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REVIEW

Recent research progress on antibacterial modifications of conventional glass ionomer cement for dental restorations: a narrative review

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Abstract

Glass ionomer cement (GIC) has been widely used in the field of oral therapy because of its excellent properties. Good oral biocompatibility and easy clinical operation are important advantages of GIC. However, GIC still faces many challenges in its application as a repair material such as secondary caries and low mechanical properties. Recent studies have shown that conventional GIC is frequently insufficient for effective antibacterial protection. Therefore, many researchers have explored improving the antibacterial properties of GIC to prevent secondary caries by incorporating various materials with antibacterial properties into GIC. In this review, the recent research on GIC modified by antibacterial materials was systematically reviewed. The antibacterial mechanisms of various types of antibacterial materials were discussed in detail, and views on future research development were presented considering the current challenges in the field of GIC antibacterial modification.

Keywords

Glass ionomer cement; Antibacterial; Modification; Narrative review

1. Introduction

Dental caries has been the most common oral disease for many years. According to The Global Burden of Disease Study at 30 years [1], approximately 2.5 billion people worldwide have permanent teeth caries and more than 570 million children have deciduous teeth caries. Moreover, the prevalence of dental caries increased from 1990 to 2020. Thus, the development of new dental restoration materials has been a subject of intensive research.

Glass ionomer cement (GIC) has been widely used in the dental restoration field and is well known for its biocompatibility, fluoride release capacity, and adhesive properties to dentin structure [2]. Many dental restorations only last approximately 5 years because of secondary caries from marginal microleakage and poor mechanical strength [3]. Cariogenic biofilm formation on GIC restorations surface and the tooth-GIC restorations bonding interface is the major reason that restricts the service life of GIC restorations [4].

Some studies reported that GIC inhibits the growth of oral bacteria by fluoride ion release [5]. However, the inhibitory effect was short-lived, and clinical research has not yet demonstrated whether fluoride release by GIC significantly reduces the formation of secondary caries [6]. Therefore, most research efforts have focused on improving the antibacterial properties of GIC to decrease the growth of oral bacteria, preventing the incidence of secondary caries, and enhancing clinical efficacy [7] by incorporating various bacteriostatic agents, such as chlorhexidine [8, 9], propolis [7], theobromine [10], silver nanoparticles [11, 12], and casein phosphopeptide-amorphous calcium phosphate [13]. Notably, many studies reported that the addition of antibacterials impacted the biocompatibility and mechanical properties of GIC, and some fillers were even impossible to use clinically because of poor stability and restoration color problems [11, 12]. Therefore, the identification and development of ideal antibacterial agents to modify GIC remains a research hotspot. Given the shortcomings of antibacterial additives, many scholars have also attempted to enhance the antibacterial properties of GIC through different methods.

In this review, we summarized the research on the strategies for antibacterial modifications of GIC from Jan 2017 to Dec 2024, with the aim to provide ideas for GIC modification with better performance.

2. Material and methods

2.1 Inclusion criteria

(1) Studies that incorporated antibacterial additives into conventional GIC were included;

(2) Scientific papers were published in English from Jan 2017 to Dec 2024, with specific inclusion criteria in the Table 1 below:

TABLE 1. PICOS.

PICOS	Description
Participants	Conventional Glass Ionomer Cements
Interventions	Antibacterial Agents
Comparisons	Convencional Glass Ionomer Cements without antibacterial
	Agents (control group)
Outcomes	Antibacterial capacity
Study designs	*In vitro* studies

Legend: PICOS: participants, interventions, comparisons, outcomes and study designs.

2.2 Exclusion criteria

(1) Studies about the antibacterial GIC used for orthodontic, adhesive, core build-up restoration were excluded;

(2) Studies whose antibacterial analysis was not clear were excluded;

(3) Studies whose research object was not conventional GIC were excluded;

(4) Studies not in the range from Jan 2017 to Dec 2024 were excluded.

2.3 Study identification

A literature search was conducted and the resulting articles were evaluated by two independent authors (QSZ and JXL). They were responsible for discarding studies that were not relevant to the subject, according to the above inclusion and exclusion criteria. Firstly, duplicate articles were removed, and then the titles and abstracts were evaluated for inclusion or not. When the titles or abstracts could not be judged, the full texts of the articles were read to make decision. Any disagreement between the two reviewers on the inclusion of the article was resolved through discussion.

3. Results

3.1 Search strategy and research methods

A search using the keywords of (glass ionomer cement OR GIC) AND (antibacterial OR antimicrobial) AND (modification OR additive) by PubMed and Web of Science databases was conducted, which identified 74 studies from Jan 2017 to Dec 2024, and there were 68 studies left after eliminating duplications. By further screening titles/abstracts, 45 studies were initially retained. Based on inclusion and exclusion criteria, 39 papers were eventually included in this review. Fig. 1 shows the flow chart of the literature retrieval method. This study adopted a narrative review approach.

3.2 Single antibacterial component-based GIC modifications

3.2.1 Metal-based antibacterial additives

3.2.1.1 Silver nanoparticles (AgNPs)

AgNPs have a broad antibacterial spectrum and strong inhibitory effects on bacteria, fungi, viruses and other pathogenic microorganisms [14]. AgNPs exhibit antibacterial effects by releasing silver ions into the pathogen biofilm to block respiratory metabolism by inactivating oxidative metabolic enzymes [2]. A recent study showed that AgNPs exerted antibacterial activity against more bacteria than previously identified, including *L. acidophilus*, *E. faecalis* and *A. actinomycetemcomitans* [14]. Therefore, AgNPs show promising application in the field of dental restorative materials.

In recent years, research on improving the antibacterial properties of conventional GICs by AgNPs has focused on changing the morphology of AgNP fillers or modifying AgNPs. Porter *et al.* [11] used α-lipoic acid-capped AgNPs to modify GIC, and the modified GIC was shown to exhibit a good inhibitory effect on bacterial biofilm growth. The authors also found that the optimal concentrations for the AgNPs differed among GICs. For example, Fuji IX with 10 μg α-lipoic acid-capped AgNPs (Ag/capsule) achieved a 99% biofilm reduction, while Ketac Molar and Riva Selfcure needed 24 μg Ag/capsule to reduce biofilm formation by 78%. Guo *et al.* [12] investigated the antibiofilm properties of a newly developed silver nanowire (AgNW)-modified GIC. The results showed that the GIC modified with 0.5 wt% AgNW had slightly better antibiofilm properties than the GIC modified with 0.5 wt% traditional AgNPs, but the difference was not statistically significant. Additionally, the color change of AgNW-modified GICs was significantly lower than that of AgNP-modified GICs. Md Imran *et al.* [15] reported that GIC modified with 1% silver nanoparticles exhibited superior antibacterial activity. Specifically, the inhibitory zone against *S. mutans* increased by 25%, and that against *L. acidophilus* increased by 20%, compared to the control group. The compressive strength of the modified GIC was preserved, and a compressive strength of 220 MPa was achieved by adding 1% silver nanoparticle, which was comparable to that of the control group (215 MPa). However, as the concentration of silver nanoparticles increased, there was a slight decrease in wear resistance.

Despite the promising findings, there are still some unresolved questions regarding AgNPs, such as the cytotoxicity of AgNP-modified GICs. Siqueira *et al.* [16] evaluated the cytotoxicity of GIC modified by AgNPs on pulp cells and showed that GIC modified by 0.1% or 0.2% AgNPs had no significant cytotoxicity compared with conventional GIC. However, whether the increase of the AgNP proportion leads to an increase in toxicity is an important question that needs to be addressed. Additionally, a recent study reported that GICs modified by AgNPs above 0.4% changed the bond quality of the dentin interface [17]. Therefore, whether it is feasible to

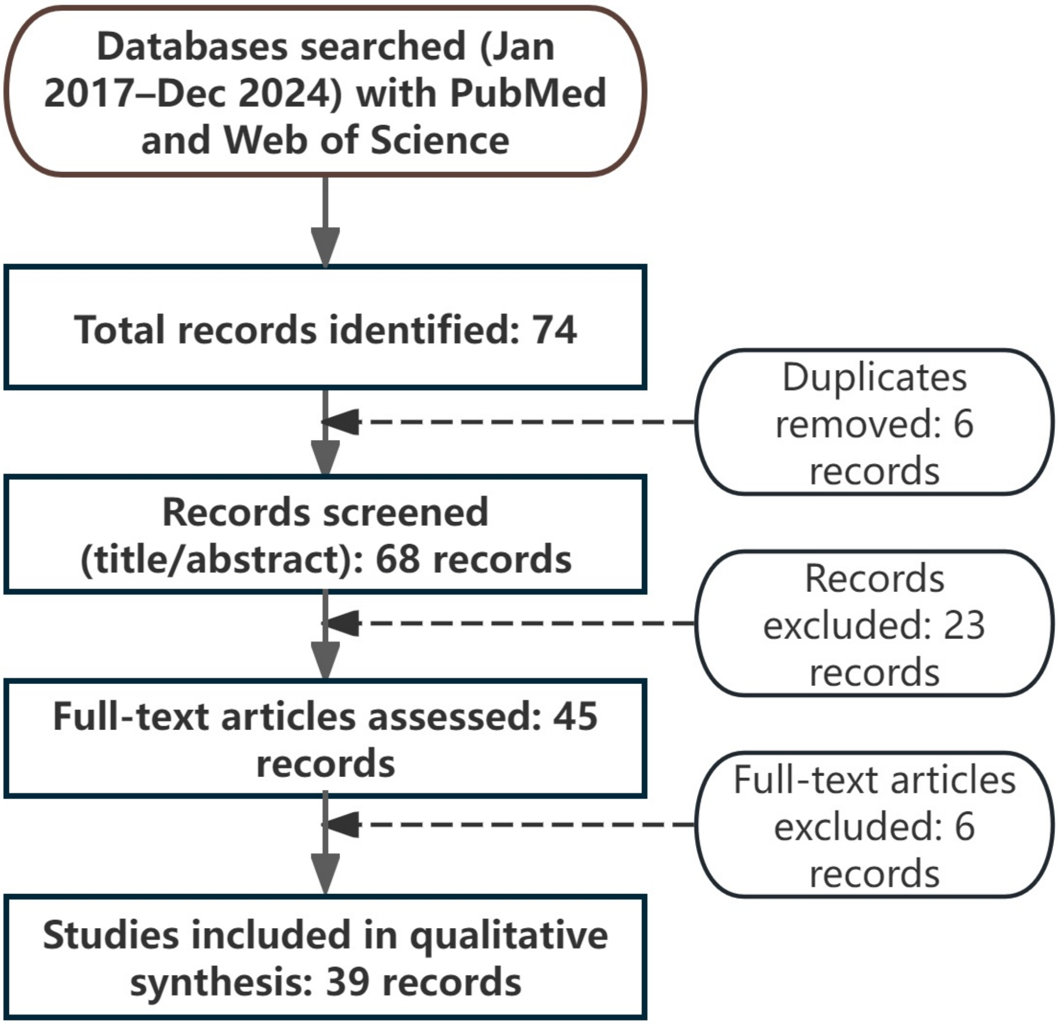

FIGURE 1. Flow chart of the literature retrieval method of this narrative review.

improve the antibacterial performance of GIC through simply increasing the concentration of AgNPs, without impacting other properties, needs to be verified.

Alshehri *et al*. [18] examined the effects of AgNP concentration on the fluoride release and recharge of GIC. The results showed that the addition of AgNPs at the concentrations of 0.1% and 0.2% significantly affected the release properties of fluoride, although the modified GICs had antibacterial effects [18]. This indicates the need to identify an appropriate concentration for the antibacterial effects of AgNPs and the remineralization effects of fluoride in clinical applications. Moreover, more studies are required to explore the antibacterial performance of AgNPs with different sizes and morphologies to help optimize the application of AgNPs in GIC in the future [19].

3.2.1.2 Copper nanoparticles (CuNPs)

As a conventional metallic element, copper has a long history of a wide range of applications in different fields. The research and application of copper in the treatment of diseases and antibacterial strategies have been a focus of medical researchers [20]. The antibacterial mechanism of copper involves its promotion of the production of reactive oxygen species (ROS), resulting in oxidative damage to cell structures, DNA degradation, and eventually cell death [20]. With the development of nanotechnology and the generation of CuNPs, the antibacterial properties of copper have been improved.

CuNPs are a type of dental filler with wide application prospects because of their antibacterial properties [21]. Numerous studies have confirmed that CuNPs exhibit antibacterial activity against many oral pathogens, such as *S. mutans*, *E. coli* and *S. aureus* [21]. Perez *et al*. [22] investigated the antibacterial activity of CuNPs incorporated into commercial GIC, and the results demonstrated that GIC with 2–4 wt% CuNPs exhibited antibacterial activity against *S. mutans* and *S. sanguinis*. However, the cell viability of Human Dental Pulp Fibroblast (HDPF) tended to decrease with the exposure time extension to GIC extracts, but there was no statistically significant difference between any GIC groups [22]. However, the cell relative growth rates (RGR) of the modified GIC groups for 48 h were in the range of 68–72%, which were all below 75%, indicating obvious cytotoxicity. Another study used musk extract to biosynthesize copper nanoparticles (TVE-CuNPs) and different concentrations of TVE-CuNPs were used to modify GIC. The 0.5% TVE-CuNP-modified GIC effectively inhibited the growth of *S. mutans* and *S. aureus* to a greater extent compared with conventional GIC; however, there was no significant difference in the antibacterial performance between 0.5% AgNP-modified GIC and 0.5% TVE-CuNP-modified GIC [23].

The main issue limiting the application of CuNPs in oral restorative materials is whether excessive CuNPs cause acute or chronic poisoning [24]. The biosafety of CuNPs in humans has been investigated in several studies. Pasha *et al.* [24] showed that adding CuNPs into dental material did not damage oral soft tissues or cause significant cytotoxicity to the dental pulp. However, Hernández-Moreno *et al.* [25] found that CuNPs showed cytotoxicity at concentrations of 0.39–25.0 μg/mL, and there were significant statistical differences compared with ZnONPs. Therefore, further experimental research is needed to apply CuNPs to improve the antibacterial properties of GIC in the clinic.

3.2.1.3 Magnesium oxide nanoparticles (MgONPs)

MgONPs have a proven antibacterial activity owing to a superoxide anion on the surface [26]. Karthik revealed that the antibacterial mechanism of MgONPs was from the production of ROS, which causes oxidative stress in bacterial cells, leading to cell death.

Noori *et al.* [27] evaluated the antibacterial and antibiofilm properties of conventional GIC modified by MgONPs against *S. mutans* and *S. sobrinus*. The results showed that GIC modified with 2.5% MgONPs exhibited a good antibacterial effect, and the antibiofilm property was significantly increased when the concentration of MgONPs was above 1% [27]. However, the application of MgONPs is limited because of agglomeration issues and decreased mechanical strength. To solve this problem, researchers have attempted several solutions. Naguib *et al.* [28] coated MgONPs with zein polymer (zMgONPs) at different concentrations (0.5%, 1% and 2%) and found that this modification strategy reduced the agglomeration problem of nanoparticles without impacting the antibacterial properties. The authors subsequently evaluated the antibacterial properties of the GIC modified with zMgONPs and found that the addition of 0.3%, 0.5% and 1.0% zMgONPs all significantly enhanced the antibacterial activity of GIC compared with the control GIC [29]. This study provided a strategy to improve the application of MgONPs in dental materials. However, while zein reduces the agglomeration effect, it has no antibacterial properties. Moreover, whether zein has a negative effect on the mechanical strength of GIC is unknown. Therefore, more research is necessary, and new strategies to reduce the aggregation problem of MgONPs in GIC and improve the antibacterial properties and mechanical strength of modified GIC are required.

3.2.1.4 Zinc oxide nanoparticles (ZnONPs)

ZnONPs are safe inorganic nanoparticles with multiple positive functions and demonstrated antibacterial activity. Previous studies have reported that ZnONPs inhibits oral microbial growth and biofilm formation by releasing zinc ions and producing reactive oxygen species and confirmed that the antibacterial activity of ZnONPs was negatively correlated with the size of nanoparticles [30]. Another report showed that resin-based dental composites modified by 10 wt% ZnONPs reduced biofilm formation by roughly 80% in a single-species dental biofilm model [31]. However, ZnONP-containing resin composites (10%) qualitatively showed less biofilm after anaerobic incubation for 1 day with a three-species biofilm model compared with unmodified composites, but did not significantly reduce biofilm growth after incubation for 3 days, indicating a poor antibacterial effect for multiple species biofilm [32].

Similarly, different conclusions have been drawn on the antibacterial properties of GICs modified by ZnONPs. Garcia *et al.* [33] reported that the antibacterial properties of modified GIC against *S. mutans* were not improved by adding 1% and 2% of ZnONPs. Conversely, Malekhoseini *et al.* [34] showed that the antibacterial properties of resin-modified glass ionomer were improved by adding 2% of ZnONPs. Additionally, previous studies found that the ZnONPs only have short-term effects of the antibacterial activity [35]. Therefore, a new type of ZnONP is still needed to endow GIC with long-lasting antibacterial properties.

3.2.1.5 Titanium dioxide nanoparticles (TiO_2NPs)

TiO_2NPs are widely used in dental materials because of their suitable biocompatibility and effective antibacterial activity. The TiO_2NP crystal surface stimulates the production of ROS, which can cooperate with anatase phase TiO_2NPs to attack polyunsaturated phospholipid bacteria and cause site-specific DNA damage to achieve antibacterial effects [36]. Various studies examined GIC modified by TiO_2NPs and showed that TiO_2NPs enhanced the mechanical properties [37], fluoride ion release, and antibacterial properties of GIC compared with traditional GIC [38].

Some studies have explored the potential role of size and shape of the modifiers in impacting antibacterial properties. Araújo *et al.* [39] evaluated the antibacterial effect of GIC modified by different concentrations of n-TiO_2 (0–7%) against *S. mutans* and the mechanisms of virulence at the cellular and molecular levels. The results showed that the modified GIC had antibacterial properties, and 5% was the most effective concentration of n-TiO_2. Incorporation of n-TiO_2 resulted in reduced expression of covR, a key gene for bacterial virulence [39]. Mahendra *et al.* [38] investigated the correlation between the release kinetics of Ti ions and the antibacterial properties of modified GIC. The results revealed that the 3% TiO_2NPs-modified GIC reached a peak Ti ion release in the first two months, after which the release was negligible. In contrast, the 5% TiO_2NPs-modified GIC demonstrated sustained Ti ion release throughout the experimental period, with the highest release in the second month. At all of four time points (24 hours, 2 months, 4 months and 6 months), both the Ti ion release levels and antibacterial property of the 5% TiO_2NPs-modified GIC were significantly higher than those of the 3% group. These results indicated that increasing the concentration of TiO_2NPs from 3% to 5% markedly enhanced the Ti ion release and antibacterial property of the modified GIC.

Studies have also compared the antibacterial activity of TiO_2NPs with other antibacterial agents. Hamid *et al.* [40] compared TiO_2NPs with cetylpyridine chloride (CPC). Both of them improved the antibacterial activity of modified GIC, and 3% TiO_2NPs showed stronger antibacterial activity than the other experimental groups. Wassel *et al.* [41] evaluated the antibacterial effect and fluoride release of GIC modified by AgNPs or TiO_2NPs. The results showed that adding 5 wt% TiO_2NPs or AgNPs into the powder component of conventional GIC significantly enhanced its antibacterial properties without impacting fluoride release. More investigation into the antibacterial durability of TiO_2NP-modified GIC is required in future research.

A list of studies in the last 5 years on antibacterial properties of GIC modified by single metal component nanoparticles is shown in Table 2 (Ref. [11, 12, 15, 22, 23, 27, 29, 33, 38–41]).

3.2.2 Antibacterial additives derived from natural sources

3.2.2.1 Propolis

Propolis is a resinous substance that is collected by bees from plant terminal buds and exudates [42]. It is a natural antibacterial material that contains phenols, flavonoids and terpenoids. There are two mechanisms for the antibacterial activity of propolis: the inhibition of bacterial RNA polymerase activity and its glucosyltransferase activity [43]. A recent study has expanded its antibacterial spectrum, demonstrating antibacterial efficacy against *Pseudomonas aeruginosa* by inhibiting its growth, biofilm formation, extracellular DNA (eDNA) release, and phenazine production [43]. In addition to its antibacterial properties, propolis also shows antifungal [44] and antiviral activities [45] and thus holds great value in the dental material field, including as an additive to improve the antibacterial properties of GIC [45].

Ideal additives for GIC should not only have excellent antibacterial properties but also not damage the mechanical properties or biocompatibility of GIC. Meneses *et al*. [7] evaluated the antibacterial effect of GIC incorporated with ethanolic extracts of propolis and also examined the mechanical properties and *in vivo* biocompatibility. The antibacterial activity of GIC modified by ethanol extract of propolis (EEP) was dose-dependent, and a commercial GIC containing 50% EPP had the best biocompatibility. No significant difference was found between EPP-modified GIC and conventional GIC regarding effects on mechanical properties.

Studies have also compared the antibacterial properties of GIC modified by propolis and other antibacterial fillers. GIC modified with 25% propolis exhibited a similar antibacterial effect compared with GIC modified with 10% chitosan, and there was no statistical difference between 50% propolis-modified and 50% Triphala-modified GIC [45], but GIC modified with 1% chlorhexidine had a better antibacterial effect [45]. Researchers also evaluated the effects of different types of propolis on GIC. An ethanolic extract of red propolis was used to modify GIC, and antibacterial efficacy was observed at the concentration of 25%, without a significant impact on mechanical properties or fluoride release [46]. However, Elmenshawy *et al.* [47] found that the GIC modified with 25% EEP had the highest antibacterial activity, while the control GIC had the lowest value. In contrast, the control GIC had the highest micro-shear bond strength, whereas the GIC modified with 25% EEP had the lowest strength. In the future, it is imperative to address the issues of high expansion rates and poor stability in propolis-modified GIC.

3.2.2.2 Essential oils

Plant essential oils are volatile oil mixtures extracted from the roots and stems of plants, such as cinnamon, clove, thyme and tea tree [48]. Plant essential oils have multiple effects such as analgesia, sedation, anti-inflammatory activity, anti-spasticity activity and local anesthesia. Although the precise antibacterial mechanism has not been fully clarified, studies have demonstrated that essential oils readily cross the cell walls and interact with the bacterial cytoplasm, causing the cytoplasm to solidify and rupture [49].

Essential oils have been found to have inhibitory effects on various oral pathogens, such as *S. pyogenes*, *S. mutans* and *C. albicans* [48]. Nunes *et al*. [50] reported the antibacterial activity and cytotoxicity of thymol oil-modified GIC. The GIC modified with thymol oil had a significant inhibitory effect on both planktonic *S. mutans* and their biofilm without cytotoxicity. Sherief *et al*. [51] investigated GIC modified by different essential oils. The authors showed that all modified GICs significantly inhibited both *S. mutans* and *C. albicans* growth, and the mechanical properties of GIC were not significantly affected by the addition of 5% cinnamon oil. Additionally, the fluoride release of all the modified GICs was significantly higher than that of traditional GIC.

In addition to the antibacterial properties, the cytotoxicity of plant essential oils also needs to be addressed. Only a few studies have investigated this question, and one report found no cytotoxicity from thymol oil-modified GIC. The cytotoxicity of GICs modified by different essential oils should be clarified in future research. Additionally, the durability of antibacterial properties of GIC modified by essential oils also requires attention.

3.2.2.3 Casein phosphopeptide-amorphous calcium phosphate (CPP-ACP)

CPP-ACP is derived from casein in milk and is the non-covalent binding product of calcium, phosphorus and casein phosphopeptide. CPP-ACP provides sufficient calcium and phosphate ions for tooth surface mineralization, and it also binds fluoride ions to delay the release of calcium and phosphorus [52].

After adding CPP-ACP to GIC, stable amorphous calcium fluoride phosphate is produced, thus improving the antibacterial performance of GIC [53]. Previous *in vitro* premolar cavity filling experiment demonstrated that 3 wt% CPP-ACP-modified GIC effectively inhibited the progress of secondary caries [53]. The 3% CPP-ACP group also showed good flexural strength. Dashper *et al*. [13] showed that 3 wt% CPP-ACP-modified GIC had an inhibitory effect on *S. mutans*. In a recent study, Mao *et al.* [54] reported an approximate 39% reduction of a mixed bacterial biofilm of three bacteria of RMGI modified by 5% CPP-ACP, with an inhibition effect of *S. mutans* and a promotion effect of *S. gordonii*. Recent studies found that CPP-ACP improved the release of calcium, phosphorus, and fluorine ions of GIC and increased the surface hardness of GIC prostheses. Kirthika *et al*. [55] evaluated the bacterial adhesion of GIC modified with CPP-ACP, bioactive glass (BAG), chitosan (CH) and methacryloyloxydodecyl pyridinium bromide (MDPB). The results showed that CPP-ACP-GIC, CH-GIC and BAG-GIC exhibited similar

TABLE 2. An overview of recent research progress in the last 5 years on antibacterial properties of GIC modified by single metal component nanoparticles.

Antibacterial agent	GIC type	Antibacterial Assay	Bacterial strain	Major outcomes	Ref.
AgNPs	Conventional glass ionomer (Fuji IX, Ketac Molar and Riva Selfcure)	Agar diffusion test	*S. mutans*	AgNP-modified GICs exhibited significant antibiofilm activity and unimpaired mechanical properties, which were equivalent or superior to non-modified GICs.	[11]
AgNPs	Conventional glass ionomer	Agar diffusion test	*S. mutans*	GIC modified with 0.5 wt% AgNW had slightly better antibiofilm properties than that modified with 0.5 wt% traditional AgNPs on *S. mutans*, but the difference was not statistically significant.	[12]
AgNPs	Conventional glass ionomer	Agar diffusion test	*S. mutans* and *L. acidophilus*	GIC modified with 1% AgNPs increased the inhibitory zones by 25% against *S. mutans* and 20% against *L. acidophilus*, compared to the control group. However, the compressive strength of the modified GIC was not affected.	[15]
CuNPs	Conventional glass ionomer	Agar diffusion test	*S. mutans* and *S. sanguinis*	GIC modified with 2–4 wt% CuNPs showed significantly antibacterial activity against *S. mutans* and *S. sanguinis*. However, the cell viability of HDPF tended to decrease with the exposure time extension to GIC extracts (68–72% viability), but there were no statistical differences between GIC groups. However, the cell RGR of the modified GIC groups for 48 h were in the range of 68–72%, which were all below 75%, indicating obvious cytotoxicity.	[22]
TVE-CuNPs or AgNPs	Conventional glass ionomer (GC Fuji IX)	Agar diffusion test	*S. mutans* and *S. sanguinis*	0.5% TVE-CuNP-modified GIC effectively inhibited the growth of *S. mutans* and *S. aureus* compared with conventional GIC, and its antibacterial property was comparable to that of 0.5% AgNPs-modified GIC.	[23]
MgONPs	Conventional glass ionomer (Ketac Molar Easymix)	Agar diffusion and CFU counting test	*S. mutans* and *S. sobrinus*	2.5% MgONPs-modified GIC showed remarkable antibacterial and antibiofilm activity against *S. mutans* and *S. sobrinus*, but 2.5% MgONPs decreased the mechanical strength of the modified GIC.	[27]
zMgONPs	Conventional glass ionomer (Fuji II, Rely X Temp E, Ionoglass Cem, Es Temp NE and System P link)	Agar diffusion and direct contact test	*S. mutans*, *E. faecalis*, *C. albicans* and *S. aureus*	Significant inhibition zones were observed in all zMgONPs groups compared to control group, and a dose-response relationship was observed only in Fuji II group. The antibacterial effect of zMgONPs-modified Rely X was most prominent against *C. albicans* and *S. aureus*.	[29]
ZnONPs	Conventional glass ionomer (Fuji II)	CFU counting test	*S. mutans*	1 and 2 wt% ZnONPs-modified GICs did not improve the antibacterial activity against *S. mutans*.	[33]
TiO_2NPs	Conventional glass ionomer	Agar diffusion test	*S. mutans*	The addition of 3% TiO_2NPs remarkably improved the antibacterial activity against *S. mutans* and the compressive strength of the modified GIC.	[40]
TiO_2NPs	Conventional glass ionomer (Ketac Molar Easymix)	Agar diffusion test	*S. mutans*	The GIC modified by 5% n-TiO_2NPs showed a higher antibacterial property compared with conventional GIC.	[39]
TiO_2NPs	Conventional glass ionomer	Agar diffusion test	*S. mutans*	At the four time points (24 hours, 2 months, 4 months, and 6 months), both the Ti ion release levels and antibacterial property of the 5% TiO_2NPs-modified GIC were significantly higher than those of the 3% group.	[38]
TiO_2NPs	Conventional glass ionomer	Agar diffusion test	*S. mutans*	GIC modified by 5 wt% TiO_2NPs significantly increased its antibacterial effect and CS, without affecting fluoride release.	[41]

GIC: Glass ionomer cement; AgNPs: Silver nanoparticles; CuNPs: Copper nanoparticles; HDPF: Human dental pulp fibroblast; RGR: Relative growth rates; TVE: Musk extract; MgONPs: Magnesium oxide nanoparticles; CFU: Colony forming unit; zMgONPs: MgONPs with zein polymer; ZnONPs: Zinc oxide nanoparticles; TiO_2NPs: Titanium dioxide nanoparticles; CS: Compression strength.

bacterial adhesion, which was significantly less than that of conventional GIC but significantly more than that of MDPB-GIC. Moreover, CPP-ACP significantly improved the flexural strength of GIC [55]. 1.56 wt% CPP-ACP-GIC had better compressive strength and wear resistance than the 1% and 2% groups. Therefore, more research is required to identify the most effective concentration to achieve the balance between the antibacterial and mechanical properties of CPP-ACP-modified GIC.

3.2.2.4 Theobromine

Theobromine is a natural polyphenol found in cocoa beans and cacao tree bark that promotes remineralization of the enamel surface by increasing the formation and crystal size of apatite, reduces dentin sensitivity through occluding dentin tubules [56], and inhibits the growth of bacteria through reducing acid production and glucan synthesis of *S. mutans* [10].

Researchers have investigated GIC modified by theobromine. Cevallos *et al.* [10] reported that 1 wt% theobromine-modified GIC inhibited the biofilm growth of *S. mutans* and improved its microhardness. Compared with traditional GIC, the modified GIC showed no significant differences in saliva adsorption, solubility and fluorine release [10]. However, considering the shortcomings of the low water solubility and poor stability of polyphenols, the long-term effect of theobromine-modified GIC remains to be clarified.

3.2.2.5 Salvia officinalis (sage) extracts

Herbal extracts have recently been widely used in oral care products and dental materials because of their environmentally friendly, safe and antibacterial properties. Sage (*Salvia officinalis*) has a long history as a medicinal plant with antibacterial, anti-inflammatory, analgesic, and other effects [57]. Sage is used as a medicinal tea in Europe to control sore throat, inflammatory oral diseases and gingivitis. Kermanshah *et al.* [58] showed that sage extract-containing mouthwash had an inhibitory effect on the growth of oral microbiota. Beheshti-Rouy *et al.* [59] demonstrated that sage extracts effectively reduced the number of *S. mutans* colonies in oral plaque. The inhibitory effects of sage extract on *Porphyria gingivalis* and *C. albicans* were also been reported [59].

Shahriari *et al.* [60] added 0.5–1.25 wt% of sage extract to GIC and examined the antibacterial effect on two main cariogenic bacteria, *S. mutans* and *L. casei*. The results showed that all the modified GICs had inhibitory effects on both bacteria in a dose-dependent manner, except for the 0.5% group that did not show an inhibitory effect on *L. casei.* However, the mechanical properties and biocompatibility of sage extract-modified GIC need to be evaluated before clinical trials. Notably, the color change of modified GIC is also a potential problem for clinical application.

A list of studies in the last 5 years on antibacterial properties of GIC modified by single natural sources component is shown in Table 3 (Ref. [7, 10, 13, 45–47, 50, 51, 55, 60]).

3.2.3 Inorganic antibacterial additives

3.2.3.1 Hexametaphosphate (HMP)

HMP is an inorganic cyclic phosphate salt that increases the permeability of the microbial wall and disperses microbial biofilm [5], so it is widely used as an antibacterial agent. While the antibacterial mechanism of HMP is not completely clear, studies have confirmed that HMP has a strong affinity for Mg^{2+} and Ca^{2+}. Moreover, the ionic complexes formed by HMP have a great influence on the permeability of microbial cell walls and also affect the activity and metabolic capacity of microorganisms, endowing HMP with unique antibacterial properties. HMP also increases the release of fluoride, phosphate and calcium ions, which play a key role in tooth remineralization. Previous studies have shown that fluoride toothpaste containing HMP had a better effect on enamel remineralization compared with toothpaste without HMP [61]. Therefore, HMP has become a potential GIC modification additive.

Hosida *et al.* [5] evaluated the fluoride ion release and antibacterial and mechanical properties of GIC modified with different concentrations of HMP and the effects on enamel demineralization. The results showed that 9% and 12% HMP-modified GIC had the best antibacterial effects and the highest level of fluoride ion release among all tested concentrations. With the increase of HMP concentration, the degree of enamel demineralization decreased. However, the addition of HMP reduced the mechanical properties of GIC.

In the future, researchers could combine HMP with other additives to modify GIC with the aim of overcoming the negative effects on mechanical strength and further improving the antibacterial activity.

3.2.3.2 Fluorinated graphene (FG)

Graphene is a two-dimensional material composed of carbon atoms with unique properties, including excellent electrical properties, thermal properties, optical properties, mechanical properties [62], chemical stability, good biocompatibility and efficient antibacterial properties [63], providing broad application prospects. Recent studies have identified several characteristics of graphene and its derivatives (especially graphene oxide, GO) that lead to some advantages in the biomedical field. For example, graphene was shown to be non-toxic to human osteoblasts and mesenchymal stromal cells, enhance the adhesion and proliferation of osteoblasts and induce the osteogenic differentiation of dental pulp stem cells [63]. However, because of the dark color of graphene and GO, their application in dental prosthetic materials has been limited.

Fluorinated graphene (FG) is a new derivative of graphene with many unique properties as observed with graphene, such as strong antibacterial activity and good biocompatibility. Sun *et al.* [64] found that 2 wt% FG-modified GIC had a bactericidal rate of more than 75% against *S. aureus* and *S. mutans*, and its microhardness and compressive strength were increased by 60.81% and 59.56%, respectively, compared with traditional GIC. The color, solubility, and fluoride ion release performance of the modified GIC were not affected [64]. Liu *et al.* [65] found that 2.0 wt% FG effectively improved the bacteriostatic effect of GIC, and these effects were proportional to the concentration of FG. Additionally, there was no statistical difference in biocompatibility between FG-GIC and conventional GIC. FC-modified GIC also showed no cytotoxicity compared with conventional GIC. While the results for FG-modified GIC are promising, the bactericidal

TABLE 3. An overview of recent research progress in the last 5 years on antibacterial properties of GIC modified by single natural sources component.

Antibacterial agent	GIC type	Antibacterial Assay	Bacterial strain	Major outcomes	Ref.
Propolis	Conventional glass ionomer (Meron and Ketac Cem)	Agar diffusion test	*S. mutans*	The antibacterial activity of GIC modified by EEP was dose-dependent, and a commercial GIC containing 50% EPP had the best biocompatibility.	[7]
Propolis	Conventional glass ionomer	Agar diffusion test	*S. mutans* and *L. acidophilus*	GIC modified with propolis exhibited a similar antibacterial effect compared with GIC modified with chitosan and Triphala against *S. mutans* and *L. acidophilus*.	[45]
Propolis	Conventional glass ionomer (Meron and Riva)	CFU counting test	*S. mutans* and *C. albicans*	The best antibacterial efficacy of GIC modified by red propolis against *S. mutans* and *C. albicans* was observed at the concentration of 25%, without a significant impact on mechanical properties and fluoride release.	[46]
Propolis	Conventional glass ionomer	Agar diffusion test	*S. mutans*	The 25% EEP-modified GIC exhibited the superior antibacterial property. However, its micro-shear bond strength was significantly lower than that of the control GIC.	[47]
Essential oils	Conventional glass ionomer	Agar diffusion test	*S. mutans*	The GIC modified with 2% thymol oil had bacteriostatic effects on *S. mutans* plankton and a significant inhibitory effect on biofilm, but without cytotoxicity.	[50]
Essential oils	Conventional glass ionomer (Fuji IX)	Agar diffusion test	*S. mutans* and *C. albicans*	All modified GICs significantly inhibited the growth of *S. mutans* and *C. albicans,* and the mechanical properties of GIC were not significantly affected by adding 5% essential oils.	[51]
CPP-ACP	Conventional glass ionomer (Fuji VII and Fuji VII EP)	Static and flow cell assays	*S. mutans*	3 wt% CPP-ACP-modified GIC had an inhibitory effect on *S. mutans*.	[13]
CPP-ACP	Conventional glass ionomer (Type II GIC)	Bacterial adhesion tests	*S. mutans*	CPP-ACP-GIC, CH-GIC and BAG-GIC exhibited similar bacterial adhesion and were statistically better than conventional GIC but weaker than MDPB-GIC from conventional GIC, while CPP-ACP significantly improved the flexural strength of GIC.	[55]
Theobromine	Conventional glass ionomer (Fuji IX)	CFU counting test	*S. mutans*	1 wt% theobromine-modified GIC inhibited the biofilm growth of *S. mutans* and improved its microhardness.	[10]
Salvia officinalis (sage) extracts	Conventional glass ionomer	Agar diffusion test	*S. mutans* and *L. Casei*	0.5–1.25 wt% sage extract-modified GICs had inhibitory effects on both bacteria in a dose-dependent manner, except for the 0.5% group that did not show an inhibitory effect on *L. casei.*	[60]

GIC: Glass ionomer cement; EEP: Ethanol extract of propolis; CFU: Colony forming unit; CPP-ACP: Casein phosphopeptide-amorphous calcium phosphate; CH: Chitosan; BAG: Bioactive glass; MDPB: Methacryloyloxydodecyl pyridinium bromide.

rate needs to be improved.

A list of studies in the last 5 years on antibacterial properties of GIC modified by single inorganic antibacterial additive is shown in Table 4 (Ref. [5, 64, 65]).

3.2.4 Organic antibacterial additives

3.2.4.1 Chlorhexidine (CHX)

Chlorhexidine is a broad-spectrum antibacterial agent, and its antibacterial mechanism is mainly through the cation on its surface to absorb bacteria with anionic ions, so as to destroy the cell membrane of bacteria to kill bacteria [66]. Oral composite resin modified by CHX was shown to efficiently kill a variety of oral pathogens, and CHX also has the effect of stabilizing and protecting dentin collagen fibers. Therefore, adding CHX to GIC as an antibacterial component has been extensively studied. However, some problems still restrict the clinical application of CHX-modified GIC, such as the decrease in mechanical strength, the increase of the solidification time, and the negative effects on the release of fluoride ions. Additionally, because of the burst effect of CHX, it is not conducive to

TABLE 4. An overview of recent research progress in the last 5 years on antibacterial properties of GIC modified by single inorganic antibacterial additive.

Antibacterial agent	GIC type	Antibacterial Assay	Bacterial strain	Major outcomes	Ref.
Hexametaphosphate (HMP)	Conventional glass ionomer (Fuji II)	Agar diffusion test	*S. mutans*, *L. acidophilus* and *A. sraelii*	9% and 12% HMP-modified GIC had the best antibacterial effects. However, the addition of HMP reduced the mechanical properties of GIC.	[5]
Fluorinated graphene (FG)	Conventional glass ionomer	CFU counting test	*S. aureus* and *S. mutans*	The colony count of modified GIC against *S. aureus* and *S. mutans* decreased with the increase of the content of FG. The antibacterial rate against *S. mutans* was up to 85.27% when the FG content was 4 wt%.	[64]
Fluorinated graphene (FG)	Conventional glass ionomer	CFU counting test	*S.aureus* and *E.coli*	2.0 wt% FG effectively improved the bacteriostatic effect of GIC, and these effects were proportional to the concentration of FG.	[65]

GIC: Glass ionomer cement; HMP: Hexametaphosphate; CFU: Colony forming unit; FG: Fluorinated graphene.

maintaining long-term antibacterial properties of GIC.

Recent studies have focused on solving the above problems with the aim of increasing the antibacterial properties of GIC without reducing the physical and mechanical properties. Yan *et al*. [9] added CHX-encapsulated mesoporous silica nanoparticles (CHX-MSN) into GIC powder. The modified GIC achieved a slow release of CHX when CHX-MSN was added at 1 wt%, which effectively inhibited the formation of *S. mutans* biofilm for a long time and did not affect the mechanical properties. Silva *et al*. [67] evaluated the effect of CHX mixed with nano-sized sodium trimetaphosphate (TMP) on the antibacterial and mechanical properties of GIC. TMP did not affect the antibacterial activity of CHX, and GIC containing 1.25% CHX and 14% TMP showed improved antibacterial properties and the ability to resist enamel demineralization, without a significant negative effect on the mechanical properties.

With the increase in research, the potential applications for CHX-modified GIC have expanded. Vamsi *et al*. [8] evaluated the antibacterial properties of chlorhexidine diacetate (CHX-D)-modified GIC against *L. casei* and *A. viscosus*, which were predominant microorganisms in deep caries. The results showed that 1% of CHX-D significantly improved the antibacterial properties of GIC against *L. casei* and *A. viscosus*, indicating the potential for its use to prevent deep caries. Besides, Ratnayake *et al*. [68] studied the efficacy and patient satisfaction of atraumatic restorative treatment (ART) of root caries with CHX-modified GIC. Compared with conventional GIC, 5% CHX-modified GIC showed significant improvements on antibacterial activity. 5% CHX-modified GIC prosthesis showed significantly better anatomical morphology continuity with dental tissue than conventional GIC conventional GIC did, and patients were satisfied with the restorative treatment by CHX-modified GIC [68]. These results have indicated the possibility of using CHX-modified GIC for ART treatment for older people and special needs groups, especially when repairing root caries.

Notably, previous studies have reported that CHX is cytotoxic to human fibroblasts, and long-term exposure causes tooth pain, taste disorders, and other adverse reactions [69]. Therefore, how to accurately control the sustained release dosage of CHX in the oral environment to avoid these side effects requires more research.

3.2.4.2 Antibiotics

The addition of antibiotics is considered to be an effective strategy to increase the antibacterial property of GIC. Previous studies have demonstrated that adding antibiotics to GIC inhibited the growth of oral microorganisms without affecting the biomechanical properties of GIC [70].

Doxycycline (DOX), a derivative of tetracycline antibiotics, has been widely used in dentistry mainly for the treatment of periodontal diseases. Morais *et al*. [70] used polymethyl methacrylate (PMMA) to encapsulate DOX (5–15%) to prepare DOX-PMMA microspheres and added 20 wt% DOX-PMMA microspheres to GIC. The DOX-PMMA microspheres provided sustained antibacterial activity for GIC, but they decreased its diametral tensile strength. At present, research on DOX-modified GIC is still in the initial stage. Moreover, *in vivo* experiments and clinical trials should also be conducted.

A list of studies in the last 5 years on antibacterial properties of GIC modified by single organic antibacterial additive is shown in Table 5 (Ref. [8, 9, 67, 70]).

3.3 Dual antibacterial component-based GIC modifications

3.3.1 Metal nanoparticle-based dual antibacterial additives

Metal nanoparticles are currently the most widely used inorganic antibacterial agents and show long-term antibacterial activity, low bacterial resistance, low volatility, high surface volume ratio and high thermal stability. However, the antibacterial effect of metal nanoparticles is relatively weak, and high concentrations of the nanoparticles affect other performances of GIC. Therefore, the combined use with other antibacterial components has been a research trend in recent years.

Studies have shown that AgNPs can be combined with amoxicillin, clindamycin, vancomycin, penicillin G and other

TABLE 5. An overview of recent research progress in the last 5 years on antibacterial properties of GIC modified by single organic antibacterial additive.

Antibacterial agent	GIC type	Antibacterial Assay	Bacterial strain	Major outcomes	Ref.
CHX-MSN	Conventional glass ionomer (Fuji IX)	Agar diffusion test	*S. mutans*	When the addition amount of CHX-MSN was 1 wt%, the modified GIC showed the slow release of CHX, and effectively inhibited the formation of *S. mutans* biofilm for a long time, without affecting its mechanical properties.	[9]
CHX-TMP	Conventional glass ionomer	CFU counting test	*S. aureus* and *S. mutans*	TMP did not affect the antibacterial activity of CHX, and GIC containing 1.25% CHX and 14% TMP showed improved antibacterial properties and the ability to resist enamel demineralization, without a significant negative effect on the mechanical properties.	[67]
Chlorhexidine diacetate (CHX-D)	Conventional glass ionomer	Agar diffusion test	*L. casei* and *A. viscosus*	The GIC modified with 1% CHX-D significantly improved the antibacterial properties of GIC against *L. casei* and *A. viscosus*.	[8]
Antibiotics (DOX-PMMA microspheres)	Conventional glass ionomer	Agar diffusion test	*S. mutans*	When prepared DOX-PMMA microspheres loaded with 15% DOX were added at the concentration of 20 wt%, the modified GIC showed sustained antibacterial activity against *S. mutans* but its diametral tensile strength was significantly decreased.	[70]

GIC: Glass ionomer cement; CHX-MSN: Chlorhexidine-encapsulated mesoporous silica nanoparticles; TMP: Trimetaphosphate; CFU: Colony forming unit; CHX-D: Chlorhexidine diacetate; DOX-PMMA: Doxycycline-polymethyl methacrylate.

antibiotics against a variety of oral microorganisms (119). Enan *et al*. [71] evaluated the antibacterial effect of AgNPs and amoxicillin on GIC and their effects on the compressive strength of GIC. Compared with conventional GIC or GICs modified with a single antibacterial component, GIC modified with AgNPs and amoxicillin showed significantly improved antibacterial effects against *S. mutans* and *S. aureus*, and there was no significant impact on the compressive strength of GIC [71]. Morais *et al*. [70] prepared PMMA microspheres loaded with silver sulfate and doxycycline (Ag-DOX-PMMA) to modify GIC. The Ag-DOX-PMMA microsphere-modified GIC had a sustained antibacterial effect on *S. mutans*, and the antibacterial effect was better than that of GIC modified with a single antibacterial component. However, Ag-DOX-PMMA microspheres reduced the diametral tensile strength of GIC [70]. Adnan *et al*. [23] studied the antibacterial effect of metal nanoparticles combined with CHX by adding 0.5% AgNPs + 1.5% CHX or 0.5% CuNPs + 1.5% CHX into GIC. The results showed that the combined applications of the two antibacterial components significantly improved the antibacterial efficiency compared with conventional GIC or GIC modified with a single antibacterial component.

Recently, the combined application of graphene derivatives and metal nanoparticles has become a trend in the antibacterial modification of GIC. Chen *et al*. [72] used reduced graphene-silver nanoparticle (R-GNs/Ag) nanocomposites, with various proportions, to improve the antibacterial and mechanical properties of GIC. The results showed that adding 1% or 2% R-GNs/Ag significantly reduced the activity of bacteria without affecting the mechanical properties of GIC. Siddiqui *et al.* [73] successfully synthesized *Salsola imbricata*-silver nanoparticle (SI-AgNPs) via a biosynthesis approach and used it as antibacterial additive in GIC. The results demonstrated that SI-AgNPs exhibited potent antibacterial activity against oral bacteria, including *S. mutans* and *L. acidophilus*, and the most effective concentration was 2 mg/mL. Additionally, the GIC modified with 0.2% SI-AgNPs substantially enhanced the antibacterial efficacy against both *S. mutans* and *L. acidophilus*.

Titanium dioxide (TiO_2) is a common antibacterial additive in the dental material field, and its combined application with other antibacterial ingredients in GIC modification is a research hotspot. Ibrahim *et al*. [74] developed a novel GIC dual antibacterial modification method using 10% chitosan (CH) in the liquid phase and 3% TiO_2 nano-powder (TiO_2NP) in the powder phase. The antibacterial properties of the dual component-modified GIC were qualitatively and quantitatively improved. The modified GIC also showed significantly improved flexural and compressive strength. The combined application of TiO_2NP and cellulose has also made some progress. Sun *et al*. [75] modified GIC by blending 2 wt% TiO_2NP and 0.4 wt% nanocellulose. Compared with single-component modified or unmodified GIC, the dual component-modified GIC showed enhanced antibacterial effects and significantly improved compressive strength and wear resistance properties. The same group subsequently evaluated the effects of TiO_2NP and sisal cellulose nanocrystals on the physical and biological properties of traditional GIC [75]. The results showed that the combination of the two antibacterial components significantly increased the compressive and shear bond strength of GIC, reduced the dissolution rate and volume wear rate, and increased the antibacterial effect against *C. albicans* by 22% compared with traditional GIC. However, the modified GIC had a slightly negative effect on the activity of L-929 cells [75].

The combined application of metal nanoparticles and other antibacterial components still has some issues that need to be addressed, such as color change and cytotoxicity. The long-term antibacterial effect of the combined application also needs experimental confirmation.

3.3.2 Organic component-based dual antibacterial additives

CHX has excellent antibacterial effects in GIC modification, but adverse impacts have been frequently reported, resulting in obstacles for its clinical application. Therefore, the combined application of CHX with other antibacterial ingredients has become a new research direction, aiming not only to enhance the antibacterial property, but also to reduce or eliminate the adverse effects on other properties of GIC. In addition to examining a combination strategy of CHX with metal nanoparticles (Ag or Cu) [23], Mishra *et al.* [76] prepared chlorhexidine-cetrimide (CHX-CT) modified GIC and evaluated the effects on the antibacterial and mechanical properties of GIC. The results showed that 2.5/2.5 wt% CHX-CT-modified GIC significantly improved the antibacterial properties without significantly affecting the mechanical properties of GIC. The dual antibacterial component strategy using low concentrations of CHX not only guarantees antibacterial effects, but also reduces the adverse influences on other properties of GIC, which is worthy of further study.

As described above, the addition of HMP reduced the mechanical properties of GIC and the antibacterial ability of HMP-modified GIC was also limited. Therefore, HMP modified by fluoride was used to modify GIC and its antibacterial performance was explored [77]. The results showed that 1% HMP modified by fluoride had a better inhibitory effect on the biofilm of *S. mutans* and *C. albicans*. These results provided theoretical support for the combined application of HMP with other antibacterial materials.

A list of studies in the last 5 years on antibacterial properties of GIC modified by dual or multiple antibacterial components is shown in Table 6 (Ref. [23, 70–80]).

3.4 Multiple antibacterial component-based GIC modifications

To improve the antibacterial properties, increase the antibacterial profile, and prolong the antibacterial activity of modified GIC, many scholars have explored the combined application of three antibacterial components. Joshi *et al.* [78] mixed DOX with an antibiotic paste containing metronidazole and ciprofloxacin and added the mixture to GIC to evaluate the antibacterial effect on *S. mutans* and *S. aureus*. The combination of the three antibiotics significantly improved the antibacterial effect of GIC compared with conventional GIC. Ashour *et al.* [79] prepared biogenic Zingiber officinale-capped AgNPs (ZOE-AgNPs) and found that GIC modified by the combination of ZOE-AgNPs and CHX together enhanced its antibacterial efficacy and compressive strength compared with GIC modified by ZOE-AgNPs or lyophilized miswak or CHX alone. Kurt *et al.* [80] evaluate the antibacterial effect of simultaneously adding antibacterial agents to powder and liquid of conventional GIC. They added CHX, cetrimide (CT) and cetylpyridinum chloride (CPC), served as an agent, to the powder, and added benzalkonium chloride (BC), as B agent, to the liquid of GIC [80]. The results showed that the GIC modified by AB agents simultaneously at the concentration of 1% had significantly higher antibacterial activities against *S. mutans* and *L. casei*. However, the microhardness of the experimental GIC was significantly impaired.

4. Discussion

This narrative review aimed to comprehensively summarize the current research progress on different antibacterial agents incorporated into conventional GICs. Therefore, it was crucial to classify antibacterial strategies for conventional GICs and reveal their antibacterial mechanisms of introduced antibacterial agents. This paper collected relevant literatures on antibacterial modification of conventional GIC from Jan 2017 to Dec 2024, and categorized them into three major types according to the number of antibacterial agents used, such as single, dual, and multiple modification. Meanwhile, for single antibacterial agent modification strategy, the literature was further classified according to the types of antibacterial agents, such as metal nanoparticles, plant extracts and organic antibacterial agents, which were relatively abundant.

Currently, the misuse of antibiotics leads to the emergence of various drug-resistant strains in clinical practice, and the antibiotic modification strategy of GICs also contribute to this problem, which limits its application [80]. Therefore, the modification method without antibiotics obtains more and more attention. Additionally, compared with single antibacterial strategy, dual and multiple antibacterial modification strategies showed a significant improvement on the antibacterial efficacy of modified GICs against oral microorganisms [23, 77–80]. In particular, the remarkable antibacterial effect of modified GICs was achieved by combining metal nanoparticles (such as AgNPs and CuNPs) with other kinds of antibacterial agents, such as antibiotics or CHX [23, 70–72]. Some studies have shown that the combined application of different antibacterial agents did not impair the mechanical and physical properties of conventional GIC [23, 71, 72, 74, 75]. Therefore, dual or multiple antibacterial modification strategies are expected to become the pupular research trend in the future. However, there were also some references pointing out that the combined application of different antibacterial agents affected the biocompatibility and partial mechanical properties of conventional GIC to some extent [70, 80]. These contradictory results may be due to differences in the types of antibacterial agents used and their methods of incorporation.

At present, most of dual or multiple antibacterial modification strategies adopted the simple mechanical blending of different components [23, 77–80]. This approach has the advantages of simple operation and low cost, but also has obvious drawbacks, such as uneven distribution of antibacterial ingredients, weak interfacial binding between the GIC substrate and antibacterial ingredients, and uncontrolled release of antibacterial components. These drawbacks will not only influence the durability and stability of the antibacterial performance, but also impair the mechanical and physical properties of GIC. This suggests that various surface treatments on the different

TABLE 6. An overview of recent research progress in the last 5 years on antibacterial properties of GIC modified by dual or multiple antibacterial components.

Antibacterial agents	GIC type	Antibacterial assay	Bacterial strain	Major outcomes	Ref.
AgNPs and amoxicillin	Conventional glass ionomer	CFU counting test	*S. mutans* and *S. aureus*	Compared with conventional GIC or GICs modified with a single antibacterial component, GIC modified with AgNPs and amoxicillin simultaneously showed significantly improved antibacterial effects against *S. mutans* and *S. aureus*, and there was no significant impact on the compressive strength of GIC.	[71]
Silver sulfate and doxycycline (Ag-DOX-PMMA)	Conventional glass ionomer	Agar diffusion test	*S. mutans*	The antibacterial effect of GIC modified by both silver sulfate and DOX was better than that of GIC modified with a single antibacterial component. However, Ag-DOX-PMMA microspheres reduced the diametral tensile strength of GIC.	[70]
AgNPs + CHX or CuNPs + CHX	Conventional glass ionomer (Fuji IX)	Agar diffusion test	*S. Aureus* and *S. mutans*	The two antibacterial components significantly improved the antibacterial efficiency of GIC compared with conventional GIC or GIC modified with a single antibacterial component.	[23]
Reduced graphene-silver nanoparticle (R-GNs/Ag)	Conventional glass ionomer (Fuji IX)	Direct contact test and CFU counting test	*S. mutans*	Adding 1% or 2% R-GNs/Ag to GIC significantly reduced the activity of bacteria, without affecting the mechanical properties of GIC.	[72]
Salsola imbricata + AgNPs	Conventional glass ionomer	Agar diffusion test	*S. mutans* and *L. acidophilus*	Compared with conventional GIC, GIC modified with 0.2% SI-AgNPs showed significantly improved antibacterial effects against both *S. mutans* and *L. acidophilus.*	[73]
Chitosan (CH) + TiO_2NP	Conventional glass ionomer	Direct contact test	*S. mutans*	The antibacterial properties of the dual component-modified GIC were significantly improved qualitatively and quantitatively. The modified GIC also showed significantly improved flexural and compressive strength.	[74]
TiO_2NP + nanocellulose	Conventional glass ionomer	CFU counting test	*C. albicans*	The dual component-modified GIC showed enhanced antibacterial effects and significantly improved compressive strength and wear resistance properties, compared with conventional GIC. However, compared with TiO_2NP-modified GIC, there was no significant difference on antibacterial properties.	[75]
CHX + CT	Conventional glass ionomer	Agar diffusion test	*S. mutans* and *L. casei*	2.5/2.5 wt% CHX-CT-modified GIC significantly improved the antibacterial properties compared with CH-modified GIC and conventional GIC, without significantly affecting the mechanical properties of GIC.	[76]
Fluoride-modified HMP	Conventional glass ionomer (Fuji II)	Agar diffusion test	*S. mutans* and *C. albicans*	The GIC modified by 1% fluoride-modified HMP had a better inhibitory effect on the biofilm of *S. mutans* and *C. albicans*.	[77]
DOX, metronidazole and ciprofloxacin	Conventional glass ionomer	Agar diffusion test	*S. mutans* and *L. casei*	The combination of the three antibiotics significantly improved the antibacterial effect of GIC compared with conventional GIC.	[78]
ZOE-AgNPs and CHX	Conventional glass ionomer (Fuji IX)	Agar diffusion test	*S. mutan* and *S. aureus*	GIC modified by the combination of ZOE-AgNPs and CHX enhanced its antibacterial efficacy and compressive strength compared with GIC modified by ZOE-AgNPs, lyophilized miswak or CHX alone.	[79]
CHX, CT, CPC and BC	Conventional glass ionomer (Ketac Molar Easymix)	Agar diffusion test	*S. mutans* and *L. casei*	The GIC modified by AB agents simultaneously in concentration of 1% had signifcantly higher antibacterial activities against *S. mutans* and *L. casei*. However, the microhardness of the experimental GIC was significantly impaired.	[80]

GIC: Glass ionomer cement; AgNPs: Silver nanoparticles; CFU: Colony forming unit; Ag-DOX-PMMA: Silver sulfate-doxycycline-polymethyl methacrylate; R-GNs/Ag: Reduced graphene-silver nanoparticle; CH: Chitosan; CHX: Chlorhexidine; CuNPs: Copper nanoparticles; TiO_2NP: Titanium dioxide nanoparticles; CT: cetrimide; HMP: Hexametaphosphate; ZOE: Zingiber officinale; CPC: Cetylpyridinum chloride; BC: Benzalkonium chloride.

antibacterial components to improve their interfacial binding force with GIC substrate or between different antibacterial components are necessary. Moreover, the unique structural morphology of antibacterial components can prevent the additive agglomeration and uncontrolled release of antibacterial agents, offering a promising solution to address the above challenges.

The synergistic effect is the key factor in determining the performance of modified GIC by dual/multi-antibacterial agents, which could be achieved by a reasonable combination of different antibacterial agents. For instance, Enan *et al.* [71]. reported that the combination of AgNPs and amoxicillin could not only synergistically enhance the antibacterial effect, but also maintain the original mechanical properties of the material. Nevertheless, it should be emphasized that simple mechanical mixing methods may lead to uneven composition distribution, which may affect the stability of material properties. To address this problem, various functionalization techniques have been developed. For example, Sun *et al.* [75] achieved uniform synthesis of TiO_2NPs and cellulose via chemical modification. Despite the promise of dual/multi-agent strategies, two major challenges persist: Firstly, the cytotoxicity of composite materials requires thorough evaluation, especially with regard to the long-term biosafety of novel materials such as fluorinated graphene, which remains uncertain. Secondly, inappropriate colors of composite materials may cause aesthetic problems, especially for dental restorative applications [75, 80]. It should be noted that most of the current studies have short experimental durations, few studies have long-term performance monitoring beyond 6 months, and systematic *in vivo* biocompatibility evaluation is lacking. These problems need to be addressed by future researches and we should always make it clear that improving the antibacterial performance of conventional GIC should not be done at the expense of other important properties.

It remains critical to maintain mechanical properties while improving antibacterial properties. A systematic review and network meta-analysis showed that zirconia enhanced GIC had better mechanical strength and durability compared to conventional GIC, providing a promising strategy to eliminate mechanical damage caused by antibacterial additives [81]. For instance, MgONPs and HMP-modified GIC often reduced compressive strength, but combining them with zirconia could alleviate these drawbacks. Future research should explore hybrid systems that combine antibacterial efficacy with mechanical reinforcement, such as zirconia-doped GIC composites [81].

Therefore, researchers should continuously search for new antibacterial agents and their combination strategy to achieve extensive and long-lasting antibacterial effects, and enhance or maintain the biocompatibility, aesthetic property and mechanical properties of conventional GIC. Moreover, the functionalization treatment of dual or multiple antibacterial agents to form a new type of complex can provide strong support for the modification research of traditional GIC.

5. Conclusions

GIC is an important material in the field of restorative dentistry. However, clinical experience has shown that the fluoride ions released by GIC are not sufficient to prevent dental secondary caries. In this study, we conducted a narrative review about three primary strategies for antibacterial modification of GIC from 2017 to 2024, including one-component, two-component and multi-component modifications. The key findings were as follows: In single-component modification, although different additives significantly enhanced antibacterial effects, their concentration-dependent cytotoxicity and adverse effects on mechanical properties must be carefully balanced. Dual/multi-component modifications can overcome some limitations of single-component strategy through synergistic effects, but some challenges remain to be addressed, such as uneven distribution of components and long-term stability of material system. Current researches are predominantly limited to short-term *in vitro* evaluations. Therefore, future work should focus on the development of functionalized composite antibacterial materials, validation of antibacterial properties by dynamic biofilm models, and long-term antibacterial and biosafety assessments to facilitate clinical translation. In summary, the key challenge in GIC antibacterial modification is achieving a balanced optimization of multiple properties, which needs interdisciplinary collaboration to facilitate the translational research of novel materials from laboratory settings to clinical applications.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

AUTHOR CONTRIBUTIONS

YWY, BL and FXS—designed the research study; provided help and advice on supervision, project administration. QSZ, YH and JXL—performed the research. RJM, XYY—analyzed the data. YWY—funding acquisition. QSZ, YH, JXL, YWY, BL and FXS—wrote the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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