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ORIGINAL

Evaluation of the Effects of Cinnamon, CuO, and ZnO Nanoparticles on the Antibacterial Properties of a Luting Glass Ionomer Orthodontic Bands Cements: A Systematic Review and Meta-analysis

Evaluación de los efectos de las nanopartículas de canela, CuO y ZnO sobre las propiedades antibacterianas de cementos para bandas de ortodoncia de ionómero de vidrio: una revisión sistemática y un metanálisis

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Abstract

Objective: Cinnamon, Zinc oxide, and Copper oxide nanoparticles have been investigated for their antibacterial effects in the current study. Systematic Review and Meta-analysis were performed to evaluate the antibacterial properties of luting glass ionomer cement used in orthodontic bands containing cinnamon, CuO, and ZnO nanoparticles.

Material and methods: Using the PRISMA 2020 checklist, a systematic review and meta-analysis are presented in this study. EBSCO, ISI Web of Knowledge, PubMed, Scopus, Web of Science, and Embase databases were searched for systematic literature until May 2023. An inverse-variance method and a fixed effect model were used for mean differences to calculate a 95% confidence interval. The meta-analysis was carried out using Stata/MP V.17.

Results: The initial review screened abstracts from 213 studies, two authors reviewed 31 full texts, 7 studies were selected for the secondary review, and duplicate studies were eliminated. The mean difference in antibacterial effect on S. mutans between 4% cinnamon NPs vs. the control group was 12.33 (MD, 12.33 95% CI 12.11, 12.55; p=0.00). The mean difference in antibacterial effect on S. mutans between 4% Copper oxide nanoparticles was 10.02 (MD, 10.02 95% CI 9.97, 10.07). The addition of 4% ZnO NPs caused a significant increase and empowered the antibacterial property against S. mutans bacteria.

Conclusion: The present meta-analysis shows that cinnamon, zinc oxide, and copper oxide nanoparticles are effective against S. mutans.

Key words: Dental Cements, Glass Ionomer Cements, Nanoparticles, Orthodontics, Streptococcus mutans.

Resumen

Objetivos: En el presente estudio se han investigado las nanopartículas de canela, óxido de zinc y óxido de cobre por sus efectos antibacterianos. Se realizaron una revisión sistemática y un metanálisis para evaluar las propiedades antibacterianas del cemento de ionómero de vidrio utilizado en bandas de ortodoncia que contienen nanopartículas de canela, CuO y ZnO.

Métodos: Utilizando la lista de verificación PRISMA 2020, en este estudio se presenta una revisión sistemática y un metanálisis. Se realizaron búsquedas de literatura sistemática en las bases de datos EBSCO, ISI Web of Knowledge, PubMed, Scopus, Web of Science y Embase hasta mayo de 2023. Se utilizaron un método de varianza inversa y un modelo de efectos fijos para las diferencias de medias para calcular un intervalo de confianza del 95%. El metanálisis se realizó utilizando Stata/MP V.17.

Resultados: La revisión inicial examinó los resúmenes de 213 estudios, dos autores revisaron 31 textos completos, se seleccionaron 7 estudios para la revisión secundaria y se eliminaron los estudios duplicados. La diferencia media en el efecto antibacteriano sobre S. mutans entre las NP de canela al 4 % versus el grupo de control fue de 12,33 (DM, 12,33; IC del 95 %: 12,11, 12,55; p = 0,00). La diferencia media en el efecto antibacteriano sobre S. mutans entre las nanopartículas de óxido de cobre al 4 % fue de 10,02 (DM, 10,02; IC del 95 %: 9,97 a 10,07). La adición de 4% de NP de ZnO provocó un aumento significativo y potenció la propiedad antibacteriana contra la bacteria S. mutans.

Conclusión: El presente metanálisis muestra que las nanopartículas de canela, óxido de zinc y óxido de cobre son efectivas contra S. mutans.

Palabras clave: Cementos Dentales, Cementos de Ionómero de Vidrio, Nanopartículas, Ortodoncia, Streptococcus mutans.

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Introduction

Orthodontic bands were an essential component of fixed orthodontic treatments introduced at the end of the 19th century[1]. These bands had disadvantages, including the higher demineralization of tooth enamel. Also, problems such as difficulty brushing teeth and plaque accumulation were other disadvantages[2]. During fixed orthodontic treatment, the incidence of white spot lesions (WSL) is high; studies show this prevalence is 45.8% to 68.4%[3]. Recently, Glass ionomer cement (GICs) has been considered one of the best options for cementing orthodontic bands, which has good biocompatibility and chemical adhesion to teeth[4]. Studies have shown that GICs have the most vital anti-caries activity among dental materials, and this advantage could be due to their fluoride-releasing ability and remineralization potential[5]. Some studies have shown that GICs have a low activity rate against microorganisms[6-8]. In order to solve this problem, adding nanoparticles to GICs is suggested to increase the antimicrobial activity of cement[9]. Studies have investigated the effect of adding ceramic bioactive particles, glass powders, and other chemicals to GIC powder to increase antibacterial properties.

Nanoparticles can facilitate antimicrobial activity due to their small size and increased surface-to-volume ratio. However, there are challenges in this regard because researchers believe that nanoparticles may change the biological metabolic pathways of human cells and lead to the development of cancer or other diseases; therefore, maintaining human health is very important[10,11]. The use of traditional and herbal materials against bacteria has been reported in some studies[12]. Cinnamon is one of the substances with anti-inflammatory properties and is known as an anti-caries substance. On the other hand, its other benefits are having antioxidant, antimicrobial, and cardioprotective propertie[13]. Studies have shown that cinnamon nanoparticles had antibacterial activity against Streptococcus mutans (S mutans)[12]. Studies have also reported the strong antimicrobial properties of zinc oxide (ZnO) nanoparticles. The literature shows antimicrobial properties when adding zinc oxide nanoparticles to dental materials[14,15]. Other nanoparticles with antimicrobial activity reported in some studies are copper oxide (CuO) nanoparticles[16,17]. In order to provide strong evidence, a comprehensive investigation of the antimicrobial effectiveness of cinnamon, CuO, and ZnO nanoparticles for cementing orthodontic bands is essential. The present study evaluates a glass ionomer cement's antibacterial properties for luting orthodontic bands using cinnamon, CuO, and ZnO nanoparticles.

Material and Methods

Search strategy

The PRISMA 2020 checklist was used for systematic reviews and meta-analyses[18]. The study used keywords related to its objectives to search all international databases, including PubMed, Scopus, Science Direct, ISI, Web of Knowledge, and Embase, until May 2022. In addition, related articles were found using the Google Scholar search engine. MeSH keywords:

("Orthodontic Appliances, Fixed"[Mesh]) OR "Orthodontic Appliances"[Mesh]) AND "Dental Cements"[Mesh]) OR "Dental Bonding"[Mesh]) OR "Glass Ionomer Cements"[Mesh]) AND "Nanoparticles"[Mesh]) OR ("Nanoparticles/microbiology"[Mesh] OR "Nanoparticles/organizationandadministration"[Mesh] OR "Nanoparticles/statistics and numerical data"[Mesh] OR "Nanoparticles/toxicity"[Mesh])) AND "Zinc Oxide"[Mesh]) AND "cupric oxide" [Supplementary Concept]) AND "cinnamon oil, leaf" [Supplementary Concept]) AND "Streptococcus mutans"[Mesh]) AND ("Anti-Bacterial Agents"[Mesh] OR "Anti-Bacterial Agents" [Pharmacological Action] OR "Microbial Sensitivity Tests"[Mesh]).

The Data items, selection process, and data collection

The checklist included the author's name, year of publication, study design, sample size, number of control groups, number of intervention groups, type of intervention group, assess the antimicrobial property and antibacterial activity assessment was extracted and reported in **table II**. Additionally, meta-analysis data were extracted from the studies, including antibacterial effects. We selected all articles based on the inclusion criteria, screened the records independently by two reviewers, and retrieved each report.

Eligibility criteria

Inclusion criteria: A response to PICO was the inclusion criterion, as shown in **table I**. Articles published in English, in-vitro, and in-vivo studies and studies that assessed the antibacterial effect of adding cinnamon CuO and ZnO nanoparticles on glass ionomer cement.

Exclusion criteria

Case studies, Review papers, and case reports. Access to full-text studies is not available.

Study risk of bias assessment

In order to assess the quality of studies, modified CONSORT criteria (Reporting guidelines for preclinical in

Table I: PICO strategy.

PICO Strategy	Description
P	Population: Orthodontic bands
I	Intervention: A luting GIC was constructed using cinnamon, zinc oxide, and copper oxide NPs
C	Comparison: Non-modified GIC
O	Outcome: Antibacterial activity

vitro studies on dental materials) were used[19]. Each study was reviewed based on 14 items, and a yes or no answer indicates the parameters. The items were as follows:

A structured summary includes the trial design, a detailed description of the research methods, results, and conclusions. Including the scientific background and explanation of rationale, specific objectives, and hypothesis, and the intervention of each group, including when and how it was administered, replicable with sufficient detail, completely defined. Measuring the outcome according to predefined primary and secondary criteria, a description of how and when they were assessed, how the sample size was determined, a method for generating random allocation sequences, the random allocation sequence mechanism, which generates random allocation sequences, who was blinded after intervention assignment, comparison of groups using statistical methods, the results for each group and estimates of the effect size and precision, the limitations of the trial, sources of potential bias, where to find the full trial protocol, imprecision, if the relevant multiplicity of analysis, funding, and other support are available.

A modified and adapted version of the Cochrane risk of bias tool was used. Scores were assigned to each item ranging from 2, 1, or 0. Scores of 0 to 3 indicate a low risk of bias, scores of 4 to 7 indicate a moderate risk, and scores of 8 to 10 indicate a high risk of bias. The lowest score in this tool was 0, and the highest score was 10[20].

Data analysis

The data analysis was carried out using STATA/MP V.17. The inverse-variance method and fixed effect models were used to calculate the 95% confidence interval. I^2 showed heterogeneity due to using random effects to deal with potential heterogeneity. Values above 50% indicate moderate or high heterogeneity, whereas values below 50% indicate low heterogeneity.

Results

Study selection

During the initial search, 213 articles related to the keywords were identified. The records of 5 studies were duplicates, 4 articles were removed due to automation tools marking them as ineligible, and 11 were removed for other reasons. As a next step, 193 abstracts were reviewed, and after that, 162 articles were excluded from the research based on the exclusion criteria. In reviewing the full texts of 31 articles, 24 studies were excluded according to the inclusion criteria, and seven studies were selected (**Figure 1**).

Study characteristics

The data extracted from the studies are presented in **table II**.

Figure 1: PRISMA 2020 Checklist.

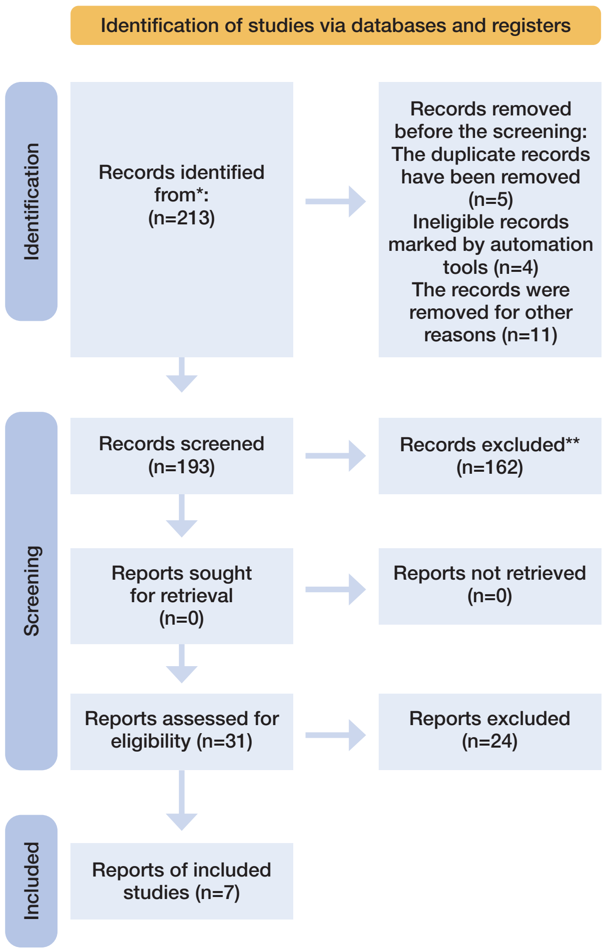


Table II: Summary of data.

No	Study. Years	Study design	Sample size	Nanoparticle type (n)	Number of the control group	Assess the antimicrobial property	Bacterial strain
1	Shafaee et al., 2022[21]	In-vitro	78	Cinnamon (26), ZnO (26), and CuO (26)	26	Agar disc diffusion test	S. mutans
2	Pourhajibagher et al., 2022[22]	Ex-vivo	50	ZnO (45)	5	Biofilm inhibition test	S. mutans
3	Malekhoseini et al., 2021[14]	Ex-vivo	50	ZnO (40)	10	Mueller-Hinton agar culture medium	S. mutans
4	Aguilar-Perez et al., 2020[6]	In-vitro	15	Cuo (12)	3	Agar diffusion test	S. mutans
5	Toodehzaeim et al., 2018[23]	In-vitro	40	Cuo (30)	10	Agar diffusion test	S. mutans
6	Garcia et al., 2017[24]	In-vitro	27	ZnO (18)	9	Antibacterial test	S. mutans and S. sanguinis
7	Vanajassun et al., 2014[25]	In-vitro	10	ZnO (5)	5	Agar diffusion test	S. mutans

S. mutans: Streptococcus mutant

The risk of bias in studies

The bias assessment tool identified four studies with a moderate risk of bias and three with a low risk of bias (**Tables III** and **IV**).

Based on the bias assessment tool, four studies were identified as moderate risk of bias and three as low risk of bias (**Tables III** and **IV**).

Antibacterial activity

Cinnamon nanoparticles

Figure 2 shows the effects of cinnamon nanoparticles on the antibacterial properties of glass ionomer cement. Mean differences of antibacterial effect on S. mutans between 1% cinnamon NPs, 2% cinnamon NPs, and 4% cinnamon NPs vs. control group was 10 (MD, 10 95% CI 9.33, 10.67; p=0.00), 11 (MD, 11 95% CI 10.94,

Table III: Quality of the included studies.

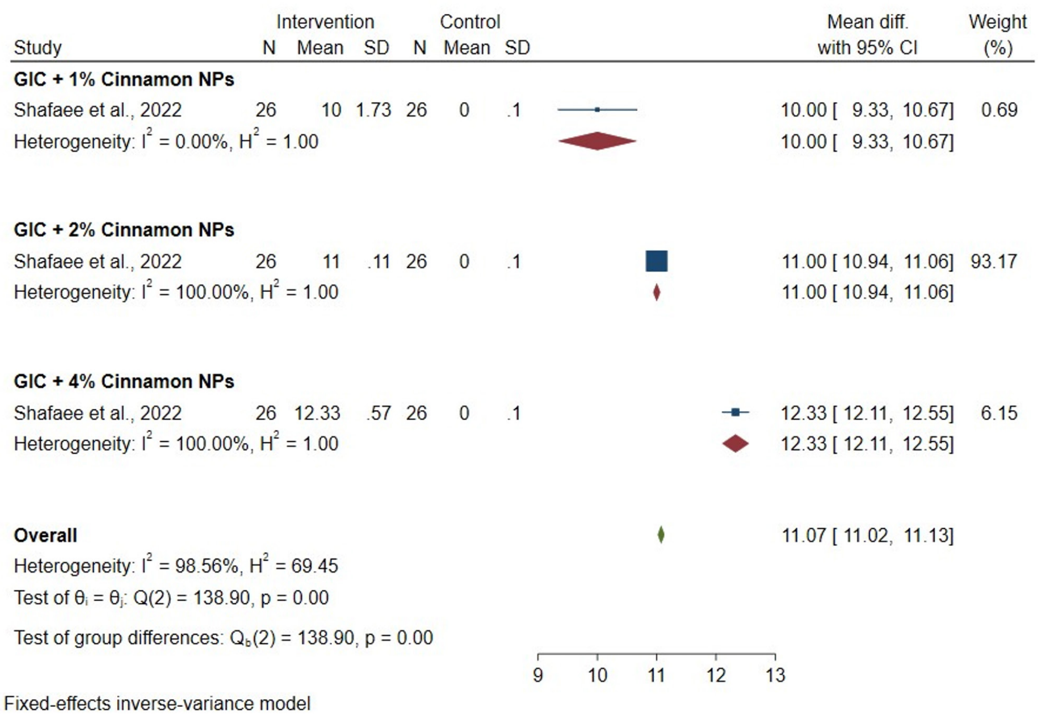
Study. Years	Item													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Shafaee et al., 2022[21]	🟢	🟢	🟠	🟠	🟠	🟠	🟠	🟠	🟠	🟢	🟠	🟠	🟠	🟠
Pourhajibagher et al., 2022[22]	🟢	🟢	🟢	🟢	🟢	🟢	🟠	🟠	🟠	🟢	🟢	🟢	🟠	🟠
Malekhoseini et al., 2021[14]	🟢	🟢	🟢	🟢	🟢	🟢	🟠	🟠	🟠	🟢	🟢	🟢	🟠	🟠
Aguilar-Perez et al., 2020[6]	🟢	🟢	🟢	🟢	🟢	🟢	🟠	🟠	🟠	🟢	🟢	🟢	🟠	🟠
Toodehzaeim et al., 2018[23]	🟠	🟠	🟠	🟠	🟠	🟠	🟠	🟠	🟠	🟢	🟢	🟢	🟠	🟠
Garcia et al., 2017[24]	🟠	🟠	🟠	🟠	🟠	🟠	🟠	🟠	🟠	🟢	🟢	🟢	🟠	🟠
Vanajassun et al., 2014[25]	🟢	🟢	🟢	🟢	🟠	🟢	🟠	🟠	🟠	🟢	🟢	🟢	🟠	🟠
	🟢	🟢	🟠	🟠	🟠	🟠	🟠	🟠	🟠	🟢	🟠	🟠	🟠	🟠

Yes: 🟢 No: 🟠

Table IV: The assessment of risks.

Study. Years	The concealment of allocations	Sample size	Blinding	Assessment methods	Reporting selective outcomes	Risk of bias
Shafaee et al., 2022[21]	1	1	2	0	0	Moderate
Pourhajibagher et al., 2022[22]	1	0	2	0	0	Low
Malekhoseini et al., 2021[14]	1	0	2	0	0	Low
Aguilar-Perez et al., 2020[6]	1	0	2	0	0	Low
Toodehzaeim et al., 2018[23]	1	1	2	0	0	Moderate
Garcia et al., 2017[24]	1	1	2	0	0	Moderate
Vanajassun et al., 2014[25]	1	1	2	0	0	Moderate

Figure 2: Cinnamon nanoparticles addition into the GIC.

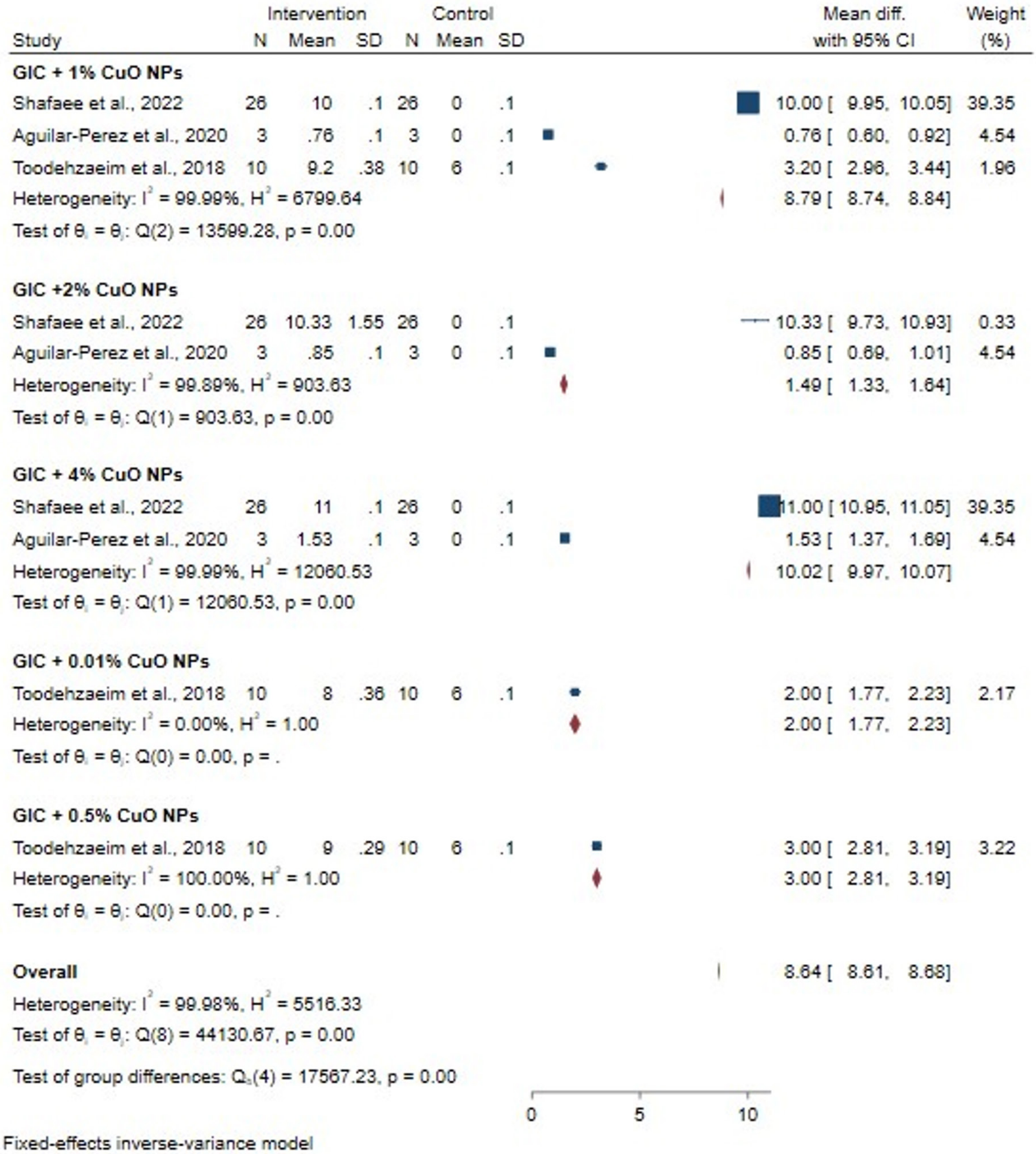


11.06; p=0.00), 12.33 (MD, 12.33 95% CI 12.11, 12.55; p=0.00), respectively. With the addition of 4% cinnamon nanoparticles, the antibacterial activity was significantly enhanced against S. mutans bacteria (**Figure 2**). Overall mean differences of antibacterial effect were 11.07 (MD, 11.07 95% CI 11.02, 11.13). The test of group differences showed significant differences between groups (p=0.00).

CuO nanoparticles

Figure 3 shows how adding CuO NPs to glass ionomer cement affects its antibacterial properties. Mean differences in antibacterial effect on S. mutans between 1% cinnamon NPs, 2% cinnamon NPs, and 4% cinnamon NPs, 0.01% cinnamon NPs, and 0.5% cinnamon NPs vs. control group was 8.79 (MD, 8.79 95% CI 8.74, 8.84; I^2=99.99%, high heterogeneity), 1.49 (MD, 1.49 95% CI 1.33, 1.64; I2=99.89%, high heterogeneity), 10.02 (MD, 10.02 95% CI 9.97, 10.07; I^2=99.99%, high heterogeneity) and 2 (MD, 2 95% CI 1.77, 2.23), 3 (MD, 3 95% CI 2.81, 3.19) respectively. The addition of 4% CuO NPs caused a significant increase and empowered the antibacterial property against S. mutans bacteria (**Figure 3**). Overall mean differences of antibacterial effect were 8.64 (MD, 8.64 95% CI 8.61, 8.68). The test of group differences showed significant differences between groups (p=0.00).

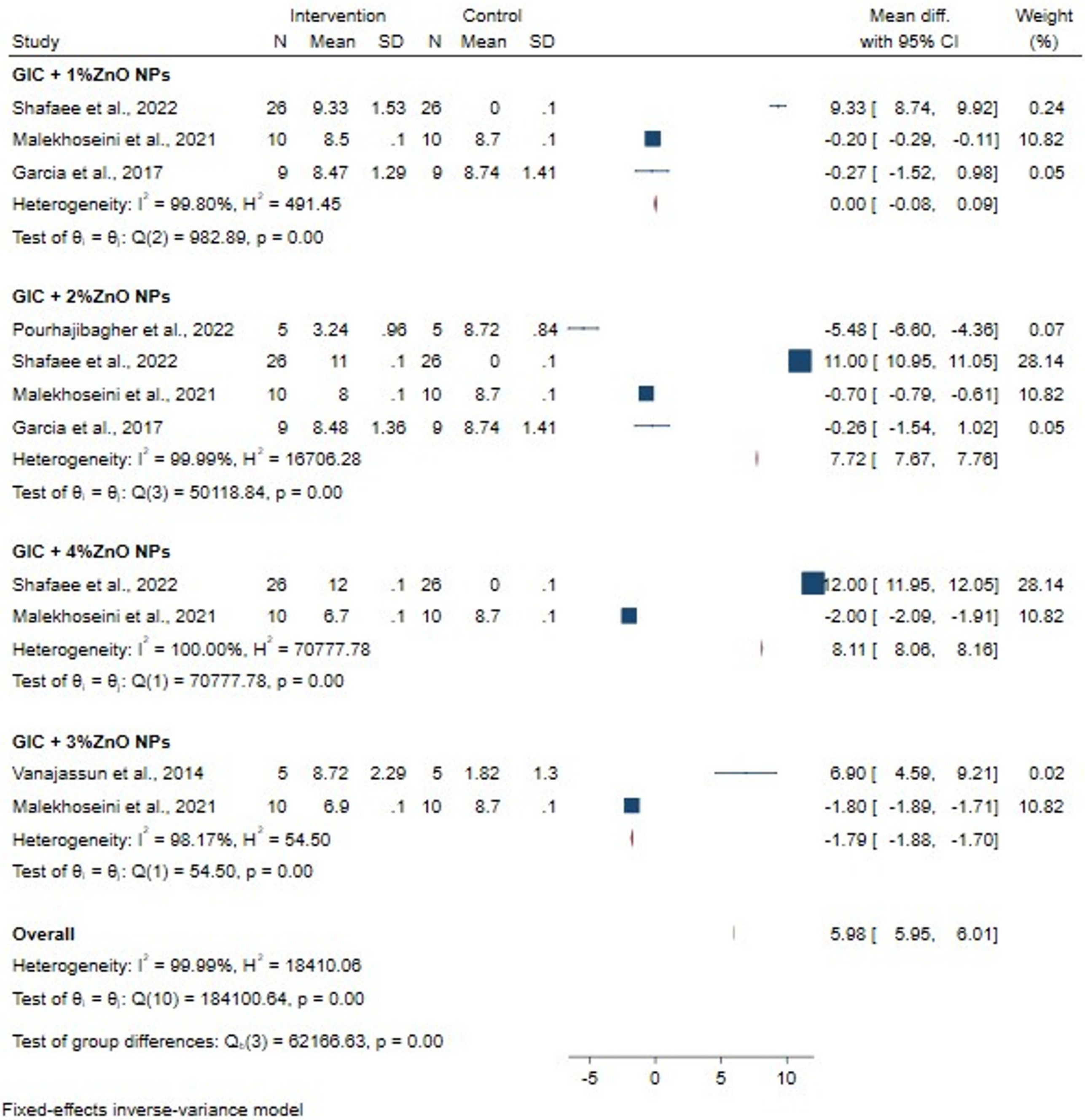
Figure 3: CuO nanoparticles addition to the GIC.



ZnO nanoparticles

Figure 4 shows how adding ZnO nanoparticles to glass ionomer cement affects its antibacterial properties. Mean differences of antibacterial effect on S. mutans between 1% ZnO NPs, 2% ZnO NPs, 4% ZnO NPs, and 3% ZnO NPs vs. control group was 0 (MD, 0 95% CI -0.08, 0.09; I^2=99.80%, high heterogeneity), 7.72 (MD, 7.72 95% CI 7.67, 7.76; I^2=99.99%, high heterogeneity), 8.11 (MD, 8.11 95% CI 8.06, 8.16; I^2=100%, high heterogeneity) and -1.79 (MD, -1.79 95% CI -1.88, -1.70; I^2=98.17%, high heterogeneity), respectively. A significant increase was observed with the addition of 4% ZnO NPs and empowered the antibacterial property against S. mutans bacteria (**Figure 4**). Overall mean differences of antibacterial effect were 5.98 (MD, 5.98 95% CI 5.95, 6.01). The test of group differences showed significant differences between groups (p=0.00).

Figure 4: ZnO nanoparticles addition into the GIC.



Discussion

According to our knowledge, this is the first meta-analysis investigating the effectiveness of GICs containing cinnamon, ZnO, and CuO nanoparticles against S. mutans. According to the present meta-analysis, the addition of 4% of cinnamon nanoparticles showed the strongest antibacterial effect against S. mutans. According to the studies, cinnamaldehyde, eugenol, benzoic acid, and cinnamic acid in cinnamon NPs have caused cinnamon NPs to have antimicrobial properties[26,27]. In a study where cinnamon nanoparticles were added to an orthodontic composite, it was observed that the induction of the antimicrobial effect of 3% cinnamon nanoparticles against S. mutans is higher than adding 1% cinnamon nanoparticles[12]. Based on the study findings, the minimum concentration used against caries-causing bacteria is 0.21 to 0.63 mg/ml[28]. The present meta-analysis showed that GIC containing 4% of ZnO NPs had the best antimicrobial properties against S. mutans bacteria compared to other percentages of ZnO NPs. ZnO NPs can prevent the growth of bacteria by destroying the cell wall and producing hydrogen peroxide[25]. Also, a meta-analysis showed that glass ionomer cement with 4% CuO NPs had stronger antimicrobial properties against S. mutans bacteria than other percentages. According to the selected studies and the analysis of their results, comparing the three investigated nanoparticles, it was observed that the cytotoxicity of CuO nanoparticles was higher than the other two nanoparticles, and the least cytotoxicity was related to cinnamon NPs[29]. A study has reported some cytotoxicity from cinnamon oil[30]. CuO nanoparticles are highly cytotoxic due to the production of reactive oxygen species, which cause oxidative stress[31]. A study that investigated the effect of zinc oxide nanoparticles on the toxicity of human gingival cells showed that high concentrations of zinc nanoparticles have high cytotoxicity in human gingival fibroblast cells[32]. Also, another study that examined the toxicity of Al2O3, CeO2, TiO2, and ZnO nanoparticles showed that the highest cytotoxicity is related to ZnO[33]. The present study had limitations; firstly, despite the small sample size of the studies, higher samples are needed for future research. Also, the selected studies were laboratory evaluations, which are needed to provide stronger evidence, showing the oral conditions completely. Only one ex vivo study was found, and future in vivo studies could help achieve better results. Also, it is important to interpret the findings of the present study with caution due to the high heterogeneity between the studies. Probably, this heterogeneity is related to the cognitive methodology of the studies.

Conclusions

According to the present meta-analysis, adding cinnamon, zinc oxide, and copper oxide nanoparticles to glass ionomer cement (GIC) for luting effectively against S. mutans, especially the use of cinnamon nanoparticles, zinc oxide nanoparticles, and copper oxide in weight percentages of 4%. It is suggested that future studies be conducted in-vivo with a larger sample size. Future studies should investigate the antibacterial properties of Cinnamon, CuO, and ZnO Nanoparticles on other bacteria. Also, more studies should be done in relation to Cinnamon.

Conflict of Interest

The authors declared that there is no conflict of interest.

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