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SYSTEMATIC REVIEW

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Antimicrobial efficacy and bonding properties of orthodontic bonding systems enhanced with silver nanoparticles: a systematic review with meta-analysis

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Abstract

The aim of this systematic review was to assess the antimicrobial effectiveness of silver nanoparticles (AgNPs) incorporated to different orthodontic bonding systems. Additionally, the review investigated the impact of AgNPs on the bonding properties of these materials. The hypothesis posed that the addition of AgNPs would enhance the antimicrobial efficacy of orthodontic bonding systems while maintaining their bonding properties. The systematic review employed a PICO-based search strategy, targeting in vitro studies focusing on the integration of nano silver particles into orthodontic bonding systems with potential antimicrobial activity. The intervention involved the use of nano silver in orthodontic bonding systems, with a comparison to systems lacking nano silver. The primary outcomes assessed were antimicrobial activity and shear bond strength (SBS). The search process, conducted without publication date restrictions, yielded 551 potential articles: 34 from PubMed, 360 from PubMed Central, 42 from Embase, 54 from Scopus, and 61 from Web of Science. Ultimately, a qualitative synthesis was conducted on 13 papers. The PRISMA diagram, visually represented the search strategy, screening process, and inclusion criteria. The study protocol was registered in PROSPERO CRD42023487656 to enhance transparency and adherence to systematic review guidelines. Quality assessment of the included studies was performed using the Newcastle-Ottawa Scale, revealing that the 13 articles meeting the inclusion criteria demonstrated a high level of evidence. Seven studies were included in the meta-analysis regarding shear bond strength. In summary, the synthesized findings from these studies strongly underscore the promising potential of orthodontic materials modified with AgNPs. These materials exhibit effective resistance against cariogenic bacteria without compromising bonding properties below clinical acceptability. Such innovative materials hold significant implications for advancing oral health within the realm of orthodontics.

Keywords Biocompatible materials, Orthodontics, Dentistry, Anti-infective agents, Inorganic Chemicals

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Introduction

The incorporation of silver nanoparticles (AgNPs) into dental materials has proven effective in inhibiting the growth of bacteria in the oral cavity, as demonstrated in various studies [1–4]. AgNPs-based materials find a wide range of applications in the oral care as nanocomposites, implant coatings, pre-formulation with antimicrobial activity against cariogenic pathogens, periodontal biofilm, fungal pathogens and endodontic bacteria, and others such as: local anesthesia and oral cancer [5].

Notably, AgNPs, in contrast to conventional silver microparticles, display enhanced antibacterial capabilities even at lower concentrations. This property is crucial for preventing significant alterations to the mechanical and color characteristics of dental materials [6]. Silver, known for its persistent antibacterial properties, also tends to induce less bacterial resistance when compared to antibiotics [7]. Moreover, silver nanoparticles demonstrated a more potent antimicrobial effect against *S. mutans* at lower concentrations compared to gold or zinc. This observation suggests that the incorporation of silver nanoparticles into dental materials could offer significant clinical advantages with a reduced risk of toxicity [4].

The effectiveness of silver nanoparticles against microorganisms strongly depends on many factors, which determine not only potential action of bacteria or fungi elimination but also cause cytotoxicity effect. Bactericidal function of nanomaterials in size between 1 and 100 nanometers always results in cytotoxicity. These two properties are inseparable and should be investigated collectively. Key aspects that directly affect the biological properties of silver nanoparticles include particle size and shape, exposure dose, coating materials, nanoparticles aggregation, surface change, release of the ionic form of silver, and the organism or the type of cells tested [8–10]. The small particle size of AgNPs corresponds to a higher toxicity degree, higher doses and agglomeration of AgNPs increase cytotoxicity, while coating of AgNPs usually decreases the cytotoxicity of AgNPs and increases their stability. Further, the surface coating with different substances usually prevents the release of silver ions and changes in the shape and size of AgNPs. For example, aggregates of AgNPs induce oxidative stress and inflammation in macrophages and lung epithelial cells [11]. The mechanism of action is that AgNPs may disrupt the cell membrane, affect adenosine triphosphate production and DNA replication, alter gene expression and oxidize biological compartments of the cell through the production of Reactive Oxygen Species (ROS). Silver ions (Ag+) released by AgNPs in a biological environment can block the respiratory chain of the microorganisms in the cytochrome oxidase and NADH–succinate dehydrogenase region [12]. In addition, AgNPs were notified to exert significant cytotoxicity including depletion of intracellular glutathione levels, increasing levels of ROS and decreasing mitochondrial membrane potential [13]. On the other hand, there are also reports in the literature of anti-inflammatory properties of AgNPs [14]. Silver nanoparticles may also accelerate the healing process of surrounded tissues after implantation of a medical device containing AgNPs [15].

In orthodontic practice, individuals with malocclusion frequently encounter difficulties in upholding proper oral hygiene. Consequently, they are prone to conditions like white spot lesions (WSL), indicative of enamel demineralization visible on tooth surfaces [16]. The shear bond strength (SBS), as recommended by Reynolds, should range between 5.9 and 7.8 MPa for orthodontic composites, achieving the balance essential to optimize both the antimicrobial efficacy and mechanical properties of orthodontic materials [17]. In the literature, dental materials with AgNPs have shown lower SBS, which may underscore the need for a careful balance between antimicrobial efficacy and mechanical characteristics in the SBS of orthodontic materials [18]. As the gold standard, an optimal material should minimize bacterial adhesion while providing sufficient SBS.

The aim of this systematic review was to assess the antimicrobial effectiveness of silver nanoparticles incorporated to different orthodontic bonding systems. Furthermore, the review examined how the inclusion of AgNPs affected the bonding properties of these materials. It was hypothesized that adding AgNPs would enhance the antimicrobial activity of orthodontic bonding systems while preserving their bonding properties.

Methods

Search Strategy

Two independent reviewers systematically conducted an extensive literature search across various databases; PubMed, PubMed Central, Embase, Scopus and Web of Science. The search string was meticulously designed to comprehensively capture relevant studies, first it was designed for Pubmed ("orthodontic*") AND ("silver nanoparticle*" or "nano silver") AND ("composite*" OR "adhesive" OR "cement") and modified for other databases, as shown in Supplement 1. Following the comprehensive search process, all identified articles were imported into Zotero to facilitate the systematic removal of duplicate records. A PRISMA diagram (Fig. 1) was then generated to visually represent the entire search strategy and the subsequent screening and inclusion process [19].

Aligned with the PICO framework [20], the structure of the current systematic review is outlined as follows:

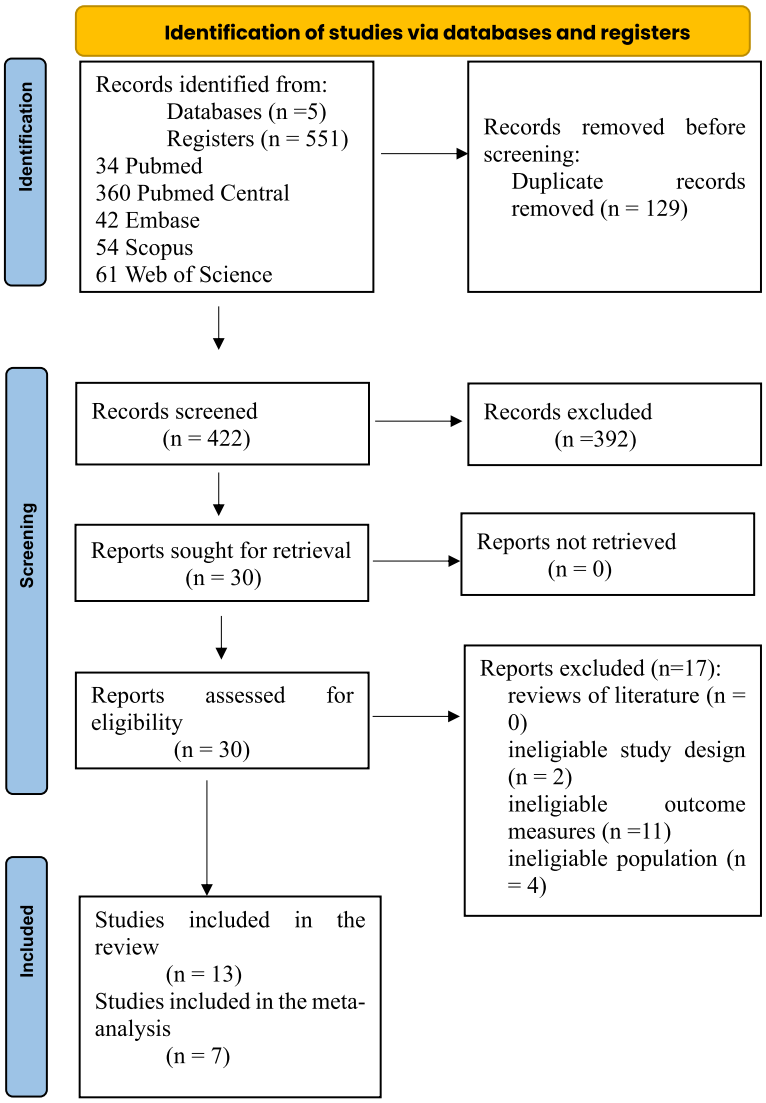

Fig. 1 Systematic review flow chart according to PRISMA Statement

Population: In vitro studies involving the incorporation of nano silver particles into orthodontic bonding systems with potential antimicrobial activity. Intervention: Utilization of nano silver in orthodontic bonding systems. Control group: Orthodontic bonding systems lacking nano silver agents. Outcome: Evaluation of antimicrobial activity and shear bond strength. Research Question: Does incorporating nano silver particles into orthodontic bonding systems enhance antimicrobial activity without compromising bonding properties, as shown in the in vitro studies?

The final literature search was concluded on February 19, 2024. Importantly, no restrictions on publication dates were imposed during the search process, and the review of pertinent publications was conducted in an unbiased manner. To enhance transparency and adherence to systematic review guidelines the study protocol was registered in PROSPERO CRD42023487656.

Eligibility criteria

Inclusion criteria

In-vitro studies assessing both the antimicrobial activity and the bond strength of experimental or commercial orthodontic bonding systems with AgNPs.

Exclusion criteria

The systematic review did not include literature and systematic reviews, case reports, guidelines, letter to the editors or conference abstracts. Only articles published in English were included in the analysis.

Animal studies. Studies involving the use of silver agents as a surface treatment. Studies exclusively assessing an antimicrobial evaluation or the bond strength of orthodontic bonding systems.

Data extraction

After removing duplicate publications, the primary author (M.S.-D.) conducted a thorough examination of the titles and abstracts of the remaining studies. Following this, the second author (L.S.-S.) also evaluated all studies to identify potentially eligible studies. The full texts of the chosen papers were meticulously scrutinized, and decisions regarding their inclusion or exclusion were made in accordance with predetermined criteria. Each stage of the screening involved the authors working separately to ensure thoroughness and accuracy. Any uncertainties or ambiguities encountered in this process were resolved through discussions between the two authors and the third author (K.W.). To compare the selected studies based on the Cochrane Collaboration guideline [21] spreadsheet was created. The level of agreement was assessed using the Cohen's Kappa statistic.

Quality assessment

The Newcastle–Ottawa Scale (NOS) served as the tool for evaluating the quality of the studies incorporated into the review [22]. The quality assessment score ranged from 0 to 9 points, with a higher score indicating a better study quality. Each characteristic evaluated earned one point, with the study eligible for 4 points for ideal object selection, 2 points for ideal comparability, and 3 points for ideal determination of outcomes.

Independent evaluation – Two reviewers (M.S.-D. and L.S.-S.) or more reviewers (K.W.) independently evaluated each study using NOS criteria.

Discussion and resolution - If discrepancies were observed between the reviewers' ratings, a discussion was held to reach consensus. Each reviewer provided their rationale for the rating assigned to each criterion and compared their interpretations of the study methodology and data.

Third-party arbitration - If consensus could not be reached through discussion, a third reviewer (K.W.) was engaged to arbitrate and provide an independent assessment.

Final evaluation - Once discrepancies were resolved, a final evaluation was agreed upon and documented for each study. To measure the agreement between the authors, the Cohen's Kappa coefficient was calculated, providing a statistical indicator of the level of agreement in the quality assessment process.

Meta-analysis

Characteristics of the sample

The sample for the meta-analysis comprises data from seven studies, each providing measurements of SBS in both experimental and control groups. The studies included range in publication year from 2009 to 2023, reflecting a broad temporal scope which allows for an assessment of trends and changes in methodologies over time.

The total number of subjects across all studies is balanced between groups, with each study contributing equally sized experimental and control groups. Specifically, the sample sizes within individual studies vary, with the smallest groups consisting of 5 metal orthodontic brackets per group and the largest comprising 30 brackets per group contributing to a cumulative total of 108 brackets in each group across all studies.

Mean SBS values reported in the studies show a range from 5.22 MPa to 14.69 MPa in the experimental groups and from 5.31 MPa to 24.67 MPa in the control groups. The standard deviations within these groups suggest variability both within and across studies, with experimental group standard deviations ranging from 1.16 MPa to 6.68 MPa, and control group standard deviations ranging from 1.46 MPa to 6.40 MPa.

In the present meta-analysis, the threshold for determining statistical significance was set at level of $\alpha = 0.05$. The distributions of the studied SBS were detailed according to the size of the groups (n), the mean values (M), and the standard deviations (SD) observed within each group.

Pooling effect size estimations

The evaluation of the SBS differences between the experimental group, which incorporated AgNPs, and the control group, devoid of AgNPs, was conducted utilizing a random effects model. This model was selected to accommodate the variability in study outcomes that extends beyond mere sampling errors. To allocate appropriate weight to each study's contribution to the cumulative effect estimate, the inverse variance method was applied. This approach emphasizes the influence of studies with more precise estimates on the aggregated result.

The restricted maximum-likelihood estimator (REML) was employed to estimate the between-study variance τ^2, an approach that is favored due to its ability to generate unbiased estimates across various scenarios, particularly in the context of the small sample sizes that are typical in meta-analyses. For more precise determination of the confidence intervals for τ^2 and τ, the Q-Profile method was implemented, which enhances the accuracy of the uncertainty associated with these estimates.

Furthermore, the adoption of the Hartung-Knapp adjustment mitigates potential biases inherent in the random effects model, especially important in analyses involving a limited number of studies, thereby bolstering the credibility of the findings derived from this meta-analysis.

Furthermore, Hedges, a bias-corrected standardized mean difference, was employed to ascertain the effect sizes. This measure, which corrects for biases associated with small sample sizes, serves as an advantageous tool for enhancing the precision and trustworthiness of the results integrated in this meta-analysis.

Heterogeneity assessment

Tau-squared (τ^2) and tau (τ) were utilized to quantify the variance and standard deviation, respectively, of the true effect sizes among the studies included. The I-squared (I^2) statistic, as delineated by Higgins & Thompson, was employed to evaluate the genuine heterogeneity of the studies, differentiating true variation from that which could be attributed to random chance. Additionally, the *H* statistic was employed to gauge the extent of heterogeneity, with values exceeding one indicating significant variability among the studies.

The assessment of heterogeneity was rigorously executed through the Q-test, which calculates the presence of heterogeneity by the weighted sum of squared differences between the effect estimates of individual studies and the aggregate effect estimate. This statistical approach ensures a thorough evaluation of variance across the included studies.

Publication bias assessment

To ascertain the presence of publication bias within the meta-analysis, multiple analytical methods were implemented. Initially, a funnel plot was utilized for the visual examination of asymmetries, which might suggest bias. This graphical approach plots observed effect sizes on the x-axis against their corresponding standard errors (*SE*) on the y-axis, providing an early indication of any irregular distribution patterns in study data that could hint at publication bias. The plot includes a vertical line representing the model-derived estimate, and a pseudo confidence interval, calculated as ± 1.96 times the SE, that surrounds this estimated value to aid in assessing data symmetry and detecting potential biases.

For a more rigorous quantitative analysis of funnel plot asymmetry, two specialized tests were employed, each adapted to different metrics of effect size. Specifically, Egger's test which conducts a regression of standardized effect estimates against their precision (the inverse of the *SE*), was used for standardized mean difference (*SMD*) effect sizes. This method strategically emphasizes studies with more precise estimates (lower *SE*), enhancing the reliability of the analysis and providing a comprehensive evaluation of the central tendency across studies. Analyses were conducted using the *R* Statistical language (version 4.3.3; R Core Team, 2024).

Results

The search strategy identified 551 potential articles: 34 from PubMed, 360 from PubMed Central, 42 from Embase, 54 from Scopus and 61 from Web of Science. Following the removal of 129 duplicates, articles underwent analysis. Subsequently, 392 papers were excluded due to not meeting the inclusion criteria. Among the remaining 30 papers, 17 were excluded for lack of relevance to the study's subject. The final qualitative synthesis included 13 papers.

The Prisma Flow Diagram (Fig. 1) provides a comprehensive overview of the entire search process, detailing each stage of the systematic review [19]. The agreement between the two reviewers was robust, as indicated by a high Cohen's Kappa coefficient of 0.96, underscoring a strong consensus in the evaluation process.

In the assessment of antimicrobial efficacy, diverse methodologies were employed across the reviewed studies, as detailed in Table 1. Various tests, including the agar diffusion test, biofilm assay, Colony Forming Unit (CFU), and metabolic activity assays, were employed. Jenabi et al. [23] assessed Master Dent and Universal Bonding with varied AgNPs concentrations using agar diffusion and CFU assessments. Kim et al. [24] utilized bioactive glass with AgNPs, tested through an agar diffusion test. Li et al. [25] studied GC Fuji ORTHO LC with varying nanoparticle ratios, using agar diffusion and direct contact tests. Mahendra et al. [26] examined Enlight with AgNPs against controls through agar diffusion, CFU, and biofilm inhibition tests. Tristán-López et al. [27] evaluated Transbond™ MIP, Transbond™ XT, and Prime & Bond with AgNPs, utilizing agar diffusion test, Minimum Inhibitory Concentration (MIC), and Minimal Bactericidal Concentration (MBC) assessments. The tested materials displayed a spectrum of AgNPs percentages, ranging from minimal concentrations such as 0.025% and 0.05 wt% [28], advancing to 0.1 wt% [29, 30] and 0.15 wt% [31, 32], and 0.3 wt% [33, 34]. Moreover, larger concentrations were examined, including 1% [26], Jenabi et al. study encompassing 0.5, 1, 2.5, and 5 wt% concentrations [23], and Kamran et al., investigation with 5 wt% [35]. Additionally, there was variation in the nanoparticle size across studies, commencing with sizes less than 5 nm [28], expanding to the range of 30–50 nm in the others [26, 34], and reaching 80 nm in the investigation conducted by Kamran [35].

Regarding shear bond strength, Table 1 provides a comprehensive overview of 13 studies conducted on

Table 1 Description of antimicrobial evaluation and the shear bond strength evaluation in in vitro studies

Authors, Year	Material evaluated with AgNPs and the control group	Antimicrobial evaluation method and the microorganism type	Time points tested	Type of teeth and number of teeth evaluated	Shear Bond Strength testing machine	Material tested
Ahn et al., 2009 [28]	Experimental composite adhesive with 0.025% and 0.05 wt%, diameter less than 5 nm The control group: Fuji Ortho LC, (GC Corporation, Tokyo, Japan), Transbond XT (3 M/Unitek, Monrovia, CA, USA)	Agar diffusion test Biofilm assay *S. mutans* (ATCC25175) *S. sobrinus* (ATCC33478)	3, 6, 9 and 24 h 3 and 6 h	Human premolars 85	Universal testing machine (Instron 4465, Canton, MA, USA)	Metal orthodontic brackets (Victory series, 3 M, Unitek)
Chen et al., 2021 [31]	GC Ortho LC, Fuji, Aichiken, Japan with 0.15wt% of AgNPs, diameter 20 nm The control group: GC Ortho LC, Fuji, Aichiken, Japan and Transbond XT	CFU Biofilm Metabolic Activity Assay Lactic acid production of biofilms *S. mutans* (ATCC 700610)	48 h 48 h plus 1 h 48 h plus 3 h	Human premolars 36	Universal testing machine	Metal orthodontic brackets (Shinye, Hangzhou, China)
Ding et al., 2021 [32]	GC Ortho LC (Fuji, Aichi-ken, Japan), at 0.15wt%AgNPs at 15 nm diameter The control group: GC and Transbond XT	CFU Biofilm Metabolic Activity Assay Lactic Acid Production Assay *S.mutans*(ATCC 700610)	48 h 48 h plus 1 h 48 h plus 3 h	Human premolars 42	Universal testing machine	Metal orthodontic brackets (Shinye, Hangzhou, China)
Eslamian et al., 2020 [33]	Transbond XT, 3 M Unitek with AgNPs Average size 50 nm at 0.3 wt% The control group: Transbond XT, 3 M Unitek	Agar diffusion test *S. mutans* (PTCC 1683)	24 h and 30 days	Human premolars 34	Universal testing machine (Z020, Zwick GmbH, Ulm, Germany)	Metal orthodontic brackets, (American Orthodontics, Sheboygan, WI, USA)
Jenabi et al., 2023 [23]	Master Dent, (Dentonics Inc., Monroe, NC, USA) and bonding agent Universal Bonding, (Dentonics Inc., Monroe, NC, USA) at 0.5, 1, 2.5, and 5 wt% concentrations of AgNPs Average size of AgNPs 17.1 nm The control group: Flowable composite Master Dent, (Dentonics Inc., Monroe, NC, USA) and bonding agent Universal Bonding, (Dentonics Inc., Monroe, NC, USA)	Agar diffusion test CFU *S. mutans* (Persian Type Culture Collection 1683)	48 h 48 h	Human premolars 54	Universal Electromechanical Testing Machine (Walter + Bai, Löhningen, Switzerland)	Fiber-reinforced composites

Table 1 (continued)

Authors, Year	Material evaluated with AgNPs and the control group	Antimicrobial evaluation method and the microorganism type	Time points tested	Type of teeth and number of teeth evaluated	Shear Bond Strength testing machine	Material tested
Jia et al., 2023 [34]	Transbond XT with0.1, 0.2, 0.3, and 0.5wt % of AgNPs (Avg. size 30–50 nm) The control group: Transbond XT	CFU *S. mutans* General Microbiological Culture Collection Center (Beijing, China)	48 h	Human premolars 50	Universal testing machine	Metal orthodontic brackets, (Hangzhou Sinya Co., Ltd. Hangzhou, China)
Kamran et al., 2022 [35]	Transbond XT with 2.5% and 5 wt% of AgNPs, (Avg. size 50–80 nm) The control group: Transbond XT	Agar diffusion test *S. mutans*	24 h	Human molars 60	Universal testing machine (Model 3343, Instron Corp., MA, USA)	Metal orthodontic brackets, 3 M, Unitek, (St. Paul, Minneapolis, USA)
Kim et al., 2018 [24]	Bioactive-glass containing 1% of Ag_2O (wt%) (Avg. size: not mention) The control group: Transbond TM XT and Charmfil TM Flow	Agar diffusion test *S. mutans* (Ingbritt)	24 h	Human premolars 60	Universal testing machine (Instron Co., Canton, MA, USA)	Metal orthodontic brackets, (K-smart; Daeseung Medical Co., Seoul, Korea)
Li et al., 2013 [25]	GC Fuji ORTHOLC (GC Corporation, Tokyo, Japan with nanoparticles diameter 5–10 nm, weight ratio of 1:99, 3:97, 5:95, 10:90 and 15:85 The control group: Fuji Ortho LC, (GC Corporation, Tokyo, Japan) and Transbond XT and Transbond Plus	Agar diffusion test Direct contact test *S. mutans*	48 h, 1 and 2 weeks 1 day and 1, 2, 3, 4, 6, 8 weeks	Human premolars 160	The Instron Universal testing instrument (8841, Instron Corp)	Metal orthodontic brackets (Masel Titan 9000TM, Roth)
Mahendra et al., 2022 [26]	Enlight, Ormco Corp, CA with 1 wt% AgNPs (diameter: 30–50 nm) The control group: Enlight, Ormco Corp, CA	Agar diffusion test CFU Biofilm Inhibition Test *S. mutans* (MTCC 497) *L. acidophilus* (MTCC 10307)	48 h 1 day, 30 days	Human premolars 80	Universal testing machine: Instron (model-8801, Norwood, MA, USA)	Metal orthodontic brackets, (Ortho Organizers)

Table 1 (continued)

Authors, Year	Material evaluated with AgNPs and the control group	Antimicrobial evaluation method and the microorganism type	Time points tested	Type of teeth and number of teeth evaluated	Shear Bond Strength testing machine	Material tested
Tristán-López et al.,2023 [27]	Transbond™ MIP 3 M, Unitek, US, Transbond™ XT 3 M, Unitek, US, Prime & Bond Denstply, Sirona, US With nanoparticles diameter 11 nm at 535 µg/mL$AgNP_S$ The control group: Transbond™ MIP 3 M, Unitek, US Transbond™ XT 3 M, Unitek, US Prime & Bond Denstply, Sirona, US	Agar Diffusion Test Minimum Inhibitory Concentration (MIC) Minimal Bactericidal Concentration (MBC) *S. mutans* (ATCC 25175) *L. acidophilus* (ATCC 4356)	24 h	Human premolars 180	Universal testing machine (Mecmesin Omnitest Universal Machine, Slinfold, UK)	Metal orthodontic brackets, (TD Orthodontics, Monterrey, NL, Mexico)
Zhang et al., 2015 [29]	Resin-modified glass ionomer cement (Vitremer, 3 M, St. Paul, MN) with 0,1% AgNPs The control group: (Transbond XT, 3 M, Monrovia, CA) and Resin-modified glass ionomer cement (Vitremer, 3 M, St. Paul, MN)	CFU Lactic acid production *S. mutans*	48 h 48 h	Human premolars 100	Universal Testing Machine (MTS, Eden Prairie, MN, USA)	Metal orthodontic brackets, (Ormco 2000, Sybron Dental, Orange, CA)
Zhang et al., 2016 [30]	Glass ionomer cement (Vitremer, 3 M, St. Paul, MN) with 0,1% AgNPs The control group: (Transbond XT, 3 M, Monrovia, CA) and Glass ionomer cement (Vitremer, 3 M, St. Paul, MN)	CFU Lactic acid production *S. mutans*	48 h 48 h	Human premolars 180	Universal Testing Machine (MTS, Eden Prairie, MN, USA)	Metal orthodontic brackets, (Ormco Series 2000, Sybron Dental, Orange, CA, USA)

CFU Colony Forming Unit, *MIC* Minimum Inhibitory Concentration, *MBC* Minimal Bactericidal Concentration

human premolars and molars using universal testing machines to measure results, establishing a standardized approach to quantifying the efficacy of modified materials.

In a comprehensive review of various studies assessing the impact of AgNPs in orthodontic materials, noteworthy findings emerge (Table 2). The studies consistently demonstrated the enhanced antibacterial efficacy of AgNPs, with reduced bacterial growth rates and substantial decreases in CFU counts. While some studies, like Ahn et al. [28], showed reduced bacterial growth without impacting SBS, others like Chen et al. [31] reported decreased CFU counts with acceptable SBS. Ding et al. [32] observed reduced CFU counts with no adverse SBS effects. Notably, Jenabi et al. [23] found outstanding antibacterial properties with 2.5% AgNPs and acceptable SBS. A statistically significant decrease in SBS was observed at a 5% concentration of silver filler, as reported by Tristán-López et al. [27], indicating beneficial antibacterial properties with no significant SBS modifications.

While AgNPs incorporation generally showcased promising antimicrobial effects, the effect on SBS varied across studies. Several investigations reported no significant SBS differences compared to controls, emphasizing the potential for maintaining adequate bonding strength. However, certain studies noted a decrease in SBS, particularly with higher concentrations of AgNPs, suggesting a delicate balance between achieving antibacterial efficacy and preserving mechanical characteristics in orthodontic adhesives [23, 33, 35]. The concentration of AgNPs emerged as a crucial factor influencing bonding strength. Overall, the incorporation of AgNPs demonstrated advantageous antibacterial properties without uniformly compromising SBS, indicating potential clinical benefits in developing orthodontic materials with enhanced resistance against cariogenic bacteria. The

Table 2 Antimicrobial and the shear bond strength results of tested materials in in vitro studies

Author and year	Conclusion
Ahn et al., 2009 [28]	The bacterial suspension with experimental composite adhesive exhibited a reduced bacterial growth rate compared to those with conventional adhesives. No significant differences were observed in SBS between conventional adhesives.
Chen et al., 2021 [31]	The incorporation of AgNPs led to a substantial decrease in CFU counts ($p < 0.05$). The bond strength of the innovative cement incorporating AgNPs falls within the acceptable range, as recommended in the literature, however was lower compared to the control group ($p < 0.05$).
Ding et al., 2021 [32]	Incorporating AgNPs greatly reduced CFU counts ($p < 0.05$). The incorporation of 0.15% AgNPs had no adverse effect on the SBS of the orthodontic cement ($p > 0.1$).
Eslamian et al., 2020 [33]	Significant antibacterial activity at 24 h and 30 days ($p < 0.001$). SBS significantly ($p < 0.009$) decreased after incorporation of AgNPs (0.3% (w/w); to 7.15 MPa, but was above the recommended SBS value.
Jenabi et al., 2023 [23]	Incorporating varying concentrations of nano silver, led to a significant reduction in *S. mutans* colony counts ($p < 0.05$). Bacterial growth was halted in samples containing 2.5% and 5% nano silver. The decrease in SBS was only notable for the 5% nano silver concentration ($p < 0.05$).
Jia et al., 2023 [34]	The orthodontic adhesive containing 0.2% AgNPs fillers showed outstanding antibacterial properties with the number of colonies decreased significantly ($p < 0.001$). The SBS of the orthodontic adhesive, enriched with 0.2 wt% NPA fillers, reached 11.89 ± 1.27 MPa, meeting the clinical shear bond strength standards.
Kamran et al., 2022 [35]	Modified samples showed more profound antimicrobial activity against *S. mutans*. The minimum SBS scores were shown by 5 wt% modified adhesive specimens ranging 8.6 ± 2.5 MPa, still meeting the clinical shear bond strength standards. Statistically significant difference in SBS between 5 wt% and 2.5 wt% samples was noticed ($p < 0.05$).
Kim et al., 2018 [24]	Testes material showed stronger antibacterial effect compared to control $p < 0.05$. The SBS showed no significant differences between groups.
Li et al., 2013 [25]	The addition of AgNPs conferred advantageous antibacterial properties. The sufficient bond strength was maintained.
Mahendra et al., 2022 [26]	Material with AgNPs showed statistically significant better antibacterial result. SBS value was greater than the clinically acceptable range but smaller than control ($p < 0.005$).
Tristán-López et al., 2023 [27]	The addition of AgNPs showed advantageous antibacterial properties. The introduction of AgNPs did not induce significant modifications in SBS for any adhesive ($p > 0.05$), and the measured forces during the SBS did not surpass the clinical acceptability.
Zhang et al., 2015 [29]	Adding 0.1% AgNPs gave good antibacterial results, as decreased biofilm CFU, compared to controls ($p < 0.05$). Adding 0.1% AgNPs did not adversely affect the SBS, compared to the unmodified control ($p > 0.1$).
Zhang et al., 2016 [30]	The addition of AgNPs showed advantageous antibacterial properties compared to control ($p < 0.05$). AgNPs did not decrease the SBS, compared to control ($p > 0.1$).

CFU Colony Forming Unit, *SBS* Shear bond strength

secondary outcomes in the studies primarily focused on cytotoxicity analysis [24, 31, 32, 34, 35] and Adhesive Remnant Index (ARI) [24, 27–30, 33–35].

Additionally, Table 3 consolidates the quality assessment results, revealing strong agreement (Cohen's Kappa coefficient 0.95) and a majority of studies scoring 7/9 on the NOS assessment [22], indicating good quality. Despite this, notable heterogeneity persists in study designs, samples, and evaluation methods. The reviewed studies collectively examined both the antimicrobial properties and SBS of orthodontic materials containing AgNPs. However, a meta-analysis was only feasible for comparing SBS between experimental and control groups due to significant heterogeneity in the microbial assessments.

Evaluation of the pooled standardized mean differences between experimental and control groups

The meta-analysis conducted to evaluate the shear bond strength between experimental and control groups based on a sample of seven studies encompassing 216 observations (108 per group).

The results from the random effects model show a mean $SMD = 0.48$, with a 95% confidence interval (*CI 95%*): -0.11–1.07. This wide confidence interval, encompassing zero, suggests that the effect size estimate is not statistically significant, $p = 0.093$. Such a result implies that the difference in shear bond strength between the experimental and control groups might not be robust across the studies analyzed.

The estimated between-study variance $\tau^2 = 0.29$, with a *CI 95%*: 0.04–1.64, indicating considerable variability in effect sizes across studies. The square root of τ^2, was $\tau = 0.5416$, with *CI 95%*: 0.19–1.28, further highlighting the presence of substantial heterogeneity. The I^2 statistic stood at 70.0%, with a *CI 95%*: 34.3 – 86.3%, suggesting that a significant proportion of the total variability in effect sizes is due to heterogeneity rather than chance. The *H* statistic, which quantifies the consistency of the studies' results, was $H = 1.83$, with a *CI 95%*: 1.23–2.70, providing further evidence of heterogeneity as it exceeds the value of one.

Furthermore, the Q-test for heterogeneity yielded a value of $Q(6) = 20.02$ with $p = 0.0028$, strongly indicating the presence of heterogeneity among the study effects. This test result supports the use of the random effects model and underscores the complexity of the underlying data structure.

In conclusion, while the analysis indicates an average effect suggesting a higher shear bond strength in the experimental group compared to the control group, the statistical significance of this effect is uncertain due to the high degree of heterogeneity observed among the included studies. The findings highlight the need for cautious interpretation of the pooled results and suggest that further research, perhaps with more stringent inclusion criteria or additional studies, might be necessary to clarify these effects.

For a graphical depiction of these findings, please consult Fig. 2, which presents a forest plot illustrating the detailed results.

Publication bias assessment

The representation of publication bias pertaining in shear bond strength (MPa) for metal orthodontic brackets is illustrated through a funnel plot in Fig. 3.

The analysis of the distribution of studies on the funnel plot reveals a relatively symmetrical arrangement around the pooled *SMD*. This symmetry is evidenced by the fact that four studies reported an *SMD* smaller

Table 3 Evaluation of the quality of the study conducted using the Newcastle-Ottawa Scale

Authors and Year	Selection	Comparability	Outcome	Total Score
Ahn et al., 2009 [28]	**	**	**	6
Chen et al., 2021 [31]	***	**	**	7
Ding et al., 2021 [32]	***	**	**	7
Eslamian et al., 2020 [33]	***	**	**	7
Jenabi et al., 2023 [23]	***	**	***	8
Jia et al., 2023 [34]	***	**	**	7
Kamran et al., 2022 [35]	**	**	**	6
Kim et al., 2018 [24]	***	**	***	8
Li et al., 2013 [25]	***	**	**	7
Mahendra et al., 2022 [26]	***	**	**	7
Tristán-López et al.,2023 [27]	****	**	**	8
Zhang et al., 2015 [29]	***	**	**	7
Zhang et al., 2016 [30]	***	**	**	7

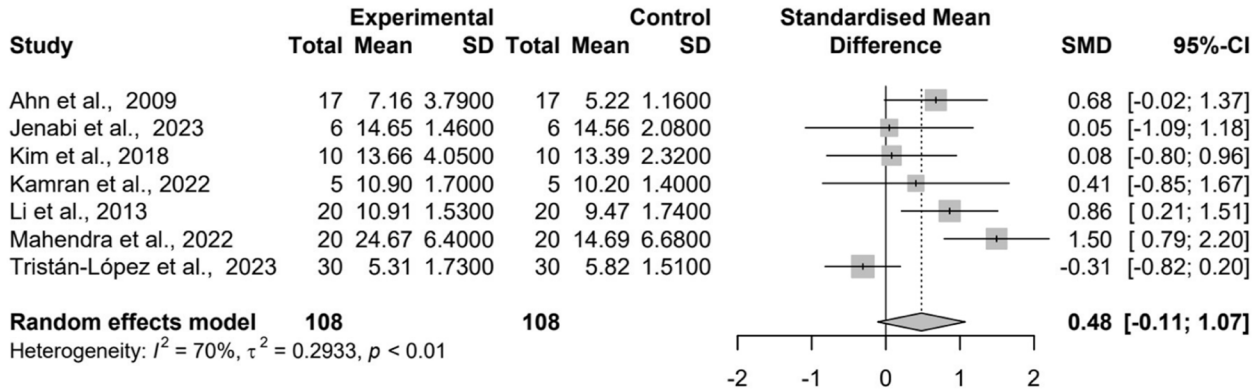

Fig. 2 Forest plot depicting the pooled standardized mean differences (SMD) in shear bond strength (MPa) for metal orthodontic brackets between control and treatment groups

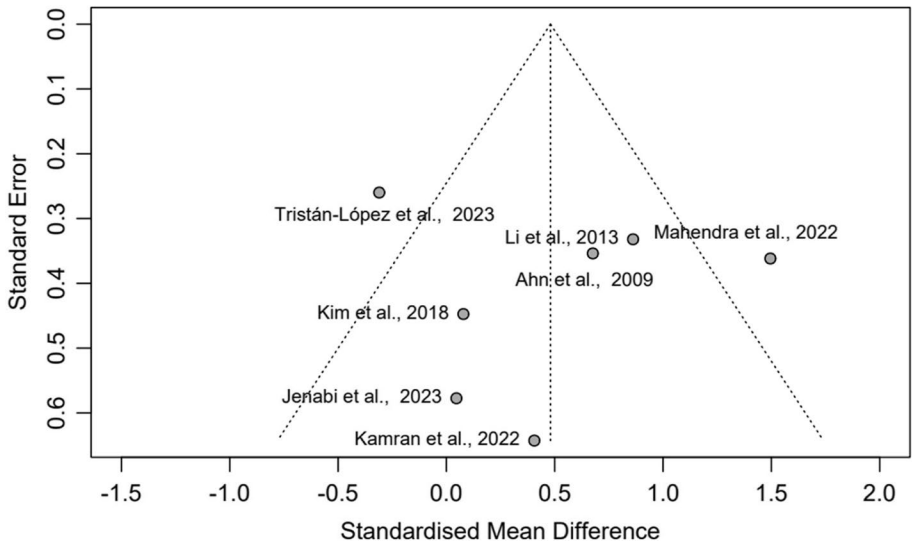

Fig. 3 Funnel plot of standardized mean differences versus standard error for assessing publication bias in studies on SBS for metal orthodontic brackets between control and experimental groups

than the pooled *SMD*, while three studies presented a larger SMD than that of the pooled result. Such a distribution suggests that there is no apparent directional skewness in the reporting of results, which often can be an indication of publication bias or other systematic errors.

Further scrutiny of the distribution of *SE* across the studies shows a range from 0.25 to 0.65. Within this context, particularly at the lower range of SE (0.25–0.35), two studies marginally exceed the expected boundaries of the funnel plot. These minor deviations occur symmetrically, with one study on either side of the funnel, which may indicate random variability rather than any systematic bias. The presence of these studies slightly outside the expected range at lower standard errors could suggest potential small-study effects or other anomalies requiring further investigation.

However, the overall symmetry observed in the larger set of studies within the funnel plot, coupled with the balanced exceedance at lower *SE* levels, supports the conclusion that the meta-analysis results are robust against significant biases related to the size or reporting of the effects. Such findings enhance the confidence in the generalizability and reliability of the meta-analysis outcomes, affirming the conclusion that the pooled *SMD* is a credible estimate of the true effect size across the analyzed studies.

The results from the Egger's regression test applied to the funnel plot asymmetry, which aimed to quantify

potential publication bias, reveal no significant evidence of bias affecting the aggregated findings. The test yielded at (5) = 0.40, $p = 0.708$. This high p-value indicates that there is no statistical significance to suggest that the funnel plot is asymmetric, a condition which would imply the presence of publication bias.

The bias estimate provided by the test is 1.08, with a relatively large standard error of $SE = 2.71$. This large standard error relative to the bias estimate further attenuates any potential concerns over the influence of bias in the studies' results. When assessing the reliability of meta-analyses, a lack of significant publication bias is crucial as it supports the validity of the conclusions drawn from the pooled data.

Additionally, the analysis accounted for residual heterogeneity, with a multiplicative residual heterogeneity variance $\tau^2 = 3.88$. This high value indicates substantial variability among the study results that is not solely attributable to sampling error, suggesting that other factors, potentially methodological or contextual differences among the studies, are contributing to the observed effects.

Discussion

The presented studies collectively investigated the antimicrobial properties of various orthodontic materials incorporated AgNPs. These materials, ranging from adhesive systems to composites and cements, underwent rigorous microbial assessment employing diverse methods such as: agar diffusion tests, CFU counts, and biofilm assays, as well as the SBS tests. The studies targeted common oral bacteria, primarily *Streptococcus mutans* and *Lactobacillus acidophilus*, known contributors to enamel demineralization and caries formation [36]. The results showcased a significant variability in the antimicrobial efficacy, influenced by factors like nanoparticles concentration, material composition, and assessment time points. Despite this variability, all materials demonstrated promising antibacterial effects, hinting at the potential to develop orthodontic products with enhanced resistance against cariogenic bacteria. Moreover, while many studies reported significant antibacterial effects, particularly against *Streptococcus mutans* and *Lactobacillus acidophilus*, the impact on SBS exhibited variation, with some studies reporting reductions in shear bond strength [23, 33, 35] and others showing no significant differences compared to control groups [24, 28–30, 32] the overall consensus leans towards a potential compromise in SBS with the incorporation of AgNPs.

In a previous study by Zhang, it was observed that the antibacterial efficacy increased as the mass fraction of AgNPs rose from 0.05 to 0.1%. However, a decrease in SBS was noted when the concentration of AgNPs reached 0.15% [37]. In the investigated studies, even the incorporation of 0.025% and 0.05 wt% nano silver into the orthodontic composite demonstrated a reduction in the growth rate of *S. mutans* [28]. In the studies conducted by Ding et al. [32], Jenabi et al. [23], Kim et al. [24], and Zhang et al. [29], the antibacterial effects were found to be statistically significant ($p < 0.05$) when compared to the control group. Eslamian et al. reported a significant antibacterial activity with a p-value less than 0.001 after incorporating 0.3 wt% AgNPs into GC Ortho LC (Fuji, Japan) [33]. Similarly, Jia et al. found the same statistical significance when adding 0.2 wt% AgNPs to Transbond XT [34].

In a study focused solely on antimicrobial efficacy, Sodagar et al. utilized higher concentrations of nano silver (1%, 5%, and 10 wt%) [38]. Interestingly, despite an escalation in nano silver concentration from 5% to 10%, they noted no significant difference in CFU counts. The studies evaluating only the antimicrobial effect of silver nanoparticles, despite obtaining positive results and demonstrating robust study designs, the papers were excluded from the review because they did not show a correlation between SBS [38–42].

In the study by Ahn et al. [28], where a minimal amount of AgNPs with small nanoparticles sizes less than 5nm was added to the tested material, as well as in the study by Ding et al. [32], no significant SBS effect was observed at the tested concentrations. Jenabi et al. [23], noted a reduction in SBS at a concentration of 5 wt%. It is worth noting that the recommended SBS values for clinical acceptability in orthodontics typically fall within the range of 5.9–7.8 MPa, as established by Reynolds [17]. Important to note the SBS reduction was higher at larger AgNPs concentrations [23, 33, 35]. This discussion underscores the delicate balance required to optimize both antimicrobial efficacy and mechanical characteristics in orthodontic materials. The variations in outcomes can be attributed to differences in nanoparticles concentrations as well as to bonding materials, and evaluation protocols. In the evaluated studies percentage ranged between 0.025 [28] reaching even in other studies 5 wt % [5, 7]. Delving deeper into shear bond strength discussions, the studies demonstrated variations in methodologies, encompassing different types of teeth; however, our discussion focused on studies evaluating SBS on human teeth and orthodontic brackets, with an emphasis on metal brackets. Noteworthy is the diverse choice of materials, including for example Transbond XT [27, 33–35], GC Ortho LC [25, 31, 32], EnlightOrmco [26] or Vitremer, 3M [29, 30] demonstrating the versatility in modifying existing orthodontic products. However, standardized evaluation methods, particularly shear bond strength tests

conducted with universal testing machines, establish a uniform approach to quantify the efficacy of the modified materials.

Studies that evaluated only SBS without microbiological results were excluded from the systematic review because they did not measure a relationship between two most important outcomes [18], these criteria for exclusion from the review proved to be correct because the most important outcome of the review is the balance between microbiological properties and SBS maintenance.

Studies evaluating SBS on bovine teeth were excluded from the analysis but they showed comparable outcomes [43–45]. Degrazia et al. [43] demonstrated that incorporating nano silver at concentrations of 0.11%, 0.18%, and 0.33 wt% into orthodontic composite materials led to a significant reduction in *S. mutans*. There was no notable difference in the bactericidal efficacy among these three concentrations, and none of them achieved complete eradication of bacterial counts and the addition of AgNPs decreased the SBS ($p < 0.001$).

Furthermore, the review underscores the necessity for standardized methodologies in assessing both antimicrobial efficacy and shear bond strength. The concentration of AgNPs fillers emerged as a critical factor influencing bracket bonding. Analyzing and determining specific quantities of AgNPs fillers incorporated into orthodontic adhesives can be crucial for maintaining optimal SBS. The collective outcomes contribute significantly to advancing the understanding of orthodontic material science and its potential implications for clinical practice.

This discrepancy may be attributed, at least in part, to the size of the nanoparticles. Various factors varied across studies, including the shape of the nanoparticles, the technique used to integrate AgNPs into the tested material, and the methodologies employed to assess the effectiveness of the nanoparticles. The key factors influencing the biological properties of AgNPs include particle size, shape, exposure dose, coating materials, nanoparticle aggregation, surface charge, release of ionic silver, and the specific organism or cell type under examination [8–10]. Smaller particle sizes correlate with increased toxicity, higher doses and agglomeration of AgNPs elevate cytotoxicity. In the evaluated studies nanoparticles size varied from less than 5 nm in the study by Ahn et al. [28], some studies evaluated materials with 30–50 nm particles [26, 34], and the largest particles (50–80 nm) were used by Kamran et al. [35]. The toxicity of nano silver is intricately linked to the size of the particles. Generally, most silver nanoparticles exhibit toxicity to the human body, primarily owing to their small particle size, which enables them to penetrate human tissues. In a study conducted by Zhang et al., the findings indicate that the 20nm silver nanoparticles demonstrate more potent toxic effects compared to their 70nm counterparts [46].

The quality assessment results, reaffirms the robustness of the included studies with a strong concordance between authors and a majority achieving good quality scores based on the Newcastle-Ottawa Scale assessment [22]. However, substantial heterogeneity in study designs, samples, and evaluation methods persists, emphasizing the necessity for standardized approaches to enhance comparability and foster a more robust evidence base.

In the summery, the reviewed studies significantly contribute to the evolving understanding of AgNPs in orthodontic materials. The potential for antibacterial benefits is promising, addressing the challenge of bacterial colonization in orthodontic settings. However, the observed variability in shear bond strength outcomes necessitates nuanced consideration of material composition, nanoparticles concentration, and assessment methods. Future research should strive for methodological consistency, exploring strategies to optimize both antimicrobial and mechanical properties in orthodontic materials containing AgNPs. Long-term effects on the mechanical properties of orthodontic materials and the potential for bacterial resistance should be thoroughly investigated to ensure the safety and efficacy of incorporating AgNPs in orthodontic practice. Overall, these findings underscore the potential of AgNPs in orthodontic materials to mitigate bacterial colonization, emphasizing the need for refining and standardizing methodologies to facilitate more meaningful comparisons across studies and enhance the translational impact of such innovations in orthodontic practice. Studies suggest that in orthodontic applications, AgNPs exhibit antimicrobial properties without significant systemic health risks. However, it is important to note that the duration of minimal or no adverse systemic health effects of AgNPs may vary depending on factors such as their concentration, exposure time and individual patient characteristics. Further studies are needed to establish the long-term safety profile of AgNPs in orthodontic materials and establish guidelines for their safe clinical use. Nanomaterials, particularly silver nanoparticles, can induce local inflammation, oxidative stress and potentially enter the circulatory system, leading to certain pathophysiological effects [47]. Moreover, integrating comparative analyses of different AgNP formulations, microbial susceptibilities and evaluation techniques can provide a more nuanced understanding of their relative effectiveness and limitations in clinical settings.

While the study provides valuable insights it is essential to acknowledge several limitations. The included studies exhibit variability in experimental designs, such

as different materials, concentrations of silver nanoparticles, and evaluation methods. This heterogeneity makes it challenging to draw direct comparisons and may also impact the generalizability of the findings. Furthermore, studies targeted different microorganisms, primarily *S. mutans* and *L. acidophilus.* The variability in microbial strains may influence the observed antimicrobial effects, and extrapolating the findings to broader microbial communities requires caution. In vitro studies, while useful for understanding basic mechanisms, may not fully replicate the complexity of biological systems in vivo.

Conclusions

In conclusion, the combined results of these studies underscore the significant potential of orthodontic materials enhanced with AgNPs to robustly combat cariogenic bacteria without compromising SBS below clinical standards. The promising antimicrobial properties exhibited by AgNPs suggest their valuable role in developing orthodontic products that effectively address bacterial challenges while maintaining the essential mechanical characteristics required for clinical efficacy. The integration of such innovative materials holds significant implications for improving oral health within the field of orthodontics. To maximize the translational impact of these advancements in orthodontic practice, it is crucial to establish standardized protocols, thereby facilitating the seamless integration of AgNPs modified orthodontic materials into routine clinical use.

In summary, the conclusions of the meta-analysis regarding the comparison of SBS between experimental and control groups can be considered reliable, as they appear not to be distorted by selective publication of studies with more favorable outcomes. This allows for a more confident interpretation of the effect sizes as reflecting true effects rather than artifacts of the publication process.

Supplementary Information

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Supplementary Material 1.

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Authors' contributions
M.S.-D. analyzed and interpreted the data, was the first investigator to evaluate the data, prepared conceptualization and methodology, wrote the paper. L.S.-S. was the second investigator to evaluate the data. M.Z. was a contributor in writing and reviewing the manuscript. G.S. and K.W. supervised the research. All authors read and approved the final manuscript.

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Declarations

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