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Evaluation of the Antibacterial Effects of the Various Nanoparticles Coated Orthodontic Brackets: A Systematic Review and Meta-analysis

Evaluación de los efectos antibacterianos de los diversos brackets de ortodoncia recubiertos con nanopartículas: Una revisión sistemática y metanálisis

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Abstract

Objectives: The antibacterial activity of zinc oxide (ZnO) and silver (Ag) nanoparticles (NPs) has been investigated in this study to present achievements in this field with the consensus of outcomes. This systematic review and meta-analysis clarified the antibacterial potential of silver, zinc-oxide NPs-coated Orthodontic Brackets.

Methods: PRISMA 2020 Checklist was the basis for performing the current systematic review and meta-analysis. The search strategy was to screen the relevant databases on PubMed, Embase, Web of Science, Scopus, ISI Web of knowledge, and EBSCO from inception until 1 November 2022. We calculated a 95% confidence interval (95%CI) for the mean difference (MD) based on the fixed effect model and Inverse-variance method. Stata/MP version 17 software was applied to conduct the meta-analysis.

Results: In the initial search, duplicate studies were removed, and the abstracts of 209 separate relevant articles were presented. Two individual authors reviewed the full text of 32 articles, resulting in the final eight articles. The mean difference (MD) of the antibacterial effect of bracket coatings against L. acidophilus between AgNPs coating and the controls was estimated at 2.71 (MD, 2.71 95%CI 2.05-3.37; p=0.00). The mean difference (MD) of the antibacterial potential of bracket coatings against S. mutans between ZnONPs coating and the controls was estimated to be -275.54 (MD, -275.54 95%CI -281.23, -269.85; p=0.00).

Conclusions: The results of our meta-analysis revealed that Ag, ZnO, and Ag/ZnO NPs-coated brackets had antibacterial activity against L. acidophilus and S. mutans compared to uncoated brackets.

Keywords: Orthodontic, Orthodontic bracket, Nanoparticles.

Resumen

Objetivos: En este estudio se investigó la actividad antibacteriana de las nanopartículas (NP) de óxido de zinc (ZnO) y plata (Ag) para presentar los logros en este campo con el consenso de los resultados. Esta revisión sistemática y metanálisis aclararon el potencial antibacteriano de los brackets de ortodoncia recubiertos con NPs de óxido de zinc y plata.

Métodos: La lista de verificación PRISMA 2020 fue la base para realizar la revisión sistemática y el metanálisis actuales. La estrategia de búsqueda fue examinar las bases de datos relevantes en PubMed, Embase, Web of Science, Scopus, ISI Web of Knowledge y EBSCO desde el inicio hasta el 1 de noviembre de 2022. Calculamos un intervalo de confianza del 95% (IC del 95%) para la diferencia de medias (MD) basado en el modelo de efectos fijos y el método de la varianza inversa. Se aplicó el software Stata/MP versión 17 para realizar el metanálisis.

Resultados: en la búsqueda inicial, se eliminaron los estudios duplicados y se presentaron los resúmenes de 209 artículos relevantes separados. Dos autores individuales revisaron el texto completo de 32 artículos, lo que resultó en los ocho artículos finales. La diferencia media (DM) del efecto antibacteriano de los recubrimientos de brackets contra L. acidophilus entre el recubrimiento de AgNP y los controles se estimó en 2,71 (DM, 2,71; IC del 95%: 2,05-3,37; p=0,00). La diferencia media (DM) del potencial antibacteriano de los recubrimientos de brackets contra S. mutans entre el recubrimiento de ZnONP y los controles se estimó en -275,54 (DM, -275,54, IC del 95%: -281,23, -269,85; p = 0,00).

Conclusiones: Los resultados de nuestro metanálisis revelaron que los brackets recubiertos con Ag, ZnO y Ag/ZnO NPs tenían actividad antibacteriana contra L. acidophilus y S. mutans en comparación con los brackets sin recubrimiento.

Palabras clave: Ortodoncia, bracket de ortodoncia, nanopartículas.

Introduction

Orthodontic treatment is usually done for cosmetic purposes; using fixed appliances in orthodontic treatment is the most common method. However, it causes changes in the oral environment[1]. These changes cause a decrease in Ph and an increase in the microbial load in the tooth cavity, which can be the retention of food particles[2]. Studies have shown that *Lactobacillus acidophilus* (L. acidophilus) and *Streptococcus mutans* (S. mutans) are among the microorganisms that increase in the graft and/or band in the oral cavity[3,4]. Evidence shows that S. mutans has a critical role in the initiation of the decay process[5], and L. acidophilus plays a more significant role in the process of caries propagation[6]. Also, the decrease in pH results in the demineralization of tooth enamel as white spot lesions (WSLs), eventually developing more cavitation. Accordingly, one of the main concerns of the patient and the orthodontist is the appearance of WSLs during bonding[7].

Oral hygiene care is recommended and emphasized to all patients during orthodontic treatment. However, the increased microbial load is still noted. The use of resin materials containing antibacterial agents[8], varnish[9], and modified orthodontic elastomers[10] are among the methods that are used to control and prevent the development of WSLs. The addition of nanoparticles (NPs) to orthodontic adhesives[10,11] has recently been of great interest. NPs with a size smaller than 100 nm and insoluble materials have been introduced[12]; Therefore, due to their small size, NPs have a greater surface-to-volume ratio and strongly interact with microbial membranes of microorganisms; which can have antimicrobial activity[13]. Since the introduction of NPs, multiple metals such as silver (Ag), gold (Au), copper (Cu), titanium (Ti), and zinc (Zn) have shown antimicrobial activity. Studies have shown that each activity has different properties and scope[3,14]. Ag, Ag ions, and Ag compounds are the most common antibacterial agents[15]. Studies have shown that AgNPs have antimicrobial properties by augmenting dental resin composites and being coated on orthodontics brackets and wires[16-18]. Using zinc oxide (ZnO) NPs can also affect the activity of bacteria[19]. A study has shown that using ZnO on the coating of orthodontic wires can have antibacterial activity[20]. Studies have shown that AgNPs have greater antimicrobial potential than ZnONPs[21]. However, studies introduced AgNPs as genotoxic and cytotoxic agents for human cells[22]. Studies show that the cost of using AgNPs is also higher in addition to the cytotoxicity of AgNPs. Therefore, the current study investigated the antibacterial performance of ZnONPs and AgNPs to present achievements in this field with the consensus of outcomes. This systematic review and meta-analysis clarified the antibacterial potential of AgNPs and ZnONPs-coated Orthodontic Brackets.

Method

The process of searching for articles

PRISMA 2020 Checklist was the basis for performing the current systematic review and meta-analysis. [23]. The search strategy was to screen the relevant databases on PubMed, Embase, Web of Science, Scopus, ISI Web of knowledge, and EBSCO using keywords related to the objectives of the study until 1 November 2022 were reviewed. Google Scholar search engine was also used to find related articles. MeSH keywords:

((((((("Orthodontic Brackets"[Mesh] OR "Orthodontic Wires"[Mesh] OR "Orthodontic Appliances"[Mesh] OR "Orthodontic Appliances, Fixed"[Mesh] OR "Dental Cements"[Mesh] OR "Dental Bonding"[Mesh]) AND "Nanoparticles"[Mesh]) OR ("Nanoparticles/microbiology"[Mesh] OR "Nanoparticles/standards"[Mesh] OR "Nanoparticles/statistics and numerical data"[Mesh] OR "Nanoparticles/toxicity"[Mesh])) AND "Silver"[Mesh]) AND "Zinc Oxide"[Mesh]) AND "Metal Nanoparticles"[Mesh]) AND ("Anti-Bacterial Agents"[Mesh] OR "Anti-Bacterial Agents" [Pharmacological Action])) AND "mutacin III, Streptococcus mutans" [Supplementary Concept]) AND "acidocin D20079, Lactobacillus acidophilus" [Supplementary Concept].

Data items, Data collection, and Selection process

Table II represents the used checklist, involving the name of the first author, year of publication, sample size, study design, control group, intervention group, and survival rate extracted and reported. Also, the data required for meta-analysis, including clinical outcome, Antibacterial effect of brackets coating, were extracted from the studies. All articles were selected based on the inclusion criteria, two reviewers independently screened each record, and each report was retrieved.

Eligibility criteria

Inclusion criteria: Inclusion criteria were a response to PICO, as reported in **table I**. Articles published in English, in-vitro studies, and studies that assessed the antibacterial effect of AgNPs and ZnONPs-coated Orthodontic Brackets.

Exclusion criteria: Case studies, case reports, and review papers. Studies without full-text access.

Table I: PICO search strategy.

PICO strategy	Description
P	Population: orthodontic brackets
I	Intervention: AgNPs and ZnONPs, Ag/ZnO NPs
C	Comparison: brackets as received without modifications
O	Outcome: clinical outcome, Antibacterial activity

Study risk of bias assessment

The quality assessment of searched articles was performed by the modified CONSORT (Guidelines for reporting pre-clinical in vitro studies on dental materials) criteria[24]; Each study was reviewed with 14 items, and the parameters were reported as yes or no. These items were:

Structured abstract of trial design, methods, findings and conclusion, introduction and causes, aims and hypotheses, the applied intervention like processes and duration, with sufficient detail to allow for replication, well-defined primary and secondary outcomes like when and how evaluated, the estimation process of sample size, the generation and implementation processes of randomized allocation, who created the randomized allocation, the blinded participants after assigning the intervention, statistical analysis for group comparison, post-intervention findings and estimated effect size and precision, limitations of the study, assessment of possible bias, lack of accuracy, and where the full trial protocol is available in case of multiplicity of analysis, funding and other support.

The modified Cochrane risk of bias tool was used, each item of which was given a score of 2, 1, or 0 with the sum of scores 0-3, 4-7, and 8-10, meaning low, moderate, and high risks of bias, respectively. In this tool, the lowest score was 0, and the highest score was 10[25].

Data analysis

Data were analyzed by STATA/MP. V17 software. We calculated a 95% confidence interval (95%CI) for the mean difference (MD) based on the fixed effect model and Inverse-variance method. Random effects were used. I2 showed possible heterogeneity, with a value of less than 50% as low and above 50% as moderate-to-high heterogeneity.

Results

The selection process of searched articles

In the initial search, 209 articles related to the keywords were found. Of these, 5 studies were Duplicate records, 8 articles were removed due to ineligibility based on automation tools, and 12 articles were deleted for other reasons. In the next step, abstracts of 184 articles were reviewed, and finally, 152 articles were omitted because of exclusion criteria. After reviewing the full text of 32 articles according to the inclusion criteria, 24 studies were excluded, and eight studies were selected (**Figure 1**).

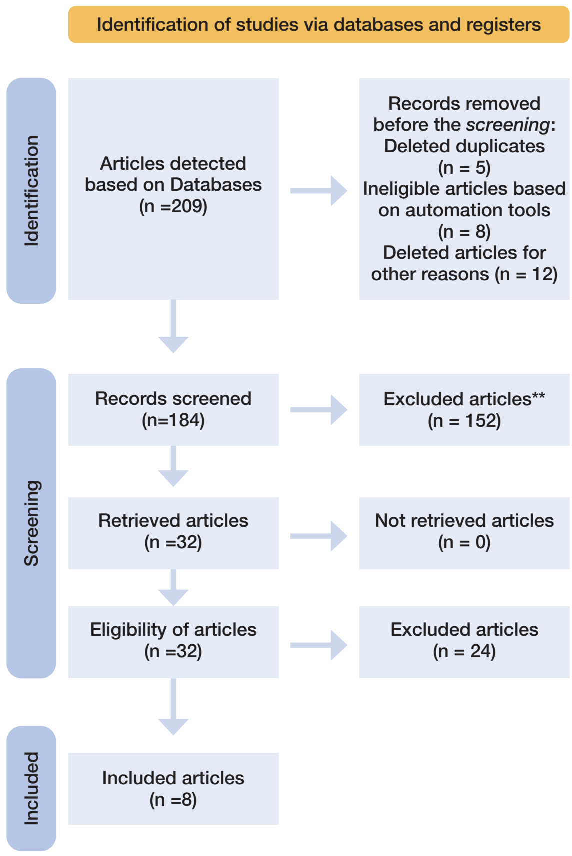
Study characteristics

A total of 566 Orthodontic Brackets were examined; the data from previous attempts are reported in **table II**.

Risk of bias in studies

According to the risk of the bias assessment tool, five studies possessed a moderate risk of bias, and three possessed a low risk of bias (**Tables III** and **IV**).

Figure 1: PRISMA 2020 Checklist.



Antibacterial testing

Antibacterial activity of brackets coating against L. acidophilus

The mean difference (MD) of the antibacterial potential of brackets coating against *L. acidophilus* between Ag NPs coating and the control group was 2.71 (MD, 2.71 95% CI = 2.05, 3.37; p=0.00) with high heterogeneity (I^2=99.84%; P =0.00). The statistical findings indicated a significantly reduced effect on the survival rate of *L. acidophilus* with Ag NPs than the control group (**Figure 2**).

The MD of the antibacterial potential of brackets coating against *L. acidophilus* between ZnO NPs coating and control group was -3.50 (MD, -3.50 95% CI = -4.38, -2.63; p=0.00) with high heterogeneity (I^2=99.81%; P =0.00). The statistical findings indicated a significantly reduced effect on the survival rate of *L. acidophilus* with ZnO NPs than the control group (**Figure 2**).

The MD of the antibacterial potential of brackets coating against *L. acidophilus* between Ag/ZnO NPs coating and controls was -58.12 (MD, -58.12 95% CI = -68.68, -47.56; p=0.00). The statistical findings indicated a significantly reduced effect on the survival rate of *L. acidophilus* with Ag/ZnO NPs than the control group (**Figure 3**).

Figures 2, 3, and **4** statistically significantly reduce the survival rate of L. acidophilus, using Ag/ZnO NPs with the highest impact and then using Ag NPs and ZnO NPs.

Table II: Summary of data.

n	Study. Years	Sample size	Nanoparticle type (n)	Number of the control group	preparation	Antibacterial activity assessment
1	Zeidan et al., 2022 [3]	48	Ag NPs [12], ZnO NPs [12], and Ag/ ZnO NPs [12]	12	Before coating the brackets, any unwanted macroscopic contamination was removed; the brackets were cleaned and underwent autoclave sterilization, then stored in a sealed container.	*S. mutans* strain (ATCC 25,175), suspension of concentration 1.5× 106 CFU/mL. Lactobacillus acidophilus
2	Tanbakuchi et al., 2021[26]	30	Ag [10], ZnO [10]	10	The ZnO suspension was prepared by dissolving ZnO powder (0.1 g) in acetone (3 mL); the same way was followed to prepare Ag suspension, followed by pumping at 10-mL/hr flow rate via a syringe pump at 3 cm from the bands.	*S. mutans* ATCC 35668, *L. acidophilus* ATCC 314 and C. albicans ATCC 14053
3	Kachoei et al., 2021 [27]	120	Ag NPs [30], ZnO NPs [30], and Ag/ ZnO NPs [30]	30	After dissolving zinc acetylacetonate (0.4 g) with absolute ethanol (20 mL), 30% starch solution (20 mL) was poured drop by drop while stirring within 4 h. The $AgNO_3$ aqueous solution was added dropwise inside the solution while stirring within half an hour and then heating in a water bath.	*S. mutans* ATCC 35668, Staphylococcus aureus ATCC 25923, Lactobacillus gasseri ATCC 33323, Escherichia coli ATCC 25922, and Candida albicans ATCC 10231
4	Yassaei et al., 2020 [28]	130	Hydroxyapatite [26], titanium oxides [26], zinc oxide [26], copper oxide [26], and silver oxide [26] NPs	6	The preparation of hydroxyapatite, zinc, titanium oxides, silver, and copper NPs was performed at the concentrations of 0.5 and 1 wt%, followed by blending with light cure orthodontics.	*S. mutans*
5	Eslamian et al., 2020 [29]	34	Ag NPs [17]	17	The groups individually underwent 0.022-inch bond stainless steel twin brackets, Transbond XT, and nano-adhesive, followed by etching with 37% phosphoric acid for 30 seconds and washing with water for 15 seconds.	*S. mutans*
6	Kambalya et al., 2018 [19]	60	Ag [15], TiO2 [15], and ZnO [15] NPs	15	Equal amounts of TiO2, Ag, and ZnO NPs (160 mg) were added to different sterile test tubes containing BHI broth (4mL), meaning 4% concentration (10mg of the test compound in 1mL BHI broth is equal to 1% of the test compound.	*S. mutans* (ATCC 25175)
7	Ramazanzadeh et al., 2015 [30]	72	nano copper oxide (CuO) [20], ZnO NPs [20], and CuO-ZnO [20]	12	Add the sodium hydroxide solution to zinc sulfate aqueous solution (at the ratio of 1:2) drop by drop while vigorously stirring for 12 hours, then filtering the resultant precipitate and washing it several times with de-ionized water.	*S. mutans*
8	Mirhashemi et al., 2013 [31]	72	ZnO NPs [36]	36	Mixing nano-powder (64 mg) with Transbond XT composite (576 mg) to prepare a dental composite bearing 10% NPs, and reaching a uniform consistency with the aid of a mixing spatula on a glass slab under a semi-dark condition	*S. mutans* ATCC 25175, S. sanguis ATCC 10556 and *L. acidophilus* ATCC 4356

Table III: Quality of the included studies.

Study. Years	Item													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Zeidan et al., 2022[3]	√	√	×	×	×	×	×	×	×	√	×	×	×	×
Tanbakuchi et al., 2021[26]	√	√	√	√	√	√	×	×	×	√	√	√	×	×
Kachoei et al., 2021[27]	√	√	√	√	√	√	×	×	×	√	√	√	×	×
Yassaei et al., 2020[28]	√	√	√	√	√	√	×	×	×	√	√	√	×	×
Eslamian et al., 2020[29]	×	×	×	×	×	×	×	×	×	√	√	√	×	×
Kambalya et al., 2018[19]	×	×	×	×	×	×	×	×	×	√	√	√	×	×
Ramazanzadeh et al., 2015[30]	√	√	√	√	×	√	×	×	×	√	√	√	×	×
Mirhashemi et al., 2013[31]	√	√	×	×	×	×	×	×	×	√	×	×	×	×

Table IV: Risk assessment.

Study. Years	Allocation concealment	Sample size	Blinding	Assessment methods	Selective outcome reporting	Risk of bias
Zeidan et al., 2022[3]	1	1	2	0	0	Moderate
Tanbakuchi et al., 2021[26]	1	0	2	0	0	Low
Kachoei et al., 2021[27]	1	0	2	0	0	Low
Yassaei et al., 2020[28]	1	0	2	0	0	Low
Eslamian et al., 2020[29]	1	1	2	0	0	Moderate
Kambalya et al., 2018[19]	1	1	2	0	0	Moderate
Ramazanzadeh et al., 2015[30]	1	1	2	0	0	Moderate
Mirhashemi et al., 2013[31]	1	1	2	0	0	Moderate

Figure 2: Forest plot showed the Antibacterial potential of Ag NPs-coated Orthodontic Brackets against *L. acidophilus*.

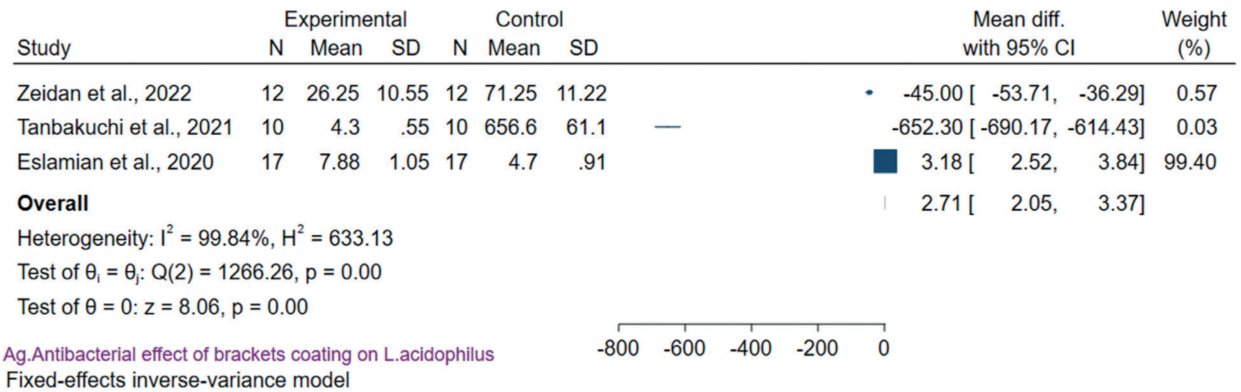


Figure 3: Forest plot showed the Antibacterial potential of ZnO NPs-coated Orthodontic Brackets against *L. acidophilus*.

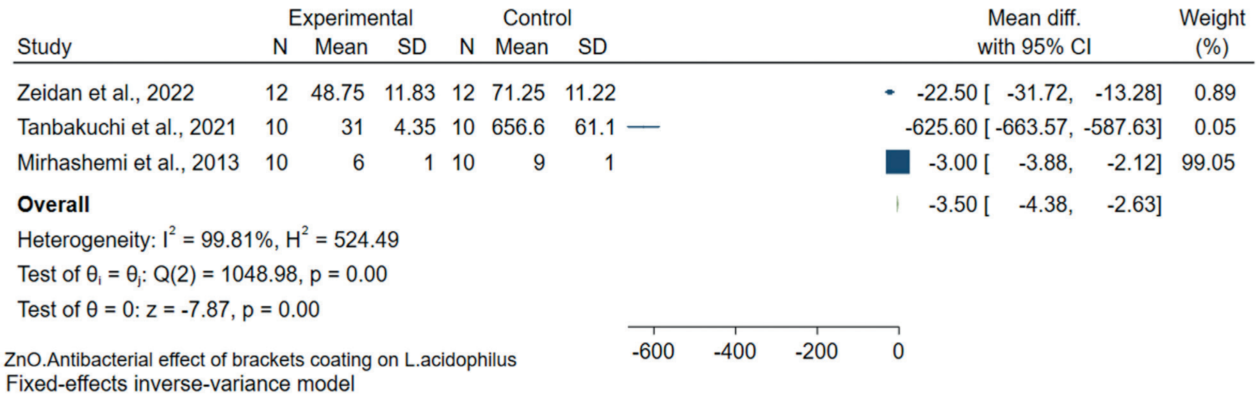
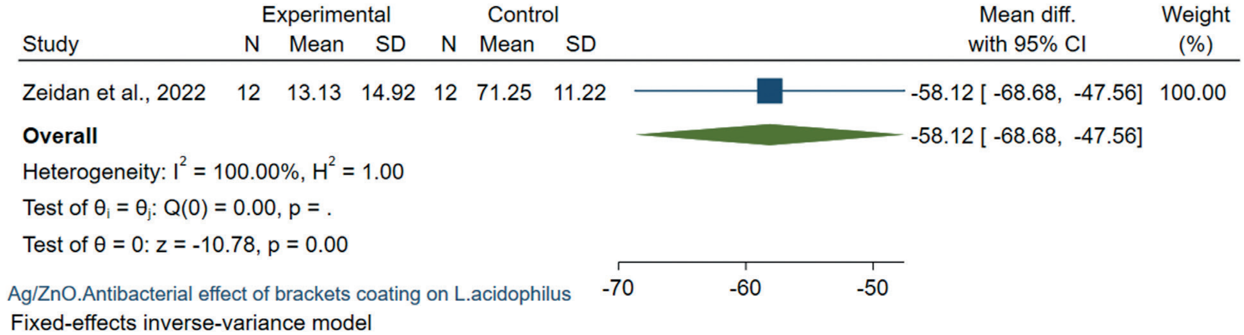


Figure 4: Forest plot showed the antibacterial potential of Ag/ZnO NPs-coated Orthodontic Brackets against *L. acidophilus*.



The MD of the antibacterial performance of brackets coating against *S. mutans* between Ag NPs coating and the controls was -2.87 (MD, -2.87 95% CI = -3.59, -2.15; p=0.00) with high heterogeneity (I^2=100%; P =0.00). The statistical findings indicated a significantly reduced effect on the survival rate of *S. mutans* with Ag NPs than control (**Figure 5**).

The MD of the antibacterial performance of brackets coating against *S. mutans* between ZnO NPs coating and controls was -275.54 (MD, -275.54 95% CI = -281.23, -269.85; p=0.00) with high heterogeneity (I^2=99.99%; P =0.00). The statistical findings indicated a significantly reduced effect on survival rate of *S. mutans* with ZnO NPs than controls (**Figure 6**).

The MD in the antibacterial performance of brackets coating against *S. mutans* between Ag/ZnO NPs coating and the controls was -574 (MD, -574 95% CI = -580.03, -567.97; p=0.00). The statistical findings indicated a significantly reduced effect on the survival rate of S. mutans with Ag/ZnO NPs than controls (**Figure 7**).

Figure 5: Forest plot showed the antibacterial potential of Ag NPs-coated Orthodontic Brackets against *S. mutans*.

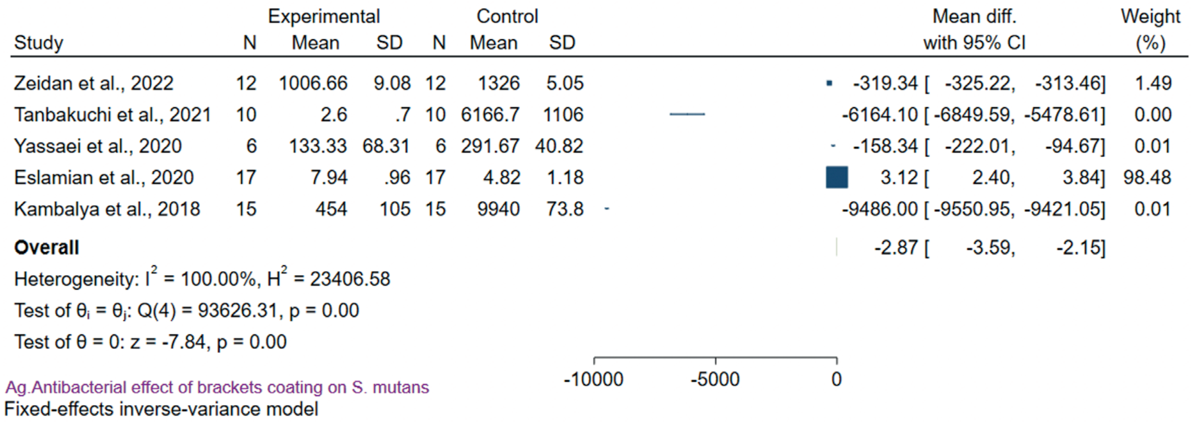


Figure 6: Forest plot showed the antibacterial potential of ZnO NPs-coated Orthodontic Brackets against *S. mutans*.

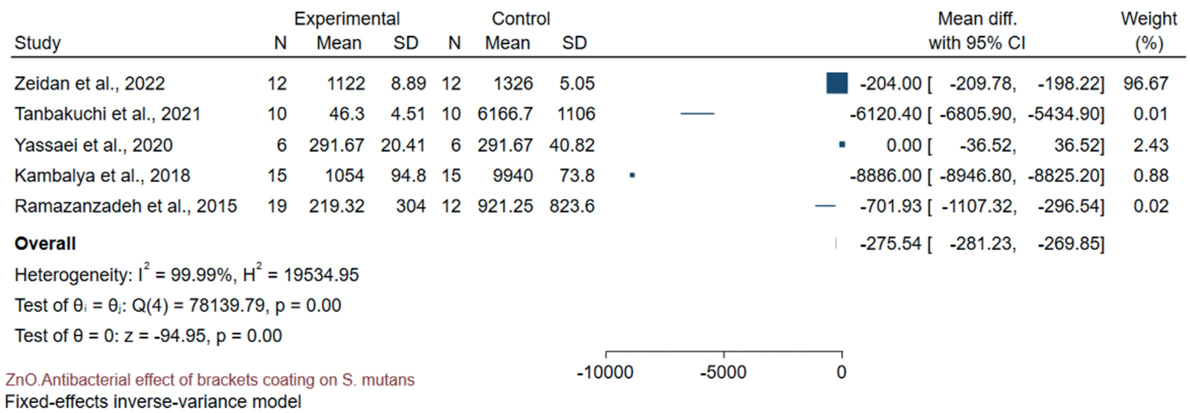
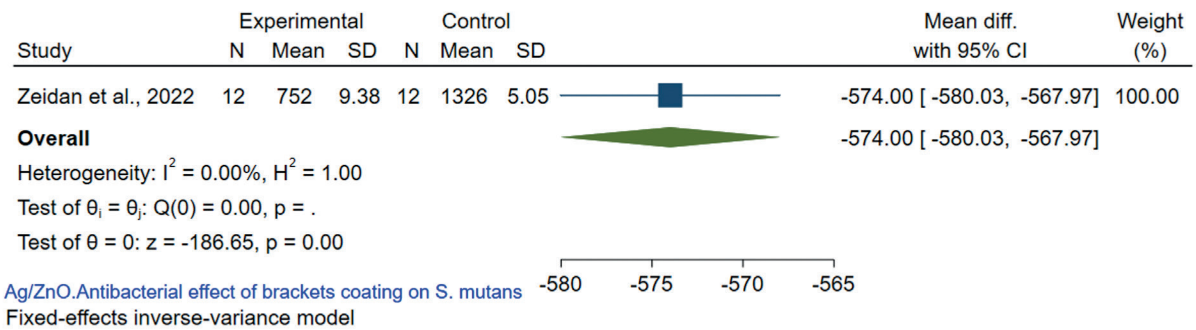


Figure 7: Forest plot showed the antibacterial potential of Ag/ZnO NPs-coated Orthodontic Brackets against *S. mutans*.



Discussion

We aimed to investigate the antibacterial potential of Ag, ZnO, and Ag/ZnO NPs-coated orthodontic brackets. One of the problems of orthodontic patients is tooth decay; Therefore, it is very important to use materials that have antibacterial activity during the orthodontic treatment process, especially in patients who do not brush their teeth[32]. Studies have shown that plaque accumulation, tooth surface demineralization, and the formation of white spot lesions are very common in orthodontic patients[33]. Based on the present meta-analysis, brackets coated with AgNPs, ZnO NPs, and Ag/ZnO NPs revealed a significant difference in antibacterial performance versus the two study bacteria. Similarly, it was shown that brackets coated with silver had an antibacterial activity versus the two study bacteria[34]. Another study showed the greater antimicrobial potential of AgNPs compared to ZnO NPs. The mentioned study investigated the antimicrobial potential of AgNPs and ZnO NPs against *S. mutans*[35]. A study showed that Ag/ZnO had an enhanced antibacterial effect against S. mutans[36]. The Ag and ZnO combination was synthesized to reduce any possible risk for cytotoxic and genotoxic impacts of AgNPs in humans[37] and to obtain the merits of its increased antibacterial activity compared to ZnO[21]. The studies selected in the present study were of medium to high quality. However, the studies had very high heterogeneity, and the reason for this could be related to the cognitive methodology and the use of different concentrations of NPs; therefore, citing our findings should be interpreted with caution. Also, the duration of the evaluation of the results was different; in some studies, the length of time was not stated. A study investigating the prolonged antibacterial performance of coated brackets was not found based on the results of studies on the two study bacteria. And then, Ag and ZnO the insignificant difference in the antimicrobial potential of the three groups over time, which means the persistence of the antimicrobial effect of the bracket coatings over time. However, the duration of the study may affect the informed results. The cognitive methodology of the studies should be the same in future studies.

Conclusion

Based on the present meta-analysis, brackets coated with silver, ZnO, and Ag/ZnO NPs had an antibacterial performance against *L. acidophilus* and *S. mutans* compared to the uncoated bracket. Further studies should be conducted to evaluate cytotoxicity and other complications for nanoparticle-coated brackets and their efficacy in clinically reducing the incidence of WSLs during orthodontic treatment. Also, more studies should be conducted to investigate the role of abrasion and friction on the NPs coating.

Conflict of Interest

The authors declared that there is no conflict of interest.

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