activity of TiO_2 NPs incorporated into the adhesives; (3) studies involving human subjects as their study participants; (4) studies including only TiO_2 NPs as their therapeutic material for testing; (5) all the reports or studies published in English, and (6) studies conducted during the time period from past 20 years (2000–2022) were included in the study.

All case reports, abstracts, short communications, letters to editorials, review of literature, and duplicate articles were excluded, as were abstracts and studies published in other than English language were also excluded from consideration.

Search Strategy, Study Selection, and Data Extraction

The following literature search methodology for Medline/PubMed was devised to extract all articles using controlled vocabulary and natural language related to the use of TiO_2 NPs and orthodontic bracket adhesives for the purpose of collecting and testing quest terms. A similar search strategy was used with other databases such as Web of Science, Google Scholar, Scopus, and SciELO, and the search approach for PubMed/Medline was explained in detail. The design of the study and publication date were not constrained in any way (Table 1).

Table 1: Keywords used for electronic database search

Search strategy
Search terms
(“Bracket Cement” [tw] OR “Bracket Adhesive” [tw] OR “Bracket Resin” [tw] OR “Bracket Bonding” OR “Orthodontic Cement” [tw] OR “Orthodontic Adhesive” [tw] OR “Orthodontic Resin” [tw] OR “Orthodontic Bonding” OR “Orthodontic Bracket Cement” [tw] OR “Orthodontic Bracket Adhesive” [tw] OR “Orthodontic Bracket Resin” [tw] OR “Orthodontic Bracket Bonding”)
(“Titania Nano” OR “Titania Nanoparticle” [tw] “Titanium dioxide” OR “TiO_2 Particle” [tw])
“Tooth Remineralization” OR “Tooth Demineralization”
“Remineralization” [tw] OR “Demineralization” [tw]
#1 OR #2
#3 OR #4
#5 AND #6

Study Selection

Two investigators carried out the selection of the articles who were aware of the study outcome, but not the journals or authors' identities. Initially, the title and abstract of the study were screened, and then the full text of the study was retrieved and reviewed. Studies with more than one exclusion criterion were not included. When disagreements between the two evaluators arise, the disagreements are resolved through a collaborative discussion.

Extraction of Data

The data were retrieved from the specific articles, which include the author's name and published year; the list of microorganisms tested; the tooth type; the method of sampling; the media used for preserving the teeth; methodology of NPs synthesis; the NPs size and concentration; the number of testing groups; the percentage of zone of growth inhibition; the mean SBS; the results; and the study's significant findings.

Quality Assessment/Bias

For *In Vitro* Studies

The excellence of the included trials was investigated by two evaluators using CONSORT guidelines for randomized clinical trials (RCTs).[14] The quality score of each included RCT was estimated using the Cochrane Handbook for Systematic Reviews of Interventions.[15]

Results

Study Selection

The PRISMA-based search methodology is illustrated in Flowchart 1. On exploring the database, a total of 93 studies were obtained, out of which 56 articles were left for full-text screening following the removal of duplicate articles. After subjecting to the present study inclusion criteria, 30 articles were excluded, and 26 articles were further evaluated, with 16 studies being excluded as (1) they were a review of the literature; (2) the articles lack of clinical application; (3) the studies that did not investigate the antibacterial properties of TiO_2 NPs adhesives; and (4) the studies that do not have a control group. Finally, 10 articles fulfilled the criteria—(1) nine *in vitro* studies and (2) one animal study (Table 2).[4,16–24]

Microbiological Outcomes of TiO_2 NPs

The predominant bacteria responsible for enamel decalcification are *S. mutants*, *Lactobacillus acidophilus,* and *S. sanguinis*. Orthodontic adhesives containing TiO_2 NPs were investigated for their antibacterial properties since the NPs could easily penetrate

Flowchart 1: PRISMA-based search methodology

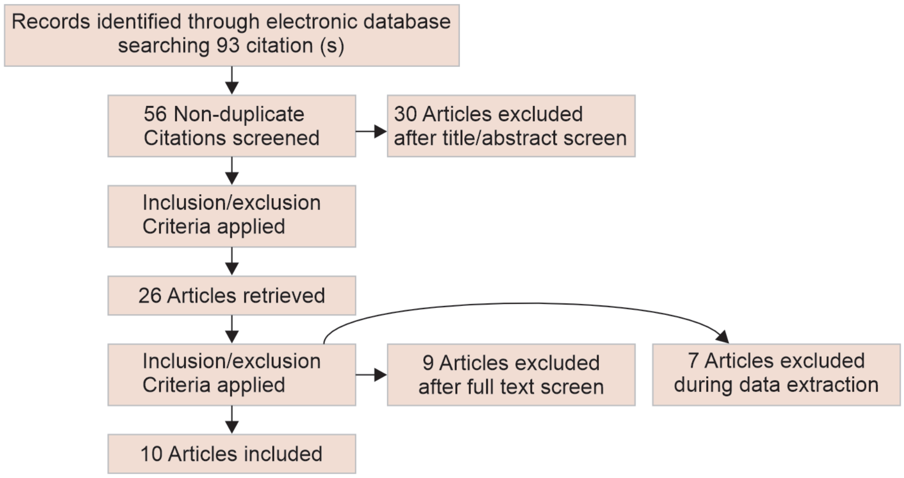

Table 2: Characteristics of the publications that were included in the study

Study	*Sample*	*Bacterial species*	*Sample type*	*Sample preparation*	*Sample storage media*	*NPs*	*Experimental groups*	*Control group*
Poosti et al., 2012	30, 45 disks	*S. mutans*	Human premolars	Cleaned for 5 seconds, with nonfluoride pumice slurry and low-speed handpiece	Immersed in deionized water for 24 hours at 37°C	Dry nanopowder, mixed rutile/ anatase phase, average primary particle size: 21 ± 5 nm; specific surface: 50 ± 10 m^2/gm; purity: >99.5%	1% (w/w) TiO_2 NPs	Transbond XT
Reddy et al., 2016	30	–	Human premolars	Pumice and water for 5 seconds, rinsed for 10 seconds, air-dried	Artificial saliva	Average size 21 ± 5 nm Purity of 99.5% 1% w/w	Transbond XT-TiO_2 NPs	Transbond XT
Sodagar et al., 2017	48, 180	*S. mutans* *S. sanguinis* *L. acidophilus*	Bovine central incisors Composite disks	Cleaned with a prophylaxis brush without powder, rinsed, and dried	0.5% chloramine-T solution (4°C) for 1 week	1, 5, and 10% (w/w) of TiO_2 nanocomposite preparation	Transbond XT plus TiO_2	Transbond XT
Felemban and Ebrahim 2017	30	–	Human premolars	Polished for 10 seconds with nonfluoridated pumice using prophylactic rubber cups	0.1% thymol	< 50 nm, 0.5% wt, 1% wt	Transbond XT mixed with ZrO_2-TiO_2	Transbond XT
Andriani and Purwanegara 2017	40	–	Human premolars	–	BHI solution containing *S. mutans* and placed in an incubator at 37°C for 30 days	Dry nano powder, particle size: 21 nm)	Transbond XT with TiO_2 NPs, 1 and 2% w/w	Transbond XT
Behnaz et al., 2018	120	–	Human premolars	Polished with fluoride-free pumice paste, and was rinsed and dried	0.5% chloramine T solution at room temperature	Anatase TiO_2 NPs in 0.1 wt% concentration	Transbond XT-TiO_2 Resilience composite-TiO_2	Transbond XT Resilience

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Study	*Sample*	*Bacterial species*	*Sample type*	*Sample preparation*	*Sample storage media*	*NPs*	*Experimental groups*	*Control group*
Reddy et al., 2018	15	*S. mutans*	Sectioned teeth	BHI broth dispensed in test tubes containing sectioned tooth and to this bacterial inoculum was added	–	Serial dilution method 1, 0.5, and 0.25% concentrations		
Moustafa et al., 2018	20 healthy albino rats	*S. mutans*	Lower central incisior			Nanopowder anatase and rutile phases, particle size of 21 ± 5 nm, 1% wt	Transbond XT-TiO_2 NPs	Transbond XT
Assery et al., 2019	90, 12	*S. mutans*	Human premolars, disks	Polished using nonfluoridated pumice slurry	1% thymol sol	30–50 nm, anatase, 1 and 3% wt	TiO_2 NPs mixed with composite	Nonreinforced resin composite
Putri et al., 2021	10	*S. mutans*		–	Specimens immersed in a test tube with bacterial solution containing sterile sucrose, liquid BHI, *S. mutans*	–	Adhesive mixed with TiO_2 NPs	Adhesive

bacteria and inhibit growth. Antibacterial activity was assessed in five of the 10 included studies (Table 3).[4,16,20,23,24]

Shear Bond Strength

Shear bond strength (SBS) was only evaluated in seven of the 10 included studies (Table 3).[4,16–21,23] Poosti et al.[16] observed that the SBS between the control and experimental adhesive groups were not significantly different. In contrast, seven studies showed a significant difference with respect to the SBS values.[4,17–21,23] The overall mean SBS scores ranged between 9.43 ± 3.03 MPa and 34.4 ± 6.7 MPa among the control group of included studies, while in the experimental group, it extended between 6.33 ± 1.51 MPa and 25.05 ± 0.5 MPa.

Bias/Quality Assessment

The *in vitro* studies were further subdivided into SBS and antibacterial studies, and the possibility of bias was stratified as low, moderate, and high. Of the seven articles included, five had a low bias and two had a moderate bias with respect to SBS. A total of five *in vitro* studies were evaluated for antibacterial activity with four showing a low bias, while one showed a high bias (Tables 4 and 5).

Based on the included articles, TiO_2 NPs embedded in orthodontic bracket adhesives may be beneficial in eradicating different microorganisms without significantly affecting SBS.

Discussion

Metallic NPs made of TiO_2 have recently received a lot of attention owing to their photocatalytic activity and less toxicity. According to Haghi et al.,[10] titanium NPs create small gaps in bacterial cell walls, increasing cellular permeability and death, which can aid in the prevention of recurrent caries and enamel decalcification. Furthermore, bacteria have a lower chance of developing resistance to TiO_2.[25]

Further, these NPs improve mechanical properties such as microhardness and bond strength that are comparable to or better than conventional composites, along with enhanced antibacterial activity.[26] As a result, a good diffusion ability into the environment is required for an optimal antibacterial NPs for use in orthodontic adhesive. The majority of the studies included in this review looked at growth inhibition zones; according to the results, five of the 10 studies found a considerable microbiological growth inhibition zone against various bacteria.

Three of the studies found that the SBS of titanium-based adhesive differed significantly from that of the adhesives used in the control group, which is in line with previous studies testing adhesives with >1 wt% NPs.[4,17,18] In contrast, two studies found no substantial difference between standard and experimental TiO_2 NPs composites.[16,23]

A range of sample preparation methods were also illustrated, including pumice washing to alcohol. A comparable tendency was detected in terms of dental storage media, which included distilled water, chloramine-T solution, thymol, and strong nitric acid. Such similarities could lead to a significant bias in all of the research considered.[27]

One of the limitations is that only *in vitro* studies were included, which requires vigilance in interpreting the data. In the included trials, a variety of adhesives were used, and the orthodontic adhesive disks' thickness and width were different. Overall, there appears to be a lack of defined techniques to follow when designing and conducting *in vitro* investigations, necessitating the implementation of steps to produce more homogeneous study outcomes.

Table 3: TiO_2 NPs incorporated orthodontic adhesive with acceptable SBS against various microorganisms

Study	*Percentage of growth inhibition zone*	*SBS*	*Result*	*Conclusion*
Poosti et al., 2012	Conventional: 69.1 ± 14.59 Nanocomposite: 8.2 ± 3.95	Conventional: 14.4 ± 1.2 Nanocomposite: 14.3 ± 1.26	Significant difference between the groups was seen only for the antibacterial activity with higher means among nanocomposite group	Adding TiO_2 NPs enhanced the antibacterial activity without compromising the physical properties
Reddy et al., 2016	–	Control = 9.43 (3.03) TiO_2 NPs = 6.33 (1.51)	The SBS was significantly higher in control compared to experimental group	Incorporation of various NPs into adhesive materials in minimal amounts can affect the SBS
Sodagar et al., 2017	*S. mutans*: 6.67 mm *S. sanguinis*: 7.33 mm *L. acidophilus*: 7.67 mm	Control = 34.4 ± 6.7 1% NP = 18.17 ± 4.6 5% NP = 13.9 ± 6.00 10% NP = 3.51 ± 3.28	SBS was significantly higher in the control and the 1% NP group than the 10% NP group *S. mutans* and *S. sanguinis* colonies were meaningfully lowered in all three groups, while the *L. acidophilus* colonies were lowered only in 10% NP containing composite	Incorporating TiO_2 NPs into composite resins confer antibacterial properties to adhesives, while the mean shear bond of composite containing 1 and 5% NPs still in an acceptable range
Andriani and Purwanegara 2017	Samples were soaked in BHI solution containing *S. mutans* to evaluate the antibacterial activity of the nanocomposite	Enamel microhradness at two points: 100 and 200 µm	Transbond XT group: 322.46 VHN and 322.34 VHN 1% TiO_2 group are 326.20 VHN and 327.04 VHN 2% TiO_2 group are 345.30 VHN and 345.78 VHN Control group are 356.76 VHN and 355.34 VHN	TiO_2 NPs in orthodontic adhesive resin have the ability to increase the antibacterial effect of the adhesive when compared to Transbond XT TiO_2 nanocomposite groups are lower than the normal enamel microhardness values
Felemban and Ebrahim 2017	–	Control = 14.75 ± 0.25 0.5% ZrO_2–TiO_2 = 20.32 ± 0.47 1% ZrO_2–TiO_2 = 25.05 ± 0.2	Orthodontic adhesive specimens with 1% weight ZrO_2–TiO_2 nanofillers showed a significantly highest SBS followed by 0.5% wt. ZrO_2–TiO_2 nanofillers, while the control group showed significantly low means of SBS	Adding ZrO_2–TiO_2 nanoparticle to orthodontic adhesive increased compressive strength, tensile strength, and SBS *in vitro*
Behnaz et al., 2018	–	Transbond XT: 14.60 ± 3.9 Transbond XT + TiO_2 NP: 12.09 ± 5.84 Resilience:12.4 ± 6.8 Resilience + TiO_2 NP: 7.8 ± 3.6	The highest SBS was found in Transbond XT composite followed by resilience without TiO_2 NPs. The lowest SBS was noted in resilience plus TiO_2 followed by Transbond XT plus TiO_2 groups	The addition of TiO_2 NPs might reduce SBS, but the adhesion might still be at an acceptable level. Thus, TiO_2 NPs may be added to Transbond XT composite
Reddy et al., 2018	1% TiO_2 = 898 ± 107.3 0.5% TiO_2 = 1300 ± 203.1 0.25% TiO_2 = 9692 ± 458.4	–	A significant difference in the colony-forming units among all three concentrations The antimicrobial effect of NPs was concentration dependent	TiO_2 showed significant antimicrobial effects and the antimicrobial effect of NPs was concentration dependent

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Study	*Percentage of growth inhibition zone*	*SBS*	*Result*	*Conclusion*
Assery et al., 2019	CFU high for the resin composite (RC) = 44.2/unit area cm^2 Least for 1% TiO_2 (RC1) = 5.2/unit area cm^2 3% TiO_2 (RC3) = 5.8/unit area cm^2	RC = 12.3 ± 0.9 RC1 = 13.2 ± 1.8 RC3 = 12.9 ± 2.7	Significant difference was observed between control and experimental resins at the baseline	Addition of 1% TiO_2 to the BPA and bis-GMA free experimental resin demonstrated promising flow and antibacterial effect without compromising the adhesion strength or chemical properties
Putri et al., 2021	Adhesive = $1{,}51 \times 10^5 \pm 1{,}24 \times 10^5$ Adhesive + TiO_2 NPs = $2{,}36 \times 10^5 \pm 1{,}94 \times 10^5$	–	No significant difference in the number of *S. mutans* colonies around the brackets that were fixated using orthodontic adhesive resin and with the resin incorporated with titanium dioxide NPs	NPs demonstrated comparable effect of antibacterial property on the number of *S. mutans*

Table 4: Assessment of individual risk of bias in the included *in vitro* studies for SBS

Study	*Sample storage medium*	*Sample randomization*	*Teeth free of caries/defects*	*Previous polishing*	*Manufacturer's instructions*	*Storage medium after bonding*	*Storage time*	*Chisel type*	*Crosshead speed*	*Risk of bias*
Poosti et al., 2012	+	+	+	+	+	+	+	+	+	Low
Sodagar et al., 2017	+	+	+	+	–	+	+	–	+	Low
Felemban and Ebrahim 2017	+	+	+	+	+	+	+	–	+	Low
Behnaz et al., 2018	+	+	+	+	–	+	+	–	+	Low
Reddy et al., 2016	+	+	+	+	–	–	–	+	+	Moderate
Andriani and Purwanegara 2017	+	+	+	+	–	+	+	–	–	Moderate
Assery et al., 2019	+	+	+	+	–	+	+	+	+	Low

Table 5: Individual risk of bias assessment for antibacterial studies

Study	*Teeth randomization*	*Sample preparation*	*Sample size calculation*	*Noncarious teeth/disk preparation*	*Blinding*	*Control group*	*Risk of bias*
Poosti et al., 2012	+	+	+	+	–	+	Low
Sodagar et al., 2017	+	+	–	+	–	+	Low
Reddy et al., 2018	+	+	–	+	–	–	High
Assery et al., 2019	+	+	–	+	–	+	Low
Putri et al., 2021	+	+	–	+	+	+	Low
Were the groups similar at baseline?					+		
Was the assignment order generated and implemented properly?					+		
Risk of bias					Low		

Conclusion

The incorporation of TiO_2 NPs in orthodontic adhesive improves its antibacterial activity, according to the studies reviewed. However, lack of consistent methods in the *in vitro* models, there was some heterogeneity throughout the investigations. TiO_2 NPs impregnated with orthodontic adhesives at a concentration of 1–5% by weight inhibit bacterial growth and exhibit excellent antibacterial properties without compromising the mean bond strength.

Author Contribution

Mahendra Venkata D Tivanani conceived and designed the study, conducted research, collected and organized data, and supervised, reviewed, and edited. Vyshnavi Mulakala provided research support and analyzed and interpreted data. Velagala S Keerthi wrote the initial and final draft of the article, review, and edit. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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