Review Article

Antimicrobial efficacy of modified gutta-percha for obturation – A systematic review

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Abstract

Gutta Percha (GP) cones are made in an aseptic environment, a number of investigations have shown the presence of bacteria in recently opened boxes and this contamination rises with incorrect handling, storage and aerosol application. Numerous physicochemical techniques have been documented aiming to boost the antibacterial activity of GP cones while ensuring its obturation requirements. This systematic review aimed to critically evaluate the efficacy of antibacterial activity of GP modified with various antibacterial agents. The protocol for this systematic review has been registered with the PROSPERO International prospective register of systematic reviews, registry No. CRD42024573067. The search was carried out across reputable databases, including PubMed/Medline, Web of Science, Scopus and it was specifically designed to include articles published until March 2024. The search queries in the database were formulated with the basis of PICO questions in combination with various Boolean operators such as AND, OR. MeSH terms used for the search included GP, antibacterial agents, nanoparticles, root canal treatment, medicated GP. The extraction of the information was done by two independent authors. The evaluation of the methodological quality of the included studies was assessed using QUIN TOOL. This systematic review was reported following the Preferred Reporting Items for Systematic Reviews (PRISMA 2020) guidelines. Initial search yielded 51 studies from database search. Out of 51, 9 articles ultimately satisfied the requirements and were therefore discussed in the current systematic review. The included studies were assessed and data were extracted and tabulated. Based on the results of the current systematic review, modified GP with various antimicrobial agents showed significantly increased antibacterial effectiveness than standard GP.

Keywords: Antimicrobial activity; *Enterococcus faecalis*; gutta-percha; modified gutta-percha; obturation; root canal treatment

INTRODUCTION

The primary objective of nonsurgical root canal therapy is to restore the health of the root canal system while promoting the healing of the periapical tissues by removing necrotic or infected remnants.[1,2] Disinfectants may not reach bacteria that are residing in root canal regions such as isthmuses, dentinal tubules, and ramifications.[3] A link between the presence of bacterial infection in the canals and periradicular rarefaction in endodontic failures were identified in a study conducted by Lin *et al*. on 150 cases of endodontic treatment failures.[4] Secondary endodontic infections are primarily caused by facultative anaerobes such as *Enterococcus faecalis* in contrast to primary endodontic infections which are polymicrobial and dominated by Gram-negative anaerobic rods.[5] Endodontic infections are polymicrobial in nature. Therefore, following effective chemo-mechanical preparation, a suitable three-dimensional obturation is necessary to provide a fluid-tight barrier and prevent the admission of any microorganisms.[6]

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Additionally, despite the fact that gutta-percha (GP) cones are made in an aseptic environment, a number of investigations have shown the presence of bacteria in recently opened boxes and this contamination rises with incorrect handling, storage and aerosol application. Immersion of GP cones in several disinfectants is a common procedure, allowing material decontamination while conferring antimicrobial activity. Since sodium hypochlorite has a broad spectrum of activity and is inexpensive, it is typically utilized in this kind of decontamination. But it might change the GP cones' elasticity, tensile strength and elongation rate, which could have an impact on root canal filling outcome.[7-9]

Modifications to GP aim to improve the effectiveness, safety and longevity of root canal treatments ultimately leading to better outcomes for patients. Therefore, numerous physicochemical techniques have been documented aiming to boost the antibacterial activity of GP cones while ensuring its filling requirements. Using antimicrobial agents such as chlorhexidine, calcium hydroxide, or bioactive phosphate glasses as well as nanoscale techniques like creating nanodiamond GP composites are a few of these processes.[10-12] These methods are predicated on the idea that the material's antibacterial qualities are primarily determined by its chemical composition and surface characteristics.[13,14] This modification is essential for reducing the bacterial load within the root canal, minimizing the risk of reinfection, and ultimately improving clinical outcomes. By integrating antibacterial materials into GP, the likelihood of posttreatment infections can be reduced. The continuous release of antibacterial agents can help prevent secondary infections that might occur if bacteria were to survive after the initial treatment.[15] The rationale of this systematic review is to evaluate the existing literature on the antimicrobial efficacy of modified GP. By methodically examining and analyzing the available literature on this issue, the review would give significant insights into the antimicrobial effectiveness of modified GP, as well as identify any gaps in current knowledge that may merit additional investigation.

Structured question

Is there any significant difference in antimicrobial efficacy of GP modified with various antimicrobial agents and conventional GP?

MATERIALS AND METHODS

This systematic review was reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines.[16]

Protocol registration

The protocol for this systematic review has been registered with the PROSPERO International Prospective Register of Systematic Reviews, Registry No. CRD42024573067.

Table 1: PICO and study design

Key element	Description
Population	GP
Intervention	Modified/coated GP
Comparison	Conventional GP
Outcome	Antibacterial activity
Study design	*In vitro* studies

GP: Gutta-Percha, PICO: Population intervention comparison outcome

Search strategy

The current systematic review employed an extensive and multidisciplinary search technique. The search was carried out across reputable databases, including PubMed/Medline, Web of Science, and Scopus, and it was specifically designed to include articles published until March 2024 [Figure 1]. A combination of keywords such as Gutta Percha, Antibacterial agents, nanoparticles, Root canal treatment, Antibacterial agents, and Medicated Gutta Percha was used for the search strategy. The search queries in the database were formulated with the basis of PICO questions [Table 1] in combination with various Boolean operators such as AND, OR. MeSH terms used for the search included Gutta Percha, Antibacterial agents, nanoparticles, Root canal treatment, and Medicated Gutta Percha. No language restriction was applied. Related articles and the reference lists of the articles that were retrieved by the search engines were manually checked for possible eligibility.

Selection criteria

The criteria for inclusion and exclusion were structured in accordance with the study design, population, intervention, comparison, and outcome. In Vitro studies that used nanoparticles for modification of GP, antimicrobial agents for modification and studies that evaluated microbial load reduction after obturation, studies that used conventional GP or other modified GP as comparison, Studies that evaluated antimicrobial activity against various microbes were included. Case reports, case series, reviews, animal studies, and randomized or nonrandomized control trials were excluded. Studies with insufficient/incomplete data were also excluded. Studies that used disinfecting solutions to increase antimicrobial efficacy, studies without antimicrobial assessment were also excluded.

Screening process

The search and screening process was carried out by two authors (Manobharathi G and Sandhya Raghu) independently. After gathering all relevant information from computer searches, we conducted a screening process to eliminate articles that did not meet our predefined inclusion and exclusion criteria.

Step 1 involved removing publications and citations that were deemed irrelevant.

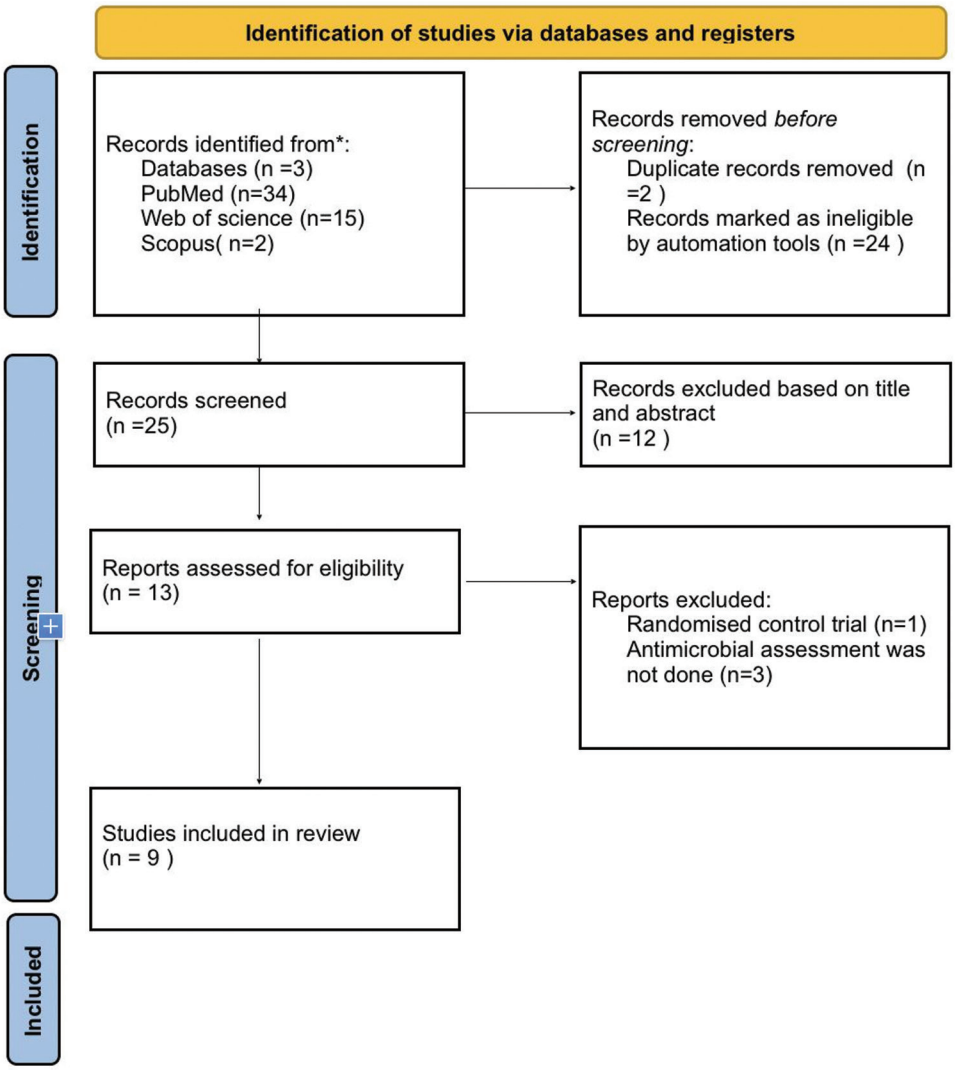

Figure 1: The Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart

In Step 2, one reviewer read the titles and abstracts of all identified studies and selected those that were pertinent. Any studies lacking statistical data or facts were immediately excluded from our review. For studies with any uncertainty, the full article was obtained and cross-checked by a second reviewer for consideration.

In Step 3, both reviewers conducted a double check of the selected studies, ensuring that any incomplete publications or those with insufficient data were eliminated. Articles that were not cited were also excluded.

Finally, Step 4 involved a thorough examination of the publications collected in Step 3, focusing specifically on those that aligned with our PICOS criteria.

Data extraction

The studies that fulfilled the inclusion criteria were processed for the extraction of data. The data were recorded as follows: first author and year of publication, type of study, sample size, study groups, antibacterial agents used, methodology, antibacterial assessment, and criteria used for evaluation. The information regarding assessment of the risk of bias was also collected. The extraction of the information was done by two independent authors (Manobharathi G and Sandhya Raghu).

Assessment of risk of bias

The evaluation of the methodological quality of the included studies was assessed using the QUIN Tool.[17] QUIN TOOL has 12 criteria for assessment. The criterias include clearly stated aim/objective, detailed explanation of sample size calculation, sampling technique, comparison of groups, operator details, randomization, method of measurement of outcome, outcome assessor details, blinding, statistical analysis, and presentation of results. According to the tool, if the criteria was adequately specified 2 points were assigned, if the criteria was inadequately specified 1 point was assigned. If not specified 0 point was assigned. Based on this the included

Table 2: Criteria assessed in QUIN tool and scores for included studies

QUIN TOOL CRITERIA	Alves *et al*.[7]	AL - Jobory & Al Hashimi[20]	Abd El Hamid *et al*.[21]	Tomino *et al*.[24]	Mohan *et al*.[5]	Bodrumlu and Alaçam[18]	Shur *et al*.[19]	Panwar *et al*.[23]	Melker *et al*.[22]
Clearly stated aim/objective	2	2	2	2	2	2	2	2	2
Detailed explanation of sample size calculation	1	1	1	1	2	1	2	1	2
Detailed explanation of sampling technique	1	1	1	1	2	1	2	1	2
Details of comparison groups	2	2	2	2	2	2	2	2	2
Detailed explanation of methodology	2	2	2	2	2	2	2	2	2
Operator details	2	2	2	2	2	2	2	2	2
Randomisation	1	1	1	1	1	1	1	1	1
Method of measurement of outcome	2	2	2	2	2	2	2	2	2
Outcome assessor details	2	2	2	2	2	2	2	1	2
Blinding	1	1	1	1	1	1	1	0	0
Statistical analysis	2	1	2	2	1	2	1	2	0
Presentation of results	2	2	2	2	2	2	2	2	2

Table 3: Risk of bias summary

Author & Year	Score	Percentage	Risk of Bias
Alves *et al*. 2018[7]	20	66	Medium risk
AL - Jobory & AL Hashimi 2021[20]	19	58	Medium risk
Abd El Hamid *et al*. 2020[21]	20	66	Medium risk
Tomino *et al*. 2016[24]	20	66	Medium risk
Mohan *et al*. 2020[5]	21	75	Low risk
Bodrumlu & Alaçam 2006[18]	20	66	Medium risk
Shur *et al*. 2003[19]	21	75	Low risk
Panwar *et al*. 2023[23]	18	58	Medium risk
Melker *et al*. 2006[22]	19	75	Low risk

articles were evaluated and scored [Table 2]. Then the scores were summarized to obtain a total score of a particular *in vitro* study. The scores thus obtained were used to grade the *in vitro* study as high, medium, or low risk (>70% = low risk of bias, 50%–74% = medium risk of bias and <50% = high risk of bias) [Table 3].

RESULTS

Search and selection

The PRISMA flowchart served as a guide for the study's article selection procedure. Initial search yielded 51 studies from database search. Subsequently, 38 articles were excluded due to their irrelevance, duplicates, and lack of accessible data. The remaining 15 articles assessed for eligibility and 3 articles were excluded due to lack of information about antibacterial assessment and 1 randomized control trial article was excluded. Nine articles ultimately satisfied the requirements and were therefore discussed in the current systematic review.

Description of included studies

The outcomes of antibacterial assessment of modified GP were examined in nine carefully chosen articles included in the current systematic review. Tables 4 and 5 provide an overview of all the detailed information from the included studies. In the systematic review, a total of nine articles were included, all of which were *in vitro* studies. These studies featured groups ranging from 2 to 6 and subgroups varying from 2 to 8. All nine studies employed different methodologies for coating GP with antimicrobial agents [Table 4]. Specifically, two studies utilized iodoform[18,19] to modify GP, while Alves *et al*. applied zinc oxide nanoparticles to GP using argon plasma treatment.[7] Four studies focused on enhancing the antimicrobial activity of GP by coating it with various nanoparticles, including zinc oxide, nano propolis, chitosan, silver nanoparticles, and nanocurcumin.[20,21,5] Each study employed distinct methodologies tailored to the specific form of nanoparticle used. This variation in methodology underscores the complexity and innovation in attempts to improve the antimicrobial performance of GP in endodontic treatments. One study explored the use of bioactive glass as a modification for GP to enhance its antibacterial effectiveness.[20,21,5,23] Three studies examined the impact of medicated GP (MGP) on its antibacterial activity which included formulations like iodoform, tetracycline.[18,19,22,23] One study focused on modifying GP using cetylpyridinium chloride (CPC), testing various concentrations of the compound, including 0.05%, 0.2%, and 0.8%.[24]

Assessment of risk of bias

According to the QUIN tool, six of the nine included *in vitro* studies showed an overall medium risk of bias. A study by Mohan *et al*.,[5] Shur *et al*.,[19] and Melker *et al*.[22] presented a low risk of bias. The investigations revealed a minimal probability of bias in all categories. Due to the small number of included studies and the variability of research design, sample sizes, and outcomes evaluated, meta-analysis was not possible. The absence of standardized techniques and limited sample numbers hampered the capacity to conduct a thorough meta-analysis.

DISCUSSION

The current systematic review focused on different methodologies of modification of GP using different antimicrobial agents and to evaluate and compare the results of antibacterial activity. Microorganisms

TABLE 4 : Characteristics of included studies

Author, Year, Country	Study Design	No of Groups	Methodology	Intervention	Comparison	Outcome	Conclusion
Alves *et al*. 2018[7] Portugal	*Invitro*	2	Argon plasma treatment	ZnO nanoparticle coating	Conventional GP	Antibacterial activity 1.direct assay 2.Indirect assay Against E.faecalis, S.aureus	Deposition of thin ZnO film on Gutta Percha cones increased its antibacterial activity against E.faecalis and S.aureus
AL - Jobory & Al Hashimi 2021[20] Iraq	*Invitro*	2	By replacing filler particles	Bioactive glass 45S5, Chitosan	Conventional GP	Antibacterial Activity (inhibition zone) against E.faecalis	Bioactive bioglass BG45S5 and chitosan showed *in vitro* highly antibacterial effects when mixing with Gutta Percha against E.faecalis
Abd EL Hamid *et al*. 2020[21] Egypt	*Invitro*	3 Sub groups -4	By immersing in coating agents	1.Nanopropolis 2.Silver curcumin	Conventional GP	Antibacterial Activity (inhibition zone) Against 1.E.faecalis 2.S.aureus 3.E. coli 4.Candida albicans	Nanopropolis and Silver curcumin coatings produced positive inhibitory action on all tested microbial species.
Tomino *et al*. 2016[24] Japan	*Invitro*	4 subgroups-8	By adding stock solution to softened thermoplastic gutta percha	Cetly pyridinium chloride 0.05%, 0.2%, or 0.8%	Conventional gp	Antibacterial activity by determining minimum inhibitory concentration	Addition of CPC significantly enhanced antimicrobial efficacy of Gutta Percha
Mohan *et al*. 2020[5] India	*Invitro*	5	Dipping in dense solution containing silver nanoparticle, chitosan nano particle	Silver nanoparticle 1%, 2%, chitosan nanoparticle 1%, 2%	Conventional gp	Antibacterial analysis 1.Growth curve analysis 2.CFU assay 3.Dead live assay 4.Reactive oxygen species analysis	The antimicrobial efficacy of the coated gutta Gercha was found in order of 2%AgNP GP>1%AgNP GP 2%Chit NP-GP>1% Chit NP-GP
Bodrumlu & Alaçam. 2006[18] Turkey	*Invitro*	3 Sub groups -4	Integrated	Iodoform	Conventional gp	Antibacterial activity (zone of inhibition)	Iodoform integrated Gutta Percha showed increased Antibacterial activity
Shur *et al*. 2003[19] USA	*Invitro*	3 Sub groups -8	Integrated	Medicated Gutta Percha	Iodoform free Gutta Percha	Antibacterial activity (zone of inhibition)	Compared to Iodoform free Gutta Percha, Iodoform containing MGP Gutta Percha had an inhibitory effect *in vitro* on S.aureus, F.nucleatum but not on E.faecalis, E. coli , P.aeruginosa
Panwar *et al*. 2023[23] India	*Invitro*	2	Manually coated	Nanocurcumin	Conventional gp	Broth dilution method, C FU (MIC)	Nanocurcumin has an antibacterial activity against E.faecalis
Melker *et al*. 2006[22] USA	*Invitro*	6	Medicated Gutta percha	Tetracycline or iodoform containing Gutta percha	Resilient points Standard Gutta percha	Agar diffusion test	Tetracycline containing Gutta Percha shows antimicrobial effectiveness over MGP or standard Gutta Percha

colonizing the root canal system play an essential role in the pathogenesis of periradicular lesions.[25,26] A link between the presence of bacterial infection in the canals and periradicular rarefaction in endodontic failure was identified in a previous studies.[3,27] The assessment and results of each included study summarized in Table 5.

According to Alves *et al*., due to the high recovery rates from infected canals in endodontic failures and after the cones' handling and storage respectively, the modified GP cones' antibacterial activity was evaluated against *E. faecalis* and *Staphylococcus aureus*.[7] The ZnO film mirrored the underlying topography, but in contrast to the film deposited on the pristine cones, the film on the pretreated

Table 5: Summation of individual parameters

Author year	Assessment	Result	Statistical analysis
Alves MJ, 2018[7]	Direct assay Indirect assay Against *E. faecalis, S. aureus*	Direct assay: Compared to untreated cones (control), ZnO coated cones caused about 30% reduction on sessile *E. faecalis* count Indirect assay: Compared to control. The eluents collected at 1 h caused growth inhibition on *E. faecalis* (−40%) and *S. aureus* (25%).The 24 hours eluents did not affect *E. faecalis* But reduced in 25% the growth of *S. aureus*	One way ANOVA followed by Tukey's HSD *post hoc* test
AL - Jobory & AL Hashimi, 2021[20]	Antibacterial activity (inhibition zone) against *E. faecalis*	The result showed that the experimental GP that mixed with chitosan and bioactive glass has best and power effect against *E. faecalis* mean 3.46±0.21	
Abd El Hamid *et al*. 2020[21]	Silver curcumin nanoparticle versus nano propolis coated GP against *E. faecalis, S. aureus, E. coli, C. albicans*	Mean and SD of the inhibition zone diameter for silver curcumin nanoparticles around disc were 12.35±0.71 mm for *E. faecalis* 20.6±0.39 mm for *S. aureus* 14.6±0.61 mm for *E. coli* 18.2±0.67 mm for *C. albicans* For Nano propolis 8.95±0.69 mm for *E. faecalis* 15.4±0.7 mm for *S. aureus* 9.75±mm for *E. coli* 14.8±0.63 mm for *C. albicans*	ANOVA followed by Student's *t*-test for group comparisons Statistically significant difference was found between the inhibitory effect of Silver curcumin nanoparticles and nano propolis against all tested microorganisms $P<0.001$
Tomino *et al*. 2016[24]	Antibacterial activity (determination of MIC)	MIC% (μg/mL) value *E. faecalis* 0.98 *S. aureus* 7.81 *S. gordonii* 0.98 *S. mutans* 0.98 *A. naeslundii* 7.81 *P. aeruginosa* 0.5 *P. gingivalis* 3.91	SNK test for multiple comparison
Mohan *et al*. 2020[5]	Growth curve analysis CFU assay Dead live assay ROS analysis	1.2% Ag-NP coated GP showed a significant reduction of bacterial count The growth curve of bacteria was found to be steeping in 1% Chitosan nanoparticle coated GP compared to control, the steepness followed by 2% Chitosan nanoparticle, 1% Ag nanoparticle, 2% Ag nanoparticle coated GP	
Bodrumlu & Alaçam 2006[18]	Zone of inhibition *E. faecalis* (ATCC29212 and ATCC 47077) *P. aeruginosa* (wild strain) *S. aureus* (wild strain) *E. coli* (wild strain) *C. albicans*	The largest mean inhibition zone with MGP occurred with *S. aureus* (mean diameter 10.5 mm) followed in descending order by *C. albicans* (9.3 mm), *E. faecalis* (ATCC 2921) (8.3 mm), *E. faecalis* (ATCC 47077) (7.0 mm), *E. coli* (4.0 mm) and *P. aeruginosa* (3.6 mm). However, not all of these effects continued over time, MGP did not inhibit the growth of *E. coli* or *P. aeruginosa* after 48 or 72 h	Kruskal–Wallis test was used to compare k independent samples
Shur *et al*. 2003[19]	Zone of inhibition	Povidone iodine inhibited all strains of bacteria tested. GP without iodoform inhibited *S. sanguis, A. odontolyticus*, MGP inhibited *S. sanguis, A. odontolyticus, F. nucleatum, S. aureus,* but no *E. faecalis*	
Panwar *et al*. 2023[23]	Zone of inhibition	The inhibition zones around coated GP cones were more pronounced for the nanocurcumin group by showing a larger zone of inhibition (12.5 mm) than the conventional group (2.5 mm) of the tested microorganism	Independent *t*-test for 2 groups, all statistical tests were two sided and performed at a significance level of $\alpha=0.05$
Melker *et al*. 2006[22]	Zone of inhibition	GP with tetracycline showed the greatest antibacterial activity against all bacteria tested except for *Fusobacterium*. The zone of inhibition with *Fusobacterium* was 21.6 mm with tetracycline GP and 70 mm with the MGP	

SD: Standard deviation, GP: Gutta-percha, MGP: Medicated GP, ROS: Reactive oxygen species, MIC: Minimum inhibitory concentration, SNK: Student–Newman–Keuls test, HSD: Honestly significant difference, *E. faecalis: Enterococcus faecalis, P. aeruginosa: Pseudomonas aeruginosa, E. coli: Escherichia coli, S. aureus: Staphylococcus aureus, F. nucleatum: Fusobacterium nucleatum, C. albicans: Candida albicans, S. sanguinis: Streptococcus sanguinis, A. odontolyticus: Actinomyces odontolyticus, S. mutans: Streptococcus mutans, S. gordonii: Streptococcus gordonii, A. naeslundii: Actinomyces naeslundii, P. gingivalis: Porphyromonas gingivalis*

cones had smaller particles and a higher specific surface area-to-volume ratio, which increased surface reactivity.[28] The ZnO film's antibacterial properties are mostly due to interfacial processes, therefore it makes sense that the plasma pretreatment increased the antimicrobial efficacy. According to In the study conducted by AL-Jobory and AL-Hashimi, methylthiazol tetrazolium (MTT) assays were used to examine the cytotoxic effects of modified bioactive and antimicrobial GP on fibroblast cells at various time intervals (24, 48, and 72 h).[20] MTT experiments revealed that the bioactive bioglass BG45S5 and chitosan had harmful effects *in vitro* when mixed with GP in fibroblast

cells, but the toxic effect was primarily observed as the same to control GP.

According to Abd El Hamid, silver-curcumin nanoparticles were bound to GP using polyvinylpyrrolidone (PVP) while propolis was bound to GP using polyvinyl alcohol.[21] Silver nanoparticle and Nano Propolis have been reported to have antibacterial activity against endodontic microorganisms.[29,30] Despite this, silver-curcumin nanoparticles' impact was much more noticeable. CPC, a quaternary ammonium compound and a cationic surfactant, was used in a wide variety of antiseptic products and drugs, including mouth rinses, dentifrices, and lozenges. CPC appears to harm microbial membranes, ultimately killing microorganisms, despite the fact that its antibacterial mechanisms are poorly known.[31,32] According to Tomino *et al*, the antibacterial activity of CPC coated GP against every microorganism tested in this investigation was considerably dose-dependently increased by the addition of CPC.[24] Furthermore, even after replacing the bacterial culture six times with new culture, the antibacterial efficacy was exhibited..

Silver nanoparticles, chitosan nanoparticles having a larger surface to volume ratio than their parent material, have demonstrated stronger antibacterial activity.[33] Because silver nanoparticles and chitosan nanoparticles suppress the formation of biofilms, many researchers have reported using them as an antibacterial agent when paired with root canal sealers. Based on Mohan et al, the silver nanoparticle coated GP (AgNP-GP) demonstrated superior antibacterial activity compared to the GP coated with chitosan nanoparticles (Chit NP-GP). Mechanistic evaluation revealed that the antibacterial effects were driven by induced oxidative stress and membrane damage to the bacteria caused by the coated nanoparticles. The antimicrobial efficacy of the coated Gutta percha was reported to be: 2% AgNP-GP > 1% AgNP-GP > 2% Chit NP-GP > 1% Chit NP-GP.[5]

Literature review reveals povidone-iodine has been assessed as a root canal disinfectant and for obturation.[35,36] It has been tested against endodontic microorganisms. Bodrumlu and Alaçam[18] incorporated povidone iodine to modify GP cones. In their assessment, the inoculation plates were covered with disks impregnated with povidone-iodine, standard GP cones, and MGP cones of the same size. The dishes were aerobically incubated at 37 degrees C. Growth inhibition zones were observed and measured at 24, 48, and 72 h. Over a 24-hour period, MGP suppressed the development of all bacteria. However, in certain instances, these effects persisted for longer. In particular, the MGP cones' antibacterial effects against Pseudomonas aeruginosa and Escherichia coli vanished after 48 and 72 h. In a study by Shur *et al*.,[19] 10% povidone-iodine inhibited all eight bacterial strains, but the growth of S. aureus and Fusobacterium nucleatum was only inhibited by MGP compared to iodoform free GP. MGP contains 10% iodoform, that iodoform in the MGP is inert until it comes into contact with tissue fluids, which in turn activate the free iodine and make it available to inhibit bacteria remaining in the canal.

In Panwar *et al*.,[23] minimum inhibitory concentration of nanocurcumin was observed at 50 mg/ml for *E. faecalis*. Nanocurcumin-coated GP showed a larger zone of inhibition when compared to conventional GP which showed a smaller zone of inhibition ($P < 0.0001$). Nanocurcumin-coated GP showed moderate antimicrobial activity, while conventional GP showed weak activity. In Melker *et al*.[22] the most antibacterial GP tested contained tetracycline, which prevented *Actinomyces*, *Fusobacterium,* and *E. faecalis* from growing by interfering with the ribosomal activity of bacteria. The positive and negative controls employed in the study were tetracycline disks/ E-tests and Resilion points. No antibacterial qualities were shown by Resilon points. *F. nucleatum*, *Actinomyces naeslundii,* and *Actinomyces israelii* were suppressed by standard GP and MGP, respectively. All four of the bacterial species studied showed growth inhibition in response to tetracycline and GP. The different methods of bacterial culture lead to diverse, nonuniform, and non comparable counts of microorganisms in their study. In future studies, it is imperative for researchers to standardize laboratory conditions. The findings of this review can guide clinicians in making informed decisions regarding the most suitable approach for endodontic retreatment, ultimately enhancing patient care and treatment outcomes.

The quality of a systematic review with most included studies at medium risk of bias is characterized as moderate. The data in a systematic review are heterogeneous, it means that the included studies have significant variations in their methods, populations, interventions, or outcomes. This heterogeneity can complicate the process of performing a meta-analysis. The future of selenium-coated GP is promising, with potential advancements in antimicrobial effectiveness, biocompatibility, and tissue healing. Continued research and clinical validation will be essential for its successful integration into endodontic treatments. Emphasis on standardizing methodologies, assessing long-term effects, and understanding the biological implications of new materials will be crucial for future advancements in endodontic treatment.

Limitations

The findings are based on *in vitro* studies, which may not accurately reflect the complex *in vivo* conditions, potentially limiting the applicability of the results. The lack of randomized controlled trials limits the strength of the evidence and the ability to draw definitive conclusions about the clinical efficacy of modified GP. The study heterogeneity, variability in study design, methodologies, and antimicrobial agents used across the included studies may affect the comparability of results and the overall conclusions. Different concentrations and combinations of

antimicrobial agents used in the modifications may lead to inconsistent results, complicating direct comparisons.

CONCLUSION

Based on results and limitations of the included studies, GP modified with antimicrobial agents demonstrated enhanced antibacterial effectiveness compared to conventional GP. However, when comparing the various modifications against each other, no significant differences were observed; all modifications exhibited increased antibacterial activity. Although further studies are needed to evaluate the physical and mechanical properties of the modified GP cones, it appears promising in preventing the ingress of microorganisms and the formation of biofilm, when following a strict asepsis protocol during endodontic treatment.

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Conflicts of interest
There are no conflicts of interest.

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