

Influence of TiO₂, ZnO, and Ag Nanoparticles on the Antibacterial and Mechanical Properties of Modified Conventional Glass Ionomer Cements: A Systematic Review

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ABSTRACT

Background/Objectives: Glass ionomer cement (GIC) materials have inherent limitations regarding mechanical properties and antibacterial characteristics. This review aimed to collate *in vitro* evidence on the effect of titanium dioxide (TiO₂), zinc oxide (ZnO), and silver (Ag) nanoparticle concentration on the antibacterial and mechanical properties of modified GIC. **Methods:** Following PRISMA 2020 guidelines, we searched the Scopus, PubMed, and Web of Science databases for eligible studies published between 2021 and 2026. The inclusion criteria were *in vitro* studies reporting the nanoparticle concentration and at least one antibacterial or mechanical property. After initial screening, 26 studies were eligible for inclusion and grouped by additive type for narrative analysis due to methodological heterogeneity. The risk of bias (ROB) was evaluated using the QUIN tool. **Results:** The antibacterial properties of all three additives were positively correlated with the concentration. In contrast, the mechanical properties exhibited a threshold effect, with higher concentrations often resulting in reduced performance due to agglomeration. TiO₂ (14/26) demonstrated consistent evidence for an optimal concentration between 3- 5 wt%, while Ag (5/26) showed antibacterial efficacy at lower concentrations with a negative impact on the restoration's physical properties. The antibacterial properties of ZnO (2/26) could not be consistently demonstrated due to insufficient evidence. Overall, 19% of the studies were assessed as low, 50% as moderate, and 31% as high ROB. **Conclusions:** TiO₂ at a concentration of 3-5% demonstrated the most promising antibacterial and mechanical properties in the modification of GIC. Due to the lack of sufficient evidence, further preclinical and clinical investigations are required for ZnO.

Keywords: glass ionomer cement; titanium dioxide; zinc oxide; silver; nanoparticles; antibacterial activity; mechanical properties

INTRODUCTION

Dental caries continues to be a major global oral health issue, arising from the fermentation of carbohydrates by bacteria, which in turn produces acidic byproducts that demineralize the enamel of the tooth [1]. *Streptococcus mutans* is a gram-positive bacterium recognized as one of the primary causative agents of caries in human teeth due to its ability to form biofilm on tooth surfaces [2]. Beyond its clinical burden, caries experience, which includes untreated cavities and tooth loss, has been shown to unfavourably affect oral health-related quality of life, particularly in schoolchildren [3].

Glass ionomer cement is one of the most widely used restorative materials in modern dentistry to combat this problem. First introduced by Wilson and Kent in

1968, this material is often valued for its chemical adhesion to tooth structure, biocompatibility, and sustained fluoride-releasing capacity, helping protect against secondary caries, which, combined, supports its use in minimally invasive and paediatric restorative approaches [4,5]. Despite these advantages, GIC remains limited by its comparatively low mechanical strength, limited wear resistance, and modest inherent antibacterial activity relative to other options such as resin-based composites, making it vulnerable to fracture, wear, and secondary caries over time, especially in load-bearing posterior restorations [4,6].

To address these shortcomings, researchers have increasingly explored the idea of incorporating metal and metal oxide nanoparticles such as titanium.

dioxide (TiO₂), zinc oxide (ZnO), and silver (Ag), as an effective additive to GIC formulations, considering their characteristic of having a higher surface-to-volume ratio, which allows closer interaction with microbial membranes, and also mechanically, where the small size of nanoparticles helps them occupy spaces that are available between macromolecules [7,8]. For example, TiO₂ nanoparticles have been shown to improve GIC's mechanical and antimicrobial properties, improve fluoride release, and, in addition, reduce microcracks and air voids by enhancing the homogeneity and consistency of the cement matrix [9,10]. ZnO nanoparticles can also improve the antibacterial and mechanical properties of GIC by increasing concentrations that enhance mechanical performance, with the rod-shaped nanoparticles potentially increasing their interaction with *S. mutans* cells [11]. In addition, Ag nanoparticle incorporation into GIC has been reported to significantly reduce *S. mutans* adhesion and biofilm development through its antibacterial effects, while also generally maintaining compressive strength comparable to unmodified GIC [12,13].

Nonetheless, there is an implication that the impact of nanoparticle inclusion on the mechanical properties of GIC seems to vary according to concentration levels. Low to moderate concentrations could improve mechanical properties, while high concentrations could lower mechanical properties owing to nanoparticle agglomeration, which would cause matrix heterogeneity, surface roughness, increased porosity, and microfractures [14,15]. Likewise, research concerning antimicrobial modifications of GIC has shown insignificant changes in mechanical properties, underscoring the need for proper adjustment of additive concentration to maximize the benefits of the modification without weakening the composite structure [13].

Despite the existence of an extensive literature related to TiO₂, ZnO, and Ag-modified GIC in terms of *in vitro* experiments, there is still a great level of fragmentation of research results in relation to differences in the methods used for nanoparticle synthesis, which include chemical, green/plant-mediated, or biogenic/microbial methods, as well as various brands of GIC, their bases, and the types of antibacterial and mechanical effects observed. Currently, no synthesis of the relevant literature is available to conduct a comparison between the concentration-dependent effects of these nanoparticles within a common framework or to verify the consistency of the optimal concentrations recommended independently in separate studies.

OBJECTIVES

The purpose of this systematic review is to compile existing *in vitro* literature concerning the effect of TiO₂, ZnO, and Ag nanoparticle concentration on the antimicrobial and mechanical characteristics of modified glass ionomer cement. This review will specifically seek to:

- 1) Describe the dose-response association between the concentration of the nanoparticles

and the antibacterial activity of the additives.

- 2) Point out the concentration thresholds at which the mechanical properties (compressive strength, flexural strength, microhardness, and shear bond strength) become affected.
- 3) Determine the optimal concentration of each nanoparticle, depending on the available data on its antibacterial efficacy and mechanical properties.
- 4) Pinpoint the research gaps that exist in relation to the currently available literature.

METHODS

Protocol

This systematic review was conducted in accordance with the PRISMA 2020 guidelines [16]. Eligibility criteria, search methods, and risk of bias assessment (QUIN) were determined prior to full-text screening. This study was not registered in any public repository due to the lack of acceptance of *in vitro* studies by PROSPERO. This is a limitation of the current study.

Search Strategy

A systematic literature search was performed through three electronic databases: Scopus (n = 145), PubMed (n = 80), and Web of Science (n = 90), yielding 315 records. The search was limited to articles published in English from 2021 to 2026. The search string used in all the databases, with small variations to adapt the syntax to each database's search engine, was: ("glass ionomer cement" OR "GIC") AND ("TiO₂" OR "titanium dioxide" OR "ZnO" OR "zinc oxide" OR "Ag" OR "silver" OR "nanoparticle") AND ("antibacterial" OR "mechanical properties")

Eligibility Criteria

The inclusion of a study was based on its compliance with four main criteria: use of conventional glass ionomer cement (GIC) as the matrix material for restorations, rather than investigating the effect of nanoparticle addition to a resin-modified GIC or another matrix material entirely; inclusion of TiO₂, ZnO, or Ag nanoparticles for material modification; specification of the amount of nanoparticles (expressed or converted as wt%); and provision of a numerical measure of antibacterial activity or mechanical behaviour of the composite material. A relevant control group was also required for each included study. This control group should be either GIC without nanoparticle addition or GIC with a different concentration of nanoparticles.

Exclusion criteria included studies focusing on restorative materials that are non-GIC in nature or do not involve GIC chemistry and are composed of materials such as composite resins, ceramics, or adhesives. Studies using resin-modified GIC (RMGIC) rather than conventional GIC were also excluded, given differences in setting reaction and matrix chemistry that could confound nanoparticle-related effects. In addition, the inclusion of nanoparticle additives, other than TiO₂, ZnO, and Ag, was not considered. Literature reviews, meta-analyses, and case reports were not considered as secondary literature.

The inclusion of studies that did not compare with a control, either in the form of pure GIC or another nanoparticle composition, was ruled out since there would be insufficient comparison in such cases. Non-English articles were excluded as well. Moreover, considering the scope of the study, human studies and clinical trials were not included.

PICO Framework

PICO is a framework that helps formulate research questions in systematic reviews; this is an adaptation of the PICO framework for a materials-based (non-clinical) study. The PICO statement for the research question "How do the TiO₂, ZnO, or Ag nanoparticle contents affect the antibacterial and mechanical properties of *in vitro* glass ionomer cement?" was formed as follows:

- i. Population (P) – Conventional glass ionomer cements (GIC) studied *in vitro*;
- ii. Intervention (I) – Conventional glass ionomer cements (GIC) with additions of TiO₂, ZnO, or Ag nanoparticles at different concentrations;
- iii. Comparison (C) – Unmodified (traditional) glass ionomer cement (GIC) or glass ionomer cement with different nanoparticle contents;
- iv. Outcome (O) – Antibacterial effect (e.g., zones of inhibition, bacterial viability or colony formation), or mechanical properties (e.g., compressive strength, flexural strength or microhardness).

Data Screening and Extraction

All 315 records were exported to Mendeley Reference Manager to remove duplicates, then double-checked in Rayyan AI before being stored. After de-duplication, the titles and abstracts were screened based on the eligibility criteria defined in the Eligibility Criteria section, with the exclusion criteria coded as wrong population, intervention, study design, or outcome. The full-text articles that remained were then collected and assessed based on all the eligibility criteria defined, including the reasons for exclusion.

The following data items were extracted from each study selected: author(s) and year of publication, brand of GIC, type of nanoparticle and concentration, method of study, quantitative antibacterial and/or mechanical outcomes. All concentrations expressed in units other than weight percentage (wt%) were converted to wt%. For instance, mg/g was divided by 10. Any study using a combination of one of the target nanoparticles (TiO₂, ZnO, or Ag) with another additive but not having an arm testing the nanoparticles alone compared to GIC was not included.

Quality Assessment

Risk of Bias Assessment was done using the QUIN tool, a tool intended for the particular purpose of evaluating *in vitro* dental studies, in contrast to clinical tools such as Cochrane RoB 2, which are used for randomized controlled trials and are not applicable to this study [17]. These 12 areas, which comprised objectives, rationale for sample size, sampling methods, comparison group details, methodology explanation, operator information, randomization and blinding process, outcome measures, statistical appropriateness, findings, and sources of funding, were graded either adequate (2 points) or inadequate/non-existent (0 points), and the maximum score obtainable was 24. Studies scoring $\geq 70\%$, 50-69%, and $< 50\%$ were considered to have low, moderate, and high risks, respectively. The review was done by one reviewer only, using AI-assisted full-text screening, without an additional reviewer; this is considered a weakness (Section Limitations of This Review).

RESULTS

Selection and Characteristics of The Study

Figure 1 demonstrates the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram that shows the systematic approach in choosing relevant studies for the review. There were 315 total articles obtained through database searches, including PubMed (n=80), Scopus (n=145), and Web of Science (WOS) (n=90). None of the articles were found in other registers. After excluding 117 duplicate articles, there were 198 articles left to screen. In the screening step, 157 articles were excluded due to being off-topic. Thereafter, 2 articles could not be accessed, resulting in 39 articles for eligibility assessment. During the eligibility assessment, 13 reports were excluded for the following reasons: wrong study design, including clinical/human studies (n = 2); ineligible GIC formulation, specifically studies using resin-modified rather than conventional GIC (n = 2); wrong additive/intervention, including studies using additives other than TiO₂, ZnO, or Ag, or combinations that did not allow the target nanoparticle's effect to be isolated (n = 4); wrong outcome, in which the tested variables did not meet the predefined outcome criteria (n = 4); and wrong incorporation method, in which the nanoparticle was not incorporated into the GIC powder/liquid matrix (n = 1).

In the end, 26 articles passed the inclusion criteria and were selected for the review. The rigorous study selection process ensured that the selected articles were related to the topic under investigation and met the inclusion criteria. The process of selecting articles is shown in Figure 1, and the characteristics of the selected articles are shown in Table 1, Table 2, Table 3, and Table 4.

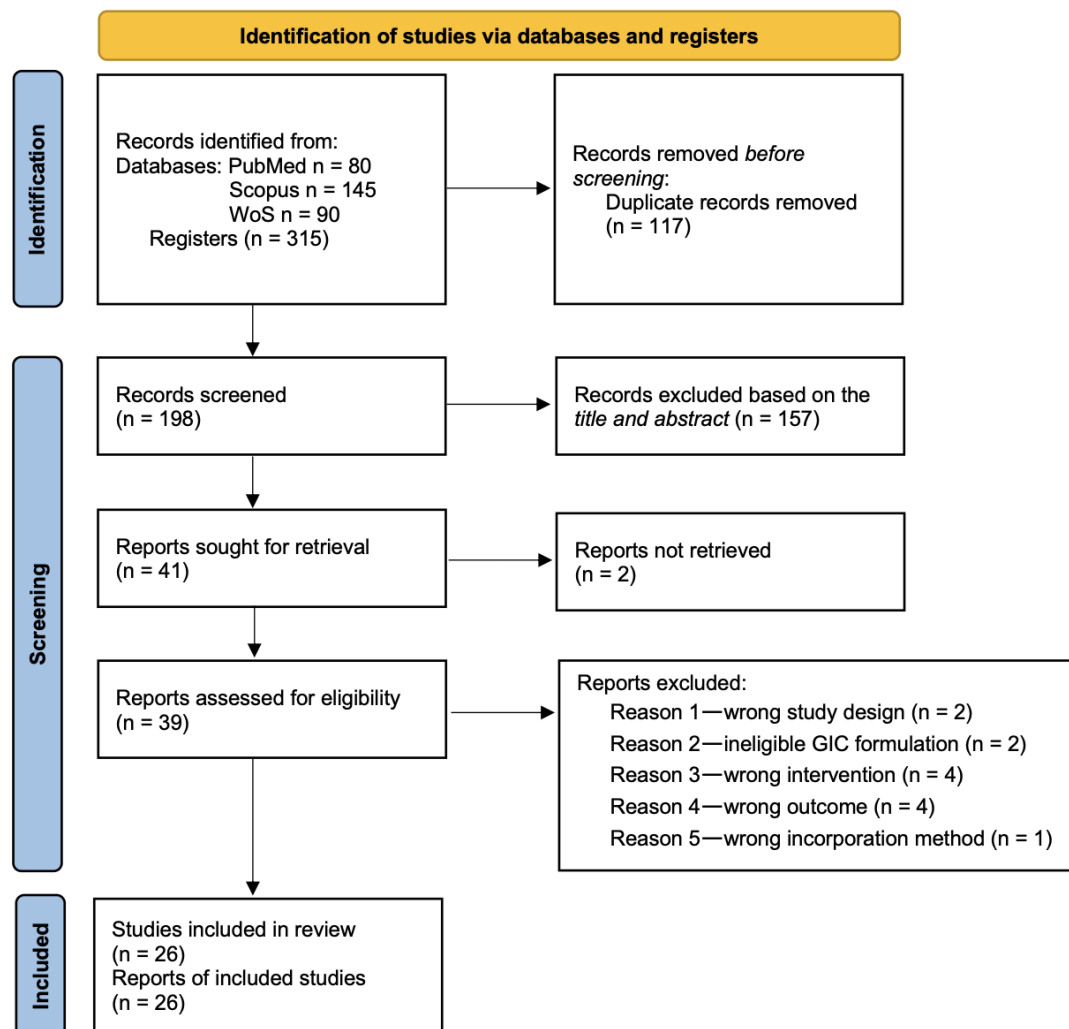


FIGURE 1: PRISMA Flowchart.

Quality Assessment and Risk of Bias of the Included Articles

Quality assessment was done using the QUIN (Quality Assessment Tool for *In Vitro* Studies in Dentistry), an instrument that was developed for laboratory-based dental research and not clinical quality tools such as Cochrane RoB 2, because the latter can hardly be applied to non-clinical *in vitro* studies. All twelve domains of the studies, clear definition of the aims/objectives, sample size calculation, sampling method, comparison group description, methodology description, operator description, randomization, outcomes measure method, outcome assessor description, blinding, statistics, and results presentation, were assessed as adequate (2 points), inadequate (1 point), or missing (0 points), thus making the highest attainable score equal to 24 per study. Studies receiving $\geq 70\%$ were considered to have low risk of bias, 50-69% to have moderate risk, and $<50\%$ to have high risk. The assessment process was done by one person assisted by artificial intelligence without any additional reviewer.

All 26 studies were evaluated with respect to the twelve domains (D1-D12), as outlined in Table 5 and the traffic light chart in Figure 3. Five studies (19%) had low risk, thirteen (50%) moderate risk, and eight (31%) high risk.

Domain one, which required a clear statement of aims; domain three, which required the use of an appropriate sampling technique; and domain four, which required detailed information about the comparison group, were adequately described in most of the studies. Domain two, which required an adequate sample size calculation; domain six, which required detailed information about the operators; domain seven, which required randomization; domain nine, which required details about the outcome assessor; and domain ten, which required blinding, were poorly described in most of the studies – possibly a universal convention *in vitro* dental material research rather than a characteristic peculiar to this literature.

Eight papers, namely Enan et al. [18], Fathi et al. [19], Guo et al. [13], Jaber et al. [11], Showkat et al. [20], Mahendra et al. [21], Ramić et al. [22], and Ekrikaya et al. [23], were categorized as being at high risk of bias because of the collective lack of sample size calculation, randomization, assessor information, blinding, and methodological detail. None of the papers excluded from the review were excluded on the grounds of having a high risk of bias. Rather, this criterion was used as an interpretive element to help understand the confidence in the review results. Importantly, studies consistently found concentration-dependent effects of TiO₂ throughout studies in all three risk-of-bias categories.

TABLE 1: Characteristics of included studies on TiO₂-modified GIC.

Author(s) & Year	GIC Type	Concentration	Outcomes Measured	Key Findings
Araújo et al., 2021 [10]	Ketac Molar EasyMix	3%, 5%, 7% TiO ₂ nanotubes	Mechanical (compressive strength, breaking strength)	TiO ₂ addition significantly reduced compressive/breaking strength vs. control
Fathi et al., 2022 [19]	Cavex	3%, 5% TiO ₂	Mechanical (compressive strength, flexural strength); cytotoxicity (non-antibacterial)	Both compressive strength (15.51 MPa) and flexural strength (26.39 MPa) peaked at 5%; declined at 7–10% due to increased porosity/microcracks (SEM-confirmed); nanoparticles non-cytotoxic (cell viability >90% at all time points)
Ganesh et al., 2026 [24]	Fuji IX	5% TiO ₂ (green-synthesized) ($\pm$ Chi)	Mechanical (enamel shear bond strength), compositional analysis (EDX/spectrum mapping)	Non-linear dose-response; 5% TiO ₂ gave highest shear bond strength (4.93 MPa vs. 2.17 MPa control, $p < 0.05$); 10% gave lowest among NP groups (3.44 MPa) but still higher than control; SEM showed fewest surface voids/cracks at 5%, worsening again at 7–10%
Ivanišević et al., 2021 [25]	Fuji IX GP Extra	3% TiO ₂ ($\pm$ HAp)	Mechanical (microhardness, cell viability)	5% gave highest microhardness; non-cytotoxic (>90% viability)
Karamüftüoğlu et al., 2026 [14]	Ketac Molar Easymix / Ketac Cem Radiopaque	1%, 3%, 5% TiO ₂ (green-synthesized)	Mechanical (flexural strength, microhardness, solubility)	Increased microhardness at both %; no significant flexural strength change; reduced water solubility
Mahendra et al., 2024 [21]	Fuji II	3%, 5% TiO ₂	Antibacterial + Mechanical (microhardness, compressive strength, roughness)	TiO ₂ -GIC improved mechanical properties the most; chitosan-GIC had higher antibacterial activity.
Mansoor et al., 2022 [15] (Nanomaterials)	GIC restorative (brand not specified)	0%, 3%, 5%, 7%, 10% TiO ₂ (biogenic, <i>Bacillus subtilis</i>)	Mechanical (fracture toughness, flexural strength, microhardness)	TiO ₂ increased fracture toughness and microhardness in some formulations
Mansoor et al., 2024 [26] (Odontology)	GIC restorative (brand not specified)	5% TiO ₂ (biosynthesized, <i>Bacillus coagulans</i>)	Mechanical (flexural strength, hardness)	No significant change in flexural strength; hardness decreased vs. control
Mansoor et al., 2025 [27] (CSBJ)	GIC restorative (brand not specified)	0%, 3%, 5%, 7%, 10% TiO ₂ (green-synthesized, corn silk)	Antibacterial (<i>L. acidophilus</i> viability)	5–7% reduced bacterial viability; no change in inhibition zone
Panahandeh et al., 2023 [9]	Fuji II	3%, 5%, 10% TiO ₂	Antibacterial (inhibition, viability, gene expression)	5% showed the highest antibacterial effect; 3–5% affected <i>S. mutans</i> viability/virulence genes
Ramić et al., 2024 [22]	Fuji IX / Ketac Molar	5% TiO ₂ (vs. HAp)	Mechanical/Physical (setting time, solubility, radiopacity)	7% increased setting time; 5% reduced solubility, increased radiopacity
Sena et al., 2025 [28]	Ketac Molar EasyMix	3%, 5%, 7% TiO ₂ nanotubes	Antibacterial (ion release, CFU)	5% showed higher/more sustained Ti ion release and antibacterial effect than 3%
Showkat et al., 2023 [20]	GIC (brand not specified)	3% TiO ₂ (isolated arm)	Mechanical (roughness, microhardness, flexural strength)	1–3% enhanced strength/hardness; 5% reduced performance (agglomeration)
Shubha et al., 2025 [29]	Fuji II	5%, 10% TiO ₂ (w/w) ¹	Mechanical (flexural strength)	TiO ₂ +chitosan combination gave the highest flexural strength among groups

¹Originally reported as 50 mg/g and 100 mg/g; converted to wt% for consistency with other included studies.

TABLE 2: Characteristics of included studies on ZnO-modified GIC.

Author(s) & Year	GIC Type	Concentration	Outcomes Measured	Key Findings
Jaber et al., 2023 [11]	Riva Self Cure	~0.024–0.041% ZnO (est. wt%) ²	Antibacterial (<i>S. mutans</i> inhibition zone), Mechanical (compressive strength, hardening)	Slight antibacterial improvement; antibacterial activity, compressive strength (~50% increase), and hardening (~20% increase) all increased with concentration (p<0.05). Compressive strength increased up to 50% with concentration.
Shafae et al., 2022 [30]	GIC (luting)	2% ZnO (vs. cinnamon, CuO)	Antibacterial (inhibition zone), cytotoxicity	ZnO showed antibacterial activity similar to cinnamon NPs; moderate cytotoxicity.

²Initial results were given as the mass concentration of the colloidal suspension (0.45–0.77 mg/mL) based on the number of laser pulses. The weight percent was then estimated by assuming that the standard scoop of Riva Self Cure powder weighs 0.45 g (according to the manufacturer's IFU) and that the density of the suspension is 1 g/mL.

TABLE 3: Characteristics of included studies on Ag-modified GIC.

Author(s) & Year	GIC Type	Concentration	Outcomes Measured	Key Findings
Ashour et al., 2022 [31]	Fuji IX	0.5% AgNP (isolated arm; vs. TVE-CuNP, metronidazole combinations)	Antibacterial (<i>S. aureus</i> , <i>S. mutans</i> via disc diffusion, MDCT), compressive strength	AgNP+metronidazole combo most effective; CS comparable across groups
Ekrikaya et al., 2025 [23]	Fuji IX	0.05% AgNP / Ag@MoS2 nanocomposite (green & chemically synthesized)	Antibacterial (viability, CFU, lactic acid, metabolic activity), microhardness, color	Ag@MoS2 highest antibacterial efficacy; no adverse effect on microhardness/color, even after thermal aging
Enan et al., 2022 [18]	Fuji IX GP	0.5% AgNP (± amoxicillin)	Antibacterial (inhibition zone, biofilm SEM), compressive strength	Combined AgNP+amoxicillin gave highest inhibition (92%+); minimal effect on compressive strength
Guo et al., 2023 [13]	Ketac Molar EasyMix	0.05%, 0.5% AgNW / AgNP	Antibacterial (biofilm, SEM, fluorescence), compressive strength, colorimetry, compressive strength, color	AgNW superior antibiofilm effect; comparable compressive strength; less color change than AgNP
Guo et al., 2025 [32]	Ketac Molar EasyMix	0.05%, 0.1%, 0.3%, and 0.5% AgNW / 0.5% AgNP	Antibacterial (biofilm, EPS, live/dead assay), mechanical (compressive strength, hardness, roughness, wettability), cytotoxicity	AgNW-GIC: strong antibiofilm effect (5.8% vs. 100% live bacteria); mechanical properties comparable to control; no cytotoxicity
Hussein & Kareem, 2024 [33]	Ketac Molar EasyMix	0.2%, 0.5% AgNP (isolated arm; ± 5%/10% chitosan)	Antibacterial (biofilm inhibition, disc diffusion)	0.5% AgNP + 10% chitosan gave highest antibiofilm activity; AgNP-alone arms also showed enhancement
Moghadam et al., 2022 [12]	GIC (brand not specified)	2% AgNP (mint-extract synthesized)	Antibacterial (inhibition zone)	Significant antibacterial effect vs. control across multiple oral bacteria; no effect on <i>E. faecalis</i> control across multiple oral bacteria

TABLE 4: Characteristics of included studies testing multiple nanoparticle types.

Author(s) & Year	GIC Type	Concentration	Outcomes Measured	Key Findings
Agrawal et al., 2026 [34]	Fuji II	12.3% Ag, 2.46% TiO2, 1.23% ZnO (combined solution)	Antibacterial (<i>S. mutans</i> inhibition zone), Mechanical (compressive strength, microshear bond strength)	Combined solution significantly increased antibacterial inhibition; no change in compressive strength; significant decrease in shear bond strength
Fattah et al., 2021 [35]	CGIC & RMGIC	TiO2, ZnO, Ag (compared across both cement types)	Microshear bond strength	TiO2 had no significant effect either cement; Ag improved CGIC bond, ZnO improved RMGIC bond.
Wassel & Allam, 2022 [36]	Riva Self Cure	5% Ag, 5% TiO2 (isolated arms)	Antibacterial (<i>S. mutans</i>), fluoride release, compressive strength	Both Ag and TiO2 significantly increased antibacterial effect vs. control; Ag increased fluoride release, TiO2 decreased it; TiO2 gave highest CS overall

TABLE 5: Risk-of-bias assessment of included studies using the QUIN tool.

Authors and Year	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	D12	Total (/24)	Score %	Overall
Araújo et al., 2021 [10]													18	75%	
Enan et al., 2021 [18]													10	42%	
Fattah et al., 2021 [35]													21	88%	
Ivanišević et al., 2021 [25]													14	58%	
Ashour et al., 2022 [31]													14	58%	
Fathi et al., 2022 [19]													10	42%	
Mansoor et al., 2022 [15]													14	58%	

Authors and Year	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	D12	Total (/24)	Score %	Overall
Moghadam et al., 2022 [12]	+	X	+	+	+	X	+	+	X	+	+	+	18	75%	+
Shafaei et al., 2022 [30]	+	X	+	+	+	X	+	+	X	+	+	+	18	75%	+
Wassel & Allam, 2022 [36]	+	+	+	+	+	X	X	+	X	X	+	+	16	67%	-
Guo et al., 2023 [13]	+	X	+	+	-	X	-	-	X	X	-	-	11	46%	X
Jaber et al., 2023 [11]	+	X	X	X	-	X	X	-	X	X	-	-	6	25%	X
Panahandeh et al., 2023 [9]	+	+	+	+	+	X	X	+	X	X	+	+	16	67%	-
Showkat et al., 2023 [20]	+	X	+	+	-	X	X	-	X	X	-	-	10	42%	X
Hussein & Kareem, 2024 [33]	+	X	+	+	+	X	X	+	X	X	+	+	14	58%	-
Mahendra et al., 2024 [21]	+	-	+	+	-	X	X	-	X	X	-	-	11	46%	X
Mansoor et al., 2024 [26]	+	X	+	+	+	X	X	+	X	X	+	+	14	58%	-
Ramić et al., 2024 [22]	+	X	+	+	-	X	X	-	X	X	-	-	10	42%	X
Ekrikaya et al., 2025 [23]	+	-	+	+	-	X	X	-	X	X	-	-	11	46%	X
Guo et al., 2025 [32]	+	X	+	+	+	X	+	+	X	X	+	+	16	67%	-

Authors and Year	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	D12	Total (/24)	Score %	Overall
Mansoor et al., 2025 [27]	+	X	+	+	+	X	X	+	X	+	+	+	16	67%	-
Sena et al., 2025 [28]	+	X	+	+	+	X	+	+	X	X	+	+	16	67%	-
Shubha et al., 2025 [29]	+	+	+	+	+	X	X	+	X	X	+	+	16	67%	-
Agrawal et al., 2026 [34]	+	-	+	+	-	X	-	-	X	X	-	-	12	50%	-
Ganesh et al., 2026 [24]	+	+	+	+	+	X	X	+	X	X	+	+	16	67%	-
Karamüftüoğlu et al., 2026 [14]	+	+	+	+	+	+	X	+	-	X	+	+	19	79%	+

Domains

D1: Clearly stated aims/objectives

D2: Detailed explanation of sample size calculation

D3: Detailed explanation of sampling technique

D4: Details of comparison group

D5: Detailed explanation of methodology

D6: Operator details

D7: Randomization

D8: Method of measurement of outcome

D9: Outcome assessor details

D10: Blinding

D11: Statistical analysis

D12: Presentation of results

Judgement

Not specified / High risk of bias (Score = 0)

Inadequately specified / Medium risk of bias (Score = 1)

Adequately specified / Low risk of bias (Score = 2)



DISCUSSION

Summary of Main Findings

The review consolidated findings of 26 *in vitro* studies on the effects of the concentration of TiO₂, ZnO, and Ag nanoparticles on the antibacterial and mechanical performance of glass ionomer cement. The review found the same trend across all three nanoparticles: antibacterial performance was dose-dependent, whereas mechanical performance showed nonlinear, threshold-like behaviour improving at low to moderate nanoparticle concentrations and then deteriorating at high concentrations. This may reflect a reinforcement-to-agglomeration transition: nanoparticles may initially act as fillers and bonding sites for polyacrylic acid in the GIC matrix, but at higher concentrations they may agglomerate.

Additive-by-Additive Interpretation

The largest set of evidence for Group TiO₂ (14 out of 26 articles) has resulted in convergence to a critical value of about 5 wt%, which is considered an optimal/maximum concentration value from the mechanical standpoint in three different studies, with diverse results in terms of mechanics through the use of different synthesis methods but achieving the same conclusion on this critical value [14,15,27]. Consistency across articles makes 5% a highly relevant maximum level, despite some contradictory evidence [9,25].

Among the reviewed materials, ZnO appeared to be the least advanced, as only two studies focused exclusively on it. Jaber et al. [11] found that higher ZnO concentrations increased antibacterial activity, compressive strength, and hardening in ZnO-modified GIC. Shafaei et al. [30] showed that ZnO-modified GIC had an antimicrobial effect at 2 wt% ZnO. Although studies reported promising antibacterial and mechanical results, their inconsistency and limited number made it impossible to establish a dose-response relationship. Also, none of the ZnO articles were low risk of bias [30].

Ag nanoparticles showed antibacterial activity at considerably lower concentrations than TiO₂ and ZnO. Hussein and Kareem [33] observed antibacterial enhancement at 0.2 and 0.5 wt% AgNP, while Moghadam et al. [12] reported significant activity at 2 wt%. However, incorporating Ag may introduce trade-offs, particularly in colour stability and bonding properties. Notably, Guo et al. [13,32] demonstrated that silver nanowire-modified GIC provided strong antibiofilm activity with reduced discoloration relative to conventional AgNP formulations. These results indicate that Ag performance depends on both concentration and nanoparticle morphology, suggesting that future formulation development should consider both loading level and particle characteristics [13,32].

Cross-Additive Comparison

Although few studies compared the effects of two or more additives, Wassel & Allam [36] set the standard for comparison and noted that TiO₂ was most effective at producing compressive strength, while both Ag and TiO₂ enhanced antibacterial

properties. In Fattah et al. [35], the additive's effectiveness depended on the cement. Thus, Ag enhanced bond strength in GIC, while ZnO enhanced bond strength in resin-modified GIC, and TiO₂ made no difference in either. Agrawal et al. [34] used all three additives and observed enhanced antibacterial properties but low shear bond strength.

Overall, TiO₂ provided the strongest evidence, especially for mechanical properties and concentration dependence. Ag showed excellent antibacterial effects even at low concentrations but was less favourable for aesthetics and bonding [13,32,33]. Preliminary data indicated ZnO's potential, but it was represented in far fewer studies. Thus, nanoparticle selection should be based on the specific combination of antibacterial effect and the mechanical/aesthetic properties of GIC [11,30].

Trade-offs and the Underlying Reinforcement Mechanism

A common characteristic of all the studies analyzed is that increased nanoparticle content does not automatically enhance the mechanical strength of the tested material. Low or moderate contents of nanoparticles will enable uniform distribution and filling of microvoids, as well as enhancing the interaction between the particles and the cement matrix, but at higher contents, the nanoparticles might agglomerate and cause stress points [27,37]. The mechanical data from Mansoor et al. [15], Mansoor et al. [27], and Showkat et al. [20] show this trend.

However, the compromise was not confined to mechanical properties only. Nanoparticle concentration also affected surface roughness, settable, solubility, radiopacity, and colour stability. Some TiO₂ formulations showed changes in set time and solubility at different concentrations, while some Ag-containing formulations mainly showed problems with discoloration and bonding strength. These results imply that nanoparticle concentration should be assessed based on multiple material outcomes, not on a single outcome such as antibacterial or mechanical properties alone. As such, the ideal concentration for maximum antibacterial activity will not automatically mean ideal material performance [13,28,32,34].

Heterogeneity as a Limitation of the Evidence Base
Significant heterogeneity was found among the included studies in nanoparticle concentration reporting, GIC formulation, TiO₂ nanoparticle preparation, and outcome measures. Where possible, we converted concentrations measured in alternative forms to wt%, but some studies initially used different units, such as mg/g. The included studies also examined different GIC formulations, namely Fuji II, Fuji IX, Ketac Molar EasyMix, Ketac Cem, Riva Self Cure, and others that may have different mechanical and chemical properties at baseline [14,15,28,33]. In addition, TiO₂ nanoparticles can be synthesized chemically or biologically/phytochemically, which may affect their interaction with the cement matrix [12,27].

This variability becomes especially important when considering the recommended optimal concentrations. A concentration that performs well in one GIC does not automatically perform the same way in a different GIC formulation. Variations in form factors, size, and synthesis method can shift the point at which a nanoparticle concentration provides positive reinforcement to one where it promotes negative agglomeration. For this reason, it is more appropriate to consider the 3–5 wt% range of TiO₂ as a concentration range rather than a threshold value [27].

Risk of Bias Considerations

The QUIN assessment indicated that only 5 out of 26 reviewed studies (19%) could be classified as having a low risk of bias. In contrast, the overwhelming majority of reviewed studies (13 studies or 50% of the total number) had a moderate risk of bias. The significant proportion of the remaining studies (8 studies or 31%) had a high risk of bias. The domains that were frequently not reported in the studies included sample size justification, operator details, randomization, outcome assessor details, and blinding—factors that are characteristic of the convention in *in vitro* dental material testing research in general, rather than nanoparticle-GICs. In view of the fact that almost one-third of the included studies were at a high risk of bias and only a small proportion of the studies (about 19%) were low risk, the overall evidence base synthesized in this systematic review has to be interpreted with caution. However, the high risk of bias was not equally spread over different additives or outcomes since the TiO₂ concentration threshold outlined remains the same for studies with all three levels of risk.

Clinical Implications

The above results show that concentrations of nanoparticles between low and moderate give a better compromise between antibacterial and mechanical properties than high concentrations [15,20,27]. On the other hand, the literature reports TiO₂ concentrations between 3–5 wt% with good antibacterial and mechanical outcomes, but the optimal concentration depends on the specific application [20,27,28]. In turn, Ag exhibited potent antibacterial properties at about 0.2–2 wt% in accordance with the available literature; however, it raised issues related to staining and other alterations of the material [12,13,32,33]. Regarding ZnO, initial results were favourable for both antibacterial and mechanical properties; however, the limited number and quality of studies do not allow us to propose a specific concentration [11,30]. One key lesson learned is that increasing nanoparticle concentration adds no value. The aim is to find an effective formulation that provides good antibacterial effect and mechanical strength, among other factors [13,34,35]. This issue applies especially to Ag, where a good antibacterial effect can be achieved at lower concentrations while the aesthetic effect remains a problem, and to TiO₂, where higher concentrations reduce mechanical strength [13,20,32]. It would also be better to report

concentrations in wt%.

Limitations

This systematic review has several limitations that should be recognized while evaluating the results. First, the study was not registered in a public protocol database, such as PROSPERO, which does not accept laboratory reviews. This is a limitation because the initial research protocol is not publicly available; therefore, the methodology and potential deviations are not accessible. Secondly, one of the reviews included in the study did not have sufficient screening, extraction, and risk-of-bias assessment. Applying the QUIN tool with the support of artificial intelligence technologies is still prone to human error. Third, the search was limited to three databases (Scopus, PubMed, and Web of Science), a specific period (2021–2026), and a single publication language (English). As a result, some articles may have been excluded during the selection process because of search limits. At the same time, publication or language bias may affect the validity of the results. Most importantly, the review includes only articles with *in vitro* experiments; therefore, the obtained concentration ranges cannot be interpreted clinically.

Future Research Directions

Future investigations should include more dose-response work, especially for ZnO, to determine whether reproducible concentrations can be defined [11,30]. Next, the concentration of nanoparticles should be indicated in wt%, along with adequate methodological details on the size, shape, synthesis, dispersion, and also incorporation of nanoparticles into the GIC matrix [27]. Moreover, direct comparisons of TiO₂, ZnO, and Ag using the same GIC formulations and equal concentrations may help distinguish the effect of nanoparticle type from the effect of cement formulation [35]. Regarding experimental work, future investigations need to improve reporting of randomization, sample-size rationale, outcome measures, and other areas identified as weak in the current risk-of-bias assessment. Consequently, it is necessary for promising formulations that have been obtained via *in vitro* studies and whose TiO₂ concentration levels fall around 3–5 wt% to be tested in clinical settings [15,20,27,28].

CONCLUSION

This systematic review presented evidence from 26 *in vitro* studies evaluating how TiO₂, ZnO, and Ag nanoparticle concentration affects the mechanical and antibacterial properties of glass ionomer cements. Overall, higher nanoparticle concentrations increased antimicrobial properties; however, mechanical properties showed more concentration-dependent behaviour, with enhancement at low or moderate concentrations and possible degradation at higher concentrations due to nanoparticle aggregation. The TiO₂ nanoparticles appeared to have consistent results, with 5 wt% of TiO₂ being an approximate upper limit for the mechanical properties in several studies. However, formulation differences prevent using this limit as an absolute one.

Ag nanoparticles showed sufficient antimicrobial properties at lower concentrations but also had more pronounced adverse effects on material properties, including colour stability. Evidence on ZnO nanoparticles remains limited. Future studies are needed to establish optimal concentrations and evaluate the clinical relevance of the data.

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REFERENCES

- [1] Hasan F, Yuliana LT, Budi HS, Ramasamy R, Ambiya ZI, Ghaisani AM. Prevalence of dental caries among children in Indonesia: A systematic review and meta-analysis of observational studies. *Heliyon* 2024;10. <https://doi.org/10.1016/j.heliyon.2024.e32102>.
- [2] Kriswandini IL, Budi HS, Justitia FM. Examination of the Structure and Formation of *Streptococcus mutans* Biofilm Induced by Glucose, Lactose, Soy Protein, and Iron. *Eur J Dent* 2024;18:834–40. <https://doi.org/10.1055/s-0043-1776121>.
- [3] Theresia TT, Andayani LH, Souliissa AG, Lestari S. Dental caries and quality of life among primary school children. *Dent J* 2026;59:120–5. <https://doi.org/10.20473/j.djmk.v59.i2.p120-125>.
- [4] Pratiwi D, Salim RF, Putri TS, Hasan AEZ. Evaluation of the physical properties of glass ionomer cement modified by ethanolic extract of propolis. *Dent J* 2024;57:172–7. <https://doi.org/10.20473/j.djmk.v57.i3.p172-177>.
- [5] Yildiz Ş, Atas O. *In vitro* evaluation of the effectiveness of pediatric drugs and tooth brushing on the surface roughness of different restorative dental materials used in pedodontics. *Dent J* 2025;58:120–7. <https://doi.org/10.20473/j.djmk.v58.i2.p120-127>.
- [6] Zhang Y, He J. Strategies for Enhancing Conventional Glass Ionomer Cement—A Short Review. *Materials* 2026;19. <https://doi.org/10.3390/ma19040653>.
- [7] Budi HS, Jameel MF, Widjaja G, Alasady MS, Mahmudiono T, Mustafa YF, et al. Study on the role of nano antibacterial materials in orthodontics (a review). *Brazilian Journal of Biology* 2024;84. <https://doi.org/10.1590/1519-6984.257070>.
- [8] Fathi UA, Zena A, Jumana, Abduljawad A, Younis, Zena M. Compressive Strength and Surface Roughness of Nanoparticle-Enriched Glass Ionomer Cement. *Tikrit Journal for Dental Sciences* 2023;11:170–7. <https://doi.org/10.25130/tjds.11>.
- [9] Panahandeh N, Hasani E, Safa S, Hashemi M, Torabzadeh H. Effects of Incorporation of Titanium Dioxide Nanoparticles on Mechanical Properties of Conventional Glass Ionomer Cement. *Journal of Iranian Medical Council* 2023;7:99–106. <https://doi.org/10.18502/jimc.v7i1.14206>.
- [10] Araújo IJDS, Ricardo MG, Gomes OP, Giovani PA, Puppini-Rontani J, Pecorari VA, et al. Titanium dioxide nanotubes added to glass ionomer cements affect *S. mutans* viability and mechanisms of virulence. *Braz Oral Res* 2021;35:1–12. <https://doi.org/10.1590/1807-3107BOR-2021.VOL35.0062>.
- [11] Jaber GS, Khashan KS, Abbas MJ, Ibrahim NA. Improvement of glass ionomer restoration by adding ZnO nanoparticles prepared by laser: an *in vitro* study. *Journal of the Indian Chemical Society* 2023;100. <https://doi.org/10.1016/j.jics.2023.100879>.
- [12] Moghadam MG, Bagherzade A, Ghorbanzade F, Hanafi-Bojd MY, Yousefi M. *In vitro* antibacterial activity of glass ionomer cements containing silver nanoparticles synthesized from leaf extract of *Mentha piperita*. *Dent* 3000 2022;10. <https://doi.org/10.5195/d3000.2022.267>.
- [13] Guo T, Yang M, Wang D, Zheng J, Gao SS. Antibiofilm and mechanical properties of silver nanowire-modified glass ionomer cement. *J Dent* 2023;135. <https://doi.org/10.1016/j.jdent.2023.104569>.
- [14] Karamüftüoğlu N, Kuşçu S, Kuşçu İ, Korkmaz N. Green-Synthesized TiO₂ Nanoparticles Improve Mechanical Performance of Glass Ionomer Cements. *Polymers (Basel)* 2026;18:295. <https://doi.org/10.3390/polym18020295>.
- [15] Mansoor A, Khan MT, Mehmood M, Khurshid Z, Ali MI, Jamal A. Synthesis and Characterization of Titanium Oxide Nanoparticles with a Novel Biogenic Process for Dental Application. *Nanomaterials* 2022;12. <https://doi.org/10.3390/nano12071078>.
- [16] Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *BMJ* 2021;372. <https://doi.org/10.1136/bmj.n71>.

- [17] Sheth VH, Shah NP, Jain R, Bhanushali N, Bhatnagar V. Development and validation of a risk-of-bias tool for assessing *in vitro* studies conducted in dentistry: The QUIN. *J Prosthet Dent* 2024;131:1038–42. <https://doi.org/10.1016/j.prosdent.2022.05.019>.
- [18] Enan ET, Ashour AA, Basha S, Felemban NH, Gad El-Rab SMF. Antimicrobial activity of biosynthesized silver nanoparticles, amoxicillin, and glass-ionomer cement against *Streptococcus mutans* and *Staphylococcus aureus*. *Nanotechnology* 2021;32. <https://doi.org/10.1088/1361-6528/abe577>.
- [19] Fathi UA, AL-Murad MA, Ahmad ZA. The Effect of the Incorporation of Titanium Dioxide Nanoparticles on the Mechanical and Physical Properties of Glass Ionomer Cement. *J Res Med Dent Sci* 2022;10:88–91.
- [20] Showkat I, Chaudhary S, Sinha AA, Manuja N, Telgi CR, Priya N, et al. Comparative Evaluation of Flexural Strength of Conventional Glass Ionomer Cement and Glass Ionomer Cement Modified with Chitosan, Titanium Dioxide Nanopowder and Nanohydroxyapatite: An *In Vitro* Study. *Int J Clin Pediatr Dent* 2023;16:S72–6. <https://doi.org/10.5005/jp-journals-10005-2617>.
- [21] Mahendra T V.D., Rahul TS, Ramesh KSV, Pasupuleti S, Velagala SK, Mulakala V. Quantitative determination and antibacterial properties of TiO₂ nanoparticle-doped glass ionomer cement: an *in vitro* study. *Eur Oral Res* 2024;58:8–13. <https://doi.org/10.26650/eor.20231225662>.
- [22] Ramić B, Cvjetićanin M, Bajkin B, Drobac M, Milanović M, Rajnović D, et al. Physical and mechanical properties assessment of glass ionomer cements modified with TiO₂ and Mg-doped hydroxyapatite nanoparticles. *J Appl Biomater Funct Mater* 2024;22. <https://doi.org/10.1177/22808000241282184>.
- [23] Ekrikaya S, Karatas O, Yilmaz E, Ildiz N, Dadi S, Sahin DG, et al. Evaluation of the antibacterial activity, surface microhardness, and color change of glass ionomer cement containing green-synthesized Ag@MoS₂ nanocomposite after thermal aging. *Clin Oral Investig* 2025;29. <https://doi.org/10.1007/s00784-025-06437-8>.
- [24] Ganesh S, Paulraj J, Maiti S. Bioengineered Green-Synthesized Titanium Dioxide And Chitosan Nanoparticle-Modified Glass Ionomer Cement: Antimicrobial, Mechanical, And Surface Properties Evaluation. *Annals of Dental Specialty* 2026;14:1–15. <https://doi.org/10.51847/MRLjvvlef7>.
- [25] Ivanisevic A, Rajic VB, Pilipovic A, Par M, Ivankovic H, Baraba A. Compressive Strength of Conventional Glass Ionomer Cement Modified with TiO₂ Nano-Powder and Marine-Derived HAp Micro-Powder. *MATERIALS* 2021;14. <https://doi.org/10.3390/ma14174964>.
- [26] Mansoor A, Mansoor E, Mehmood M, Hassan SMU, Shah AU, Asjid U, et al. Novel microbial synthesis of titania nanoparticles using probiotic *Bacillus coagulans* and its role in enhancing the microhardness of glass ionomer restorative materials. *Odontology* 2024;112:1123–34. <https://doi.org/10.1007/s10266-024-00921-5>.
- [27] Mansoor A, Mansoor E, Mansoor E, Mansoor E, Shah AU, Asjid U, et al. Synthesis of novel titania nanoparticles using corn silky hair fibres and their role in developing a smart restorative material in dentistry. *Comput Struct Biotechnol J* 2025;29:29–40. <https://doi.org/10.1016/j.csbj.2025.01.005>.
- [28] De Góis Sena L, Meyer MD, Ricardo MG, De Souza Araújo IJ, Rontani JP, Pecorari VA, et al. Effect of titanium dioxide nanotubes incorporated into conventional glass ionomer cement on *L. acidophilus*. *Braz Oral Res* 2025;39. <https://doi.org/10.1590/1807-3107bor-2025.vol39.059>.
- [29] Shubha P, Harini K, Ganesh S, Jannu A, Kusugal P, Ruttonji Z. Biosynthesized TiO₂ Nanoparticles to Enhance the Mechanical and Antibacterial Properties of Type-II Glass Ionomer Cement for Dental Restorative Applications. *Cureus* 2025. <https://doi.org/10.7759/cureus.98281>.
- [30] Shafae H, Khosropanah H, Rahimi H, Darroudi M, Rangrazi A. Effects of Adding Cinnamon, ZnO, and CuO Nanoparticles on the Antibacterial Properties of a Glass Ionomer Cement as the Luting Agent for Orthodontic Bands and Their Cytotoxicity. *Journal of Composites Science* 2022;6. <https://doi.org/10.3390/jcs6110336>.
- [31] Ashour AA, Felemban MF, Felemban NH, Enan ET, Basha S, Hassan MM, et al. Comparison and Advanced Antimicrobial Strategies of Silver and Copper Nanodrug-Loaded Glass Ionomer Cement against Dental Caries Microbes. *Antibiotics* 2022;11. <https://doi.org/10.3390/antibiotics11060756>.
- [32] Guo T, Wang D, Gao SS. The antibiofilm effect and mechanism of silver nanowire-modified glass ionomer cement against multi-species oral biofilm. *BMC Oral Health* 2025;25. <https://doi.org/10.1186/s12903-025-05536-y>.

- [33] Hussein RM, Kareem FA. Synergistic antibacterial effect of chitosan/silver nanoparticles modified glass ionomer cement (an *in vitro* study). Oxford Open Materials Science 2024;4.
<https://doi.org/10.1093/oxfmat/itae013>.
- [34] Agrawal UO, Arora AV, Kapoor SV, Jagtap MA. Comparison of antibacterial effect, shear bond strength and compressive strength of restorative glass ionomer cement incorporated with novel nanoparticle solution: An *in vitro* pilot study. IP Indian Journal of Conservative and Endodontics 2026;11:82–7.
<https://doi.org/10.18231/j.ijce.13295.1772107260>.
- [35] Fattah Z, Jowkar Z, Rezaeian S. Microshear Bond Strength of Nanoparticle-Incorporated Conventional and Resin-Modified Glass Ionomer to Caries-Affected Dentin. Int J Dent 2021;2021.
<https://doi.org/10.1155/2021/5565556>.
- [36] Wassel MO, Allam GG. Anti-Bacterial Effect, Fluoride Release, and Compressive Strength of a Glass Ionomer Containing Silver and Titanium Nanoparticles. Indian Journal of Dental Research 2022;33:75–9.
https://doi.org/10.4103/ijdr.ijdr_117_20.
- [37] Shahpaska ZR, Markovic D, Petrovic B, Nicholson JW, Coleman NJ, Gabric D, et al. Can Addition of Nanoparticles Improve the Properties of Glass-Ionomer Cements? Bratislava Medical Journal 2026;127:3315–22.
<https://doi.org/10.1007/s44411-026-00672-5>.