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Review article

Systematic review of antibacterial potential in calcium oxide and silicon oxide nanoparticles for clinical and environmental infection control

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Abstract
A substantial threat to worldwide health, the proliferation of antibiotic-resistant bacteria compels researchers to seek innovative antibacterial substances. This systematic review assesses the role of nanoparticles, particularly Calcium oxide and Silicon oxide nanoparticles, in infection control. The article examines the mechanisms by which these nanoparticles act against various bacteria and evaluates their potential as novel agents in infection control strategies.

A systematic literature search from 2015 to 2024 encompassing Web of Science, PubMed, Wiley, Science Direct, and Google Scholar, yielded 70 publications meeting the review criteria. This comprehensive methodology provides a thorough understanding of the capabilities and limitations of Calcium oxide and Silicon oxide nanoparticles as antibacterial agents.

The review aims to build a solid foundation for the utilization of nanoparticles in addressing the obstacles presented by antibiotic resistance by combining data from various investigations. Additionally, it aims to explore the safety and environmental implications associated with their use in clinical and environmental settings, providing a comprehensive analysis that may contribute to future studies and real-world applications in the field of antimicrobial technology.

Keywords: Antibiotic resistance; Antimicrobial; Biofilm inhibition; Calcium oxide nanoparticles; Infection control; Silicon oxide nanoparticles

Highlights:
- Calcium and silicon nanoparticles offer new approaches to infection control.
- Nanoparticles enhance antimicrobial to reduce infection risks in treatments.
- Potential for targeted drug delivery to infected sites improves clinical outcomes.
- Innovative use in surgical implants may reduce post-operative infection rates.
- Research supports the role of nanoparticles to develop antimicrobial coatings.

Introduction

Nanoparticles (NPs) are highly regarded for their potential in antibacterial applications due to their unique physicochemical, biological, and optical properties. Metallic NPs, such as iron oxide, silver, and zinc oxide, exhibit broad-spectrum antibacterial activity attributed to their large surface area and the ability to generate reactive oxygen species (ROS) (Algadi et al., 2024; Yousefian et al., 2023). The multifaceted mechanisms by which NPs exert antibacterial effects inducing oxidative stress, releasing metal ions, and engaging in non-oxidative pathways, make it difficult for bacteria to develop resistance (Wang et al., 2017). Notably, calcium oxide nanoparticles (CaO-NPs) and other plant-derived NPs possess inherent cytotoxic properties, positioning them as environmentally friendly alternatives to conventional antimicrobials (Khan et al., 2023). Biogenic metal oxides NPs, such as zinc oxide and copper oxide, present a promising strategy for combating drug-resistant infections, given their photocatalytic properties and synergistic effects that enhance antibacterial efficacy (Francis et al., 2023; Jiang et al., 2023).

CaO-NPs, in particular, demonstrate notable antibacterial and anti-biofilm properties, effectively inhibiting the growth of various pathogenic bacteria (Bhattacharjee et al., 2022; Khan et al., 2023; Kumar et al., 2021). These NPs disrupt bacterial cell membranes upon infiltration, leading to cell death and demonstrating their potential as potent antimicrobial

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agents (Karunanayake et al., 2019). Similarly, silicon oxide nanoparticles (SiO_2-NPs) exhibit significant antibacterial capabilities, preventing bacterial adhesion and proliferation (Sam et al., 2023). The application of these NPs in medical settings is promising due to their ability to prevent biofilm formation, disrupt existing biofilms, and combat a broad spectrum of bacterial pathogens. Their high surface area-to-volume ratio and effectiveness at low concentrations further underscore their potential in infection control (Morelli et al., 2021; Nandhini et al., 2024).

CaO-NPs and SiO_2-NPs are selected for their distinctive properties, environmentally friendly synthesis methods, ability to enhance materials, and wide-ranging applications in industry and biomedicine. Although other nanoparticles, such as those derived from metals or carbon, also possess remarkable characteristics, the emphasis on CaO-NPs and SiO_2-NPs stems from their sustainable synthesis, cost-efficiency, and notable contributions to specific applications, making them highly attractive for current research and industrial use.

The study examines the antibacterial efficacy of NPs such as CaO-NPs and SiO_2-NPs against pathogenic bacteria related to healthcare-associated illnesses (HAIs). These NPs are recognized for their efficacy against both Gram-positive and Gram-negative bacteria, including resistant strains such as *Staphylococcus aureus* and *Klebsiella pneumoniae*. The selection is to identify bacteria that facilitate biofilm development and confer medication resistance in healthcare settings. The mechanism of action of NPs, including ROS production and membrane rupture, corresponds with the treatment of illnesses resistant to traditional antibiotics (Zaha et al., 2019).

This review aims to consolidate current research on the efficacy of these NPs against various bacterial infections, evaluate their safety and potential adverse effects, and explore their practical applications in healthcare settings. Additionally, the review identifies gaps in existing research, proposes future research directions, and discusses the implications of utilizing these NPs to develop more effective and innovative infection control strategies. Both CaO-NPs and SiO_2-NPs have the potential to become valuable tools in combating bacterial infections, potentially making a significant impact on public health.

The systematic literature review (SLR) proposed in this study seeks to provide a comprehensive assessment of the bactericidal properties of these NPs. The review will explore the interactions between these NPs and bacterial cells, elucidate the mechanisms underlying bacterial cell death, and assess their efficacy against various bacterial strains and environmental conditions. Gaining this fundamental understanding is essential for determining the potential and limitations of these NPs as antibacterial agents, thereby paving the way for their innovative applications in medical and environmental contexts.

Materials and methods

This study investigates the effectiveness, mechanisms, safety, and potential applications of CaO-NPs and SiO_2-NPs in antibacterial treatments, particularly within innovative infection control. The research question was framed using the PICO framework (Fig. 1). The SLR was conducted using several high-impact databases, including ScienceDirect, Wiley, Web of Science, PubMed, and Google Scholar, to capture a comprehensive range of studies. The search strategy employed relevant keywords such as "Nanoparticles", "Calcium Oxide Nanoparticles", "Silicon Oxide Nanoparticles", "Antibacterial Activity", and "Infection Control". A Boolean search technique was utilized with the following keywords:

("Nanoparticles" OR "Calcium Oxide Nanoparticles" OR "Silicon Oxide Nanoparticles" OR "Nanoparticles and Antibacterial Activity" OR "Antimicrobial Nanoparticles" OR "Nanotechnology in Medicine" OR "Nano-medicine" OR "Nano-scale Antibacterials" OR "Nanoparticles in Infection Control") AND ("Infection Prevention" OR "Healthcare Infections" OR "Antibacterial Potential of Nanoparticles" OR "Innovative Infection Control" OR "Advanced Disinfection Techniques" OR "Antimicrobial Activity of Nanoparticles" OR "Nanostructured Materials in Medicine" OR "Nanoparticle-Antibiotic Synergy" OR "Effect of Nanoparticles on Bacteria").

The search covered publications from January 2015 to March 2024 and retrieved 1,302 articles. After filtering duplicates and irrelevant articles, 70 articles met the inclusion and exclusion criteria. The review process, guided by PRISMA guidelines (Page et al., 2021) and detailed in (Fig. 1), shows the research question operationalised using the PICO framework, sources, screening process, inclusion and exclusion criteria, and the final number of included articles.

Results

Summary of studies on CaO-NPs and SiO_2-NPs for antibacterial applications

Recent studies have highlighted the potential of CaO-NPs and SiO_2-NPs in antibacterial applications, displaying their efficiency against several bacterial species. CaO-NPs, synthesized through chemical precipitation and laser ablation techniques, have exhibited significant antibacterial activity against both Gram-positive and Gram-negative bacteria. This activity is primarily attributed to their ability to generate ROS, which leads to microbial cell death (Abbas and Aadim, 2022; Harish et al., 2022; Pham et al., 2022). *In silico* investigations have further corroborated the antibacterial potential of CaO-NPs against *E. coli*, suggesting their utility as a therapeutic option for reducing microbial loads (Kumari et al., 2022). Additionally, CaO-NPs biosynthesized from *Ficus carica* have shown both antibacterial and antibiofilm activities against a range of bacterial strains, indicating their potential application in future pharmacological formulations (Khan et al., 2023). Another study demonstrated that CaO-NPs synthesized via direct precipitation exhibited antibacterial activity against *E. coli* and *Vibrio cholerae*, reinforcing their potential for biomedical applications (Kumar et al., 2021). Similarly, SiO_2-NPs have been studied for their antibacterial properties in diverse applications, including water purification and medical device coatings. ZnO coated with SiO_2-NPs, derived from rice husk, have shown remarkable efficiency in removing antibiotics and bacteria from water, with the process being driven by electrostatic and hydrophobic interactions. These interactions are crucial in augmenting the antibacterial effectiveness of the NPs. Electrostatic interactions mostly enable the initial attraction and adhesion of bacteria to the nanoparticle surface, while hydrophobic interactions enhance the durability and efficacy of the antibacterial effect. This dual mechanism guarantees extensive antibacterial efficacy, positioning ZnO-coated SiO_2-NPs as a potential material for water disinfection and antibacterial applications (Fonseca et al., 2022; Pham et al., 2022). In addition, SiO_2-NP coatings have demonstrated substantial antibacterial activity against selected Gram-positive and Gram-negative bacteria, underscoring their potential to prevent disease transmission via medical devices

(Torres-Ramos et al., 2022). Research on silica-based iron oxide matrix composites with ZnO has indicated enhanced antibacterial properties, emphasizing the crucial role of ROS generated by ZnO in the observed antibacterial effect (Barma et al., 2020). Moreover, modified silica NPs, enhanced with organic compounds, have been engineered to improve their antimicrobial efficacy against both Gram-positive and Gram-negative bacteria (Matusoiu et al., 2022). A novel nano-antibacterial agent, combining SiO_2 with a polyionic liquid photosensitizer, has also been developed, effectively eliminating oral biofilm infections and providing a new approach to addressing biofilm-associated challenges (Akl et al., 2020). Collectively, these findings underscore the versatility and effectiveness of CaO-NPs and SiO_2-NPs in antibacterial applications, paving the way for the development of innovative antimicrobial agents and strategies (Jiao et al., 2022) – Table 1.

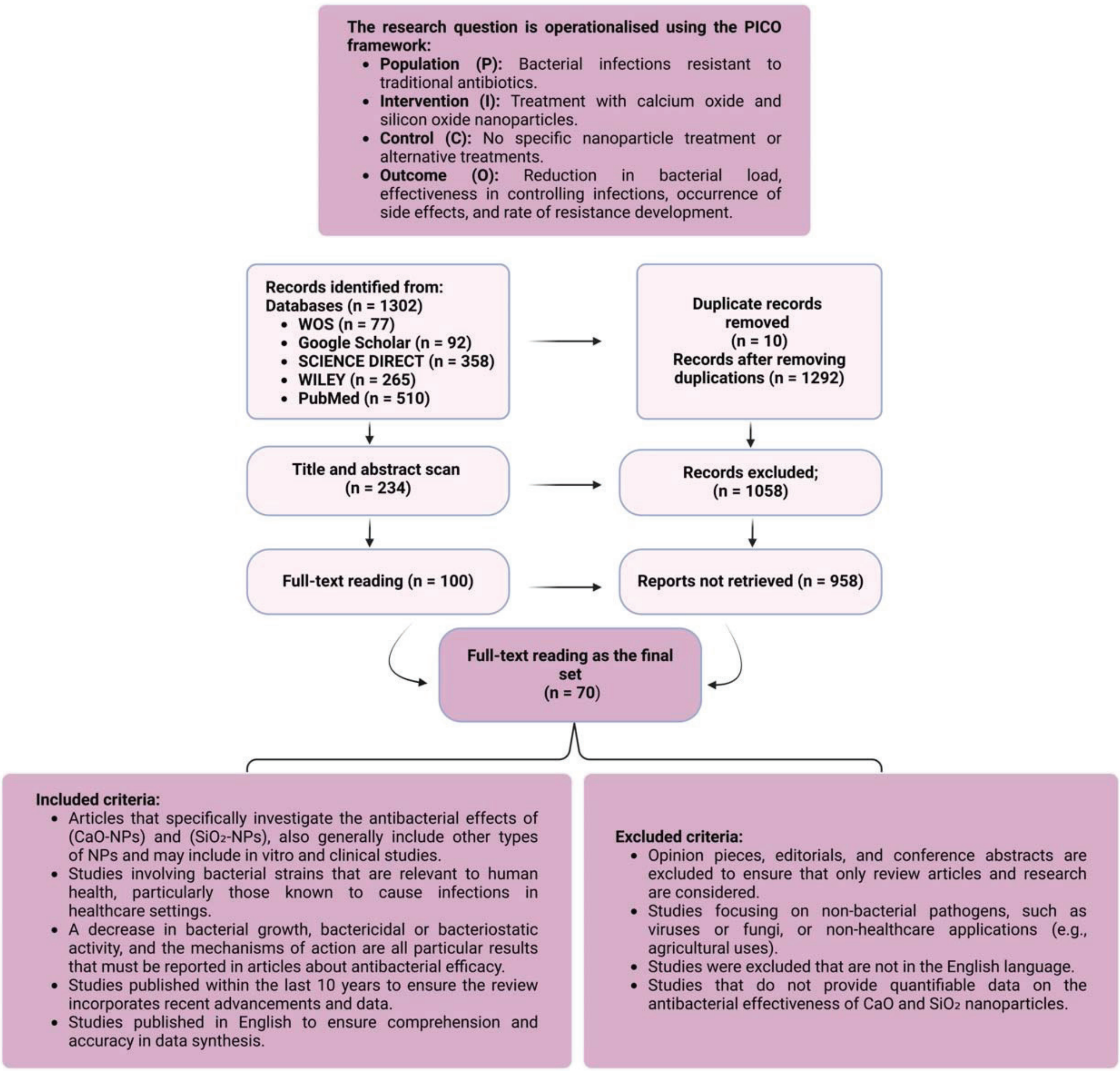

Fig. 1. PRISMA flow diagram

Table 1. Summary of studies on CaO-NPs and SiO_2-NPs for antibacterial applications

Nanoparticle type	Production method	Bacterial target	Application	Key findings	Reference
CaO-NPs	Chemical precipitation, laser ablation	Gram-positive and Gram-negative	General antibacterial use	Effective in generating ROS, leading to bacterial cell death; *in silico* studies indicate potential efficacy against *E. coli*.	Abbas and Aadim, 2022; Harish et al., 2022; Kumari et al., 2022; Pham et al., 2022
CaO-NPs	Direct precipitation technique	*E. coli*, *V. cholera*	Biomedical applications	Exhibits antibacterial activity against *E. coli* and *V. cholerae*, suggesting potential for biomedical applications.	Kumar et al., 2021
CaO-NPs	Biosynthesis from *Ficus carica*	Various bacteria	Future medications	Demonstrates both antibacterial and antibiofilm activity, indicating promise for future pharmaceutical development.	Khan et al., 2023
SiO_2	Derived from rice husk	Antibiotics and bacteria in water	Water purification	High efficiency in removing contaminants via electrostatic and hydrophobic interactions, particularly in water purification.	Fonseca et al., 2022
SiO_2-NPs	–	Gram-Positive and Gram-Negative	Medical device coatings	Coating significantly inhibits bacterial spread on medical devices, highlighting potential in healthcare settings.	Torres-Ramos et al., 2022
SiO_2-based composites (with iron oxide and ZnO)	–	–	General antibacterial use	Enhanced antibacterial capabilities with significant ROS generation, emphasizing the role of ZnO in the antibacterial effect.	Barma et al., 2020
Modified SiO_2	Involves organic chemicals	Gram-Positive and Gram-Negative	General antibacterial use	Improved antibacterial efficacy due to surface modifications that enhance microbial interactions.	Matusoiu et al., 2022
SiO_2 with poly ionic liquid photosensitizer	–	Oral biofilm infections	Dental applications	Highly effective in removing oral biofilms, providing innovative solutions for biofilm-related challenges.	Akl et al., 2020

Comparative efficacy of CaO-NPs and SiO_2-NPs against various pathogens bacteria

Both CaO-NPs and SiO_2-NPs have shown significant antibacterial efficacy against a variety of pathogens. CaO-NPs synthesized via laser ablation exhibited potent antibacterial activity against *K. pneumoniae* and *S. aureus*, achieving complete inhibition at 600 mJ. This suggests potential applications in dental health, particularly in preventing infections (Abbas and Aadim, 2022). Furthermore, CaO-NPs produced through a green synthesis approach using *Ficus carica* fruit demonstrated the ability to form protective layers against bacterial pathogens, indicating potential for future medicinal applications, especially in combating antibiotic-resistant infections (Khan et al., 2023). CaO-NPs with a particle size of 13.5 nm, synthesized through direct precipitation with a 3.48 eV optical bandgap, were found to be effective in eliminating Gram-negative bacteria such as *E. coli* and *V. cholerae*. These properties suggest their utility in drug delivery systems and environmental decontamination (Kumar et al., 2021). The bactericidal action of CaO-NPs is primarily attributed to the creation of an alkaline environment and the release of ROS, which lead to the degradation of bacterial cell walls (Bhattacharjee et al., 2022).

In contrast, SiO_2-NPs treated with trioctylphosphine oxide (TOPO) have shown efficacy against both Gram-positive and Gram-negative bacteria, including antibiotic-resistant strains such as methicillin-resistant *S. aureus* (MRSA) (Akl et al., 2020). Such modifications enhance the antibacterial efficacy of SiO_2-NPs by altering their surface characteristics, thereby improving their interaction and contact with bacterial cells. This alteration enables NPs to efficiently break bacterial cell membranes and obstruct critical cellular functions, making them effective against both Gram-positive and Gram-negative bacteria. The use of TOPO-modified NPs in medical contexts generates apprehensions about possible toxicity and environmental repercussions, needing thorough assessment and regulation (Akl et al., 2020).

These NPs also promote wound healing by releasing silicic acid, which aids in skin cell proliferation and infection prevention (Nandhini et al., 2024). Moreover, SiO_2-NPs combined with silver have demonstrated significant bactericidal activity against various bacterial strains, underscoring their potential for use in hygiene and safety applications (Khezerlou et al., 2018). Even at low concentrations, silica NPs have shown efficacy against Gram-positive bacteria, suggesting their potential integration into products such as mouthwash for enhanced oral health (Barma et al., 2020; Bhattacharjee et al., 2022).

Antimicrobial activity mechanism of CaO-NPs and SiO_2-NPs

Mechanisms of action of CaO-NPs

CaO-NPs exhibit a multifaceted mechanism of action against microbial pathogens, leveraging their physicochemical properties for both antibacterial and antibiofilm activities. A key aspect of their antibacterial efficacy is the generation of ROS, which induce oxidative stress, leading to the degradation of essential cellular components such as DNA, proteins, and lipids (Algadi et al., 2024; Mubeen et al., 2021; Westmeier et al., 2018). This ROS-mediated damage is further compounded by the ability of CaO-NPs to disrupt cell membrane integrity. This disruption is evident from the softening of amide infrared bands and the partial dissociation of lipopolysaccharide structures in Gram-negative bacteria, as well as the reduction in the integrated intensity of the C=O ester carbonyl stretch in lipoteichoic acid in Gram-positive bacteria (Khan et al., 2021;

Mosselhy et al., 2021). In addition to their direct antibacterial effects, CaO-NPs have been shown to suppress biofilm formation, a critical factor in the persistence and resistance of bacterial infections (Mosselhy et al., 2021). This anti-biofilm activity, combined with the NPs' ability to interfere with microbial efflux pumps, suggests a comprehensive approach to combating microbial resistance (Mosselhy et al., 2021). The antibacterial efficacy of CaO-NPs is also influenced by their physicochemical properties, including size distribution and surface characteristics. Smaller particles, in particular, demonstrate enhanced efficacy due to their increased surface area and reactivity (Mohanaparameswari et al., 2023; Yousefi et al., 2017). Beyond their direct antimicrobial actions, CaO-NPs have been explored for their potential in environmental applications, such as CO_2 sequestration, which can indirectly influence microbial growth by altering environmental conditions (Kadiyala et al., 2018; Yousefi et al., 2017). Their integration into polymer composites for food packaging and medical equipment highlights the broad utility of CaO-NPs, utilizing their antibacterial properties to ensure sterility and minimize contamination risks (Hu et al., 2024). Additionally, the application of CaO-NPs in plant research underscores their versatility, particularly in enhancing stress tolerance, thereby extending their relevance beyond antibacterial interventions (Bhattacharjee et al., 2023; Radulescu et al., 2023). Fig. 2 illustrates the process by which CaO-NPs exert their antibacterial effects. This mechanism provides an effective strategy for combating antibiotic resistance, modifying antibiotics, and inhibiting biofilm formation.

In summary, these studies demonstrate the complex and multifaceted mechanisms through which CaO-NPs exert their effects, encompassing direct antimicrobial actions as well as environmental and agricultural applications. This versatility positions CaO-NPs as a promising tool in the fight against microbial resistance and in promoting health and sustainability (Wang et al., 2024).

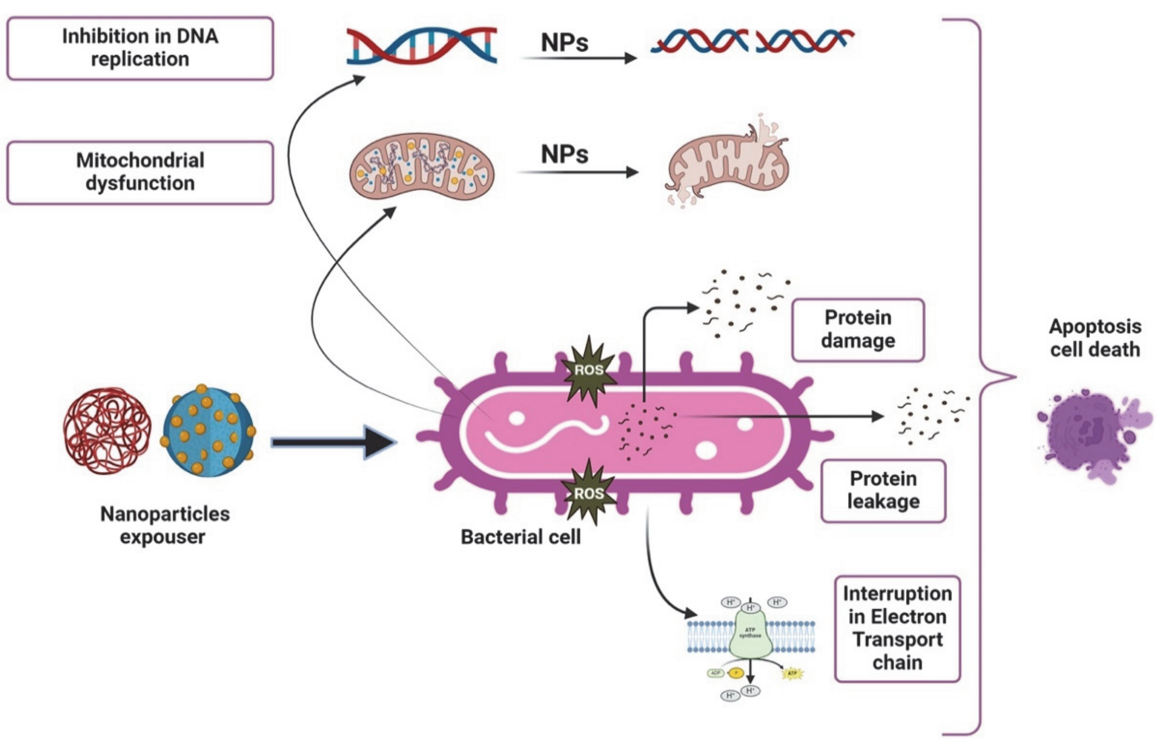

Fig. 2. Schematic mechanism: NPs interact with bacterial cells, triggering many biological pathways that lead to apoptosis

Mechanisms of action of SiO_2-NPs

The antibacterial mechanisms of SiO_2-NPs are multifaceted, involving both physical and chemical interactions with microbial cells. One notable approach involves the decoration of SiO_2-NPs with titanium dioxide (TiO_2), which significantly enhances their antibacterial activity under low-power UV radiation. This enhancement is attributed to a photocatalytic mechanism where ROS are generated, leading to damage and eventual death of bacterial cells (Vanamala et al., 2021; Velusamy et al., 2022). Similarly, combining SiO_2 with silver nanoparticles (Ag-NPs) results in a nanocomposite with strong antibacterial properties. The negatively charged nanocomposite interacts easily with microbial cells, causing physical damage to the cell membrane and leakage of cytoplasmic contents (Sangnim et al., 2024; Tsikourkitoudi et al., 2022). Furthermore, incorporating zinc oxide into silica-based iron oxide matrices increases the porosity and surface area, enhancing ROS production, which plays a critical role in the antibacterial efficacy of these composites (Sangnim et al., 2024; Srinivasan et al., 2023).

The core-shell structure of ZnO coated with SiO_2-NPs also underscores the importance of electrostatic and hydrophobic interactions in the adsorption and removal of bacteria and antibiotics from water, indicating a physical mode of action (Rashki et al., 2021). Additionally, chitosan/SiO_2 nanocomposites exhibit enhanced antibacterial properties due to the combined effects of the biopolymer and the NPs, suggesting that both physical barrier formation and chemical interactions contribute to their antimicrobial activity (Saravanan et al., 2023). Mesoporous silica nanoparticles (MSNs) loaded with pharmaceuticals have shown promise in treating bacterial infections, highlighting how the controlled release of drugs from the porous structure of SiO_2-NPs can amplify antibacterial effects (Castillo and Vallet-Regí, 2021; Malekmohammadi et al., 2022). In the context of oral health, the incorporation of silica NPs into mouthwash formulations has demonstrated increased antibacterial action against oral infections, likely due to the physical disruption of bacterial cell integrity by SiO_2-NPs (Juncker et al., 2021). Moreover, the surface treatment of silica NPs with organic groups has been found to enhance their antibacterial activity against both Gram-positive and Gram-negative bacteria, suggesting that chemical modifications can introduce unique interactions with microbial cells (Ganesan et al., 2023). The use of SiO_2-NPs for targeted drug delivery also highlights a mechanism where their large surface area and ease of functionalization facilitate the efficient transport and retention of antimicrobial agents within microbial cells (Mamun et al., 2021). Finally, the catalytic degradation of contaminants by copper oxide (CuO) coated with SiO_2-NPs, along with their significant antimicrobial activity, suggests that the catalytic generation of ROS and other reactive species on the nanoparticle surface is a crucial aspect of their antimicrobial mechanism (Bassegoda et al., 2018; Mosselhy et al., 2021).

Synergistice effects of NPs with existing antibiotics

The combination of NPs with antibiotics has emerged as a potent strategy to combat antibiotic-resistant bacteria, with significant implications for enhancing antibacterial efficacy (Table 2). Biogenic NPs such as CuO, ZnO, and tungsten trioxide (WO_3) have demonstrated strong bactericidal properties, which are further amplified when combined with antibiotics, making them highly effective against drug-resistant pathogens (Francis et al., 2023; Nandhini et al., 2024). For instance, the combination of CuO-NPs with vancomycin has been shown to reduce bacterial resistance in MRSA, suggesting that NPs can enhance antibiotic efficacy by facilitating drug penetration or adhesion to bacterial cells (Caballero Gómez et al., 2023; Fan et al., 2021). Similarly, ZnO-NPs have been reported to lower the minimum inhibitory concentrations (MIC) of vancomycin against resistant bacterial strains, indicating an effective synergy (Gupta et al., 2017; Khan et al., 2020). Additionally, the use of CuO-NPs in combination with silver nanoparticles (Ag-NPs) has been observed to enhance antibacterial effects against a variety of bacteria, including antibiotic-resistant strains (Khan et al., 2021). Furthermore, calcium carbonate NPs have been found to boost the antibacterial properties of gentamicin sulfate, suggesting that NP carriers can significantly enhance the efficacy of antibiotics (Westmeier et al., 2018). The combination of iron oxide NPs with antibiotics like ampicillin and gentamicin has also exhibited enhanced antibacterial and biofilm inhibitory properties (Khorsandi et al., 2021a). Moreover, magnesium-doped ZnO-NPs have shown improved antibacterial efficacy when combined with antibiotics, further demonstrating the potential of NP-antibiotic combinations (Sharmin et al., 2021). The pairing of CuO-NPs with chloramphenicol has also been shown to reduce the expression of resistance genes, highlighting the role of NPs in mitigating antibiotic resistance (Caballero Gómez et al., 2023). These findings underscore the ability of NPs to synergize with antibiotics, enhancing their effectiveness against drug-resistant microorganisms and suggesting potential applications for CaO-NPs in similar contexts.

Extensive research into the synergistic effects of SiO_2-NPs and antibiotics has shown promising results in improving antibiotic efficacy and addressing drug resistance. For instance, the combination of silica-magnetite nanoparticles with ciprofloxacin and humic acids has been found to enhance the removal of ciprofloxacin, reducing the mortality rate of ciliates and demonstrating the role of dissolved organic matter in environmental remediation (Amaro et al., 2021; Pham et al., 2022). Copper-doped mesoporous silica nanoparticles coated with Ag-NPs have been designed for pH-responsive delivery of tetracycline, with the production of free radicals contributing to a synergistic antibacterial effect, alongside high biocompatibility (Caballero Gómez et al., 2023; Castillo and Vallet-Regí, 2021). Hybrid silica NPs modified with amino polycarboxylate chelating groups have been shown to facilitate the delivery of vancomycin to Gram-negative bacteria, overcoming the bacterial membrane barrier (Gao et al., 2021). Moreover, multi-stimuli-responsive magnetic nanoplatforms have demonstrated improved biofilm elimination by co-delivering both large and low molecular-weight medications (Filipović et al., 2022). Additionally, the simultaneous administration of vancomycin and nano-Ag using silica NPs with a pollen-like structure has shown enhanced bactericidal activity, facilitating targeted drug release (Makabenta et al., 2021; Wang et al., 2017). Chitosan-metal ion NPs have further demonstrated a synergistic impact with antibiotics by decreasing the expression of antibiotic-resistance genes (Rashki et al., 2021). Surface-modified silica NPs have also been developed for enhanced drug release, demonstrating their antibacterial capabilities (Castillo and Vallet-Regí, 2021). Lastly, a distinct nanocarrier combining magnetic hyperthermia with controlled antibiotic delivery has shown significant reductions in viable bacteria in infections associated with biofilms (Kang et al., 2023). These studies highlight the potential of SiO_2-NPs and CaO-NPs to significantly enhance the efficacy of antibiotics against drug-resistant bacteria and biofilms.

Challenges and limitations of using CaO-NPs and SiO_2-NPs for antibacterial purposes

Although CaO-NPs and SiO_2-NPs offer promising antibacterial properties, they are not without challenges and limitations. The primary antibacterial mechanism of CaO-NPs is through the production of ROS, which can induce microbial mortality (Pham et al., 2019; Teng et al., 2023; Waktole and Chala, 2023). However, the effectiveness of CaO-NPs is highly dependent on their synthesis methods, intended applications, and the specific requirements of various microbial species, which can differ significantly (Metryka et al., 2021). Moreover, concerns about the cytotoxicity of CaO-NPs necessitate a thorough evaluation of their suitability for medical use.

Conversely, SiO_2-NPs are highly regarded for their biocompatibility, thermal stability, and large-scale synthetic availability. Their porous structure allows for the effective incorporation of antibacterial agents, making them useful in medical devices to prevent bacterial contamination (Alavi et al., 2022; Uddin et al., 2021). Despite these advantages, challenges remain regarding the functionalization of these agents and the need to balance mechanical properties with antimicrobial efficacy, particularly when incorporated into composites (Karaman et al., 2020). This challenge is especially pertinent in dental resin applications, where the inclusion of antibacterial agents can compromise aesthetic and mechanical properties. In the broader context of nanotechnology-driven antibacterial strategies, both CaO-NPs and SiO_2-NPs face additional constraints. These include concerns about the stability and toxicity of the NPs, which are critical for their safe and effective application. Additionally, the economic feasibility of implementing these technologies in clinical settings is a significant hurdle, highlighting the need for cost-effective processing and manufacturing methods (Khorsandi et al., 2021b). Furthermore, the long-term efficacy of these NPs may be compromised by the potential development of microbial resistance, underscoring the importance of continued research to understand and mitigate resistance mechanisms (Dos Santos Ramos et al., 2021; Kazem et al., 2024).

In summary, while CaO-NPs and SiO_2-NPs demonstrate promising antibacterial characteristics, their practical application is hindered by challenges related to bacterial resistance, functionalization, mechanical property compromises, and economic viability (Zohra et al., 2021). To overcome these obstacles, a multidisciplinary approach is required to optimize the design, synthesis, and application strategies of these NPs (AlMatar et al., 2018; Bharti, 2024; Uddin et al., 2021).

Table 2. Synergistic effects of NPs and antibiotics: enhancing antibacterial efficacy

Types of NPs	Antibiotics	Key finding	Reference
CaO-NPs and SiO_2-NPs	Tobramycin	NPs improve the penetration of antibiotics into bacterial cells and biofilms, offering new treatment options for drug-resistant infections.	Khan et al., 2021
MTA-NPs	Various antibiotics	NPs can alter the behavior and effectiveness of antibiotics in environmental settings.	Gao et al., 2021; Pham et al., 2022
ZnO coated with SiO_2-NPs	Various antibiotics	NPs demonstrate remarkable efficacy in eliminating antibiotics and bacteria from water, enhancing antibiotic effectiveness through adsorption and controlled delivery.	Fonseca et al., 2022
Cu-MSNs	Various antibiotics	The combination of NPs and antibiotics shows a synergistic effect against drug-resistant bacteria, with NPs enabling pH-responsive antibiotic delivery.	Juncker et al., 2021; Khan et al., 2020
Biogenic CuO-NPs, ZnO-NPs, and WO_3-NP	Various antibiotics	NPs enhance antimicrobial properties, showing a synergistic action against multi-drug-resistant (MDR) pathogens.	Francis et al., 2023; Nandhini et al., 2024
CuO-NPs	Vancomycin	The combination of NPs with antibiotics decreases resistance in MRSA.	Caballero Gómez et al., 2023
ZnO-NPs	Vancomycin	NPs reduce the MICs required for antibiotics, potentiating their effectiveness against resistant strains.	Gupta et al., 2017; Khan et al., 2020
CuO-NPs combined with Ag-NPs	Various antibiotics	NPs enhance antibacterial effects against a wide range of bacteria, including antibiotic-resistant strains.	Khan et al., 2021
$CaCO_3$-NP	Gentamicin sulfate	NPs enhance antibacterial effects.	Khan et al., 2021
Iron oxide NPs	Ampicillin and gentamicin	NPs exhibit enhanced antimicrobial and biofilm inhibitory effects when combined with antibiotics.	Mubeen et al., 2021
Magnesium-doped ZnO-NPs	Various antibiotics	NPs enhance antibacterial effects.	Anandakumar, 2023
CuO NPs	Chloramphenicol	NPs can decrease the expression of antibiotic resistance genes, making treatments more effective.	Amaro et al., 2021
Silica NPs with amino polycarboxylate	Vancomycin	NPs facilitate the effective delivery of antibiotics to Gram-negative bacteria, overcoming bacterial membrane penetration challenges.	Filipović et al., 2022
Magnetic supramolecular nanoplatforms	Large and low molecular weight drugs	NPs enhance the eradication of pathogenic biofilms, improving treatment outcomes.	Makabenta et al., 2021
MSNs	Various antibiotics	NPs enable targeted delivery of antimicrobials, reducing the required dosage and minimizing side effects.	Castillo and Vallet-Regí, 2021; Kang et al., 2023
Pollen-like Silica NPs	Vancomycin and nano-Ag	NPs promote localized drug release, resulting in enhanced bactericidal activity.	Kang et al., 2023; Wang et al., 2017
Chitosan-metal ion NPs	Various antibiotics	NPs can reduce the expression of antibiotic resistance genes, making treatments more effective.	Malekmohammadi et al., 2022
Surface-modified Silica NPs	Various antibiotics	NPs assist in controlled drug release.	Juncker et al., 2021
Magnetic-responsive nanocarrier	Various antibiotics	The combination of NPs and antibiotics significantly reduces viable bacteria in biofilm-associated infections.	Kang et al., 2023

Discussion

The exploration of CaO-NPs and SiO_2-NPs for antibacterial applications has yielded promising results, demonstrating their potential as effective agents against a wide range of bacterial pathogens. CaO-NPs, particularly those synthesized through chemical precipitation and laser ablation, have shown notable antibacterial efficacy, which is primarily driven by their ability to generate ROS. This ROS production leads to oxidative stress, resulting in the degradation of critical cellular components, including lipids, proteins, and DNA, ultimately causing bacterial cell death. These findings are supported by studies that highlight the effectiveness of CaO-NPs against both Gram-positive and Gram-negative bacteria, such as *E. coli* and *S. aureus*, suggesting their potential for therapeutic applications in combating bacterial infections, including those resistant to antibiotics (Abbas and Aadim, 2022; Harish et al., 2022; Pham et al., 2022).

Moreover, the unique properties of CaO-NPs, such as their size and surface characteristics, contribute significantly to their antibacterial activity. Smaller NPs, with their increased surface area, exhibit enhanced reactivity, which further amplifies their antimicrobial effects (Mohanaparameswari et al., 2023; Yousefi et al., 2017). Additionally, the ability of CaO-NPs to disrupt biofilm formation and interfere with microbial efflux pumps presents a comprehensive approach to addressing microbial resistance. These characteristics, combined with their potential applications in environmental decontamination and CO_2 sequestration, underscore the versatility of CaO-NPs in various fields beyond traditional antibacterial therapies (Hu et al., 2024; Kadiyala et al., 2019; Yousefi et al., 2017).

On the other hand, SiO_2-NPs have been extensively studied for their antibacterial properties, particularly in applications such as water purification and medical device coatings. The integration of SiO_2-NPs with other antimicrobial agents, like silver and zinc oxide, has led to the development of nanocomposites with enhanced bactericidal properties. These composites leverage both physical and chemical mechanisms, including ROS generation and electrostatic interactions, to disrupt bacterial cell membranes and inhibit bacterial growth (Fonseca et al., 2022; Torres-Ramos et al., 2022). The biocompatibility and thermal stability of SiO_2-NPs make them particularly suitable for use in medical devices, where they can prevent bacterial contamination and improve overall hygiene standards (Alavi et al., 2022; Uddin et al., 2021).

The study by Hao et al. (2024) on the synergistic antibacterial mechanisms of silver-copper bimetallic nanoparticles investigates the use of metals and compounds to enhance the antibacterial properties of SiO_2-NPs. Key factors include copper, silver, cobalt, and titanium dioxide. Copper exhibits antibacterial activity against *S. aureus* and *E. coli*, silver has broad-spectrum properties, cobalt contributes to multimetallic nanohybrids, and TiO_2 provides photocatalytic properties (Hao et al., 2024).

In comparing the efficacy of CaO-NPs and SiO_2-NPs, it is evident that both NPs offer distinct advantages depending on the application. CaO-NPs, with their potent ROS-mediated antibacterial action, are particularly effective against a broad spectrum of bacteria and hold potential for use in drug delivery systems and environmental applications. SiO_2-NPs, on the other hand, excel in medical and water treatment contexts due to their ability to be functionalized and combined with other antimicrobial agents, enhancing their effectiveness and versatility (Barma et al., 2020; Bhattacharjee et al., 2022).

NPs offer a promising alternative to traditional antibiotics for addressing multidrug resistance and biofilm formation in bacteria and infections. Zinc oxide NPs have shown strong antibacterial and antibiofilm activity against CRE and non-fermentative Gram-negative bacteria. Metal NPs, such as silver and selenium, have demonstrated efficacy against multidrug-resistant organisms like *Acinetobacter baumannii* and *K. pneumoniae*. NPs can also disrupt biofilm formation in *Pseudomonas aeruginosa*, enhancing their ability to treat chronic infections (Singh et al., 2022).

Despite the promising potential of CaO-NPs and SiO_2-NPs, several challenges remain that must be addressed to fully realize their applications in antibacterial treatments. The cytotoxicity of CaO-NPs, for instance, raises concerns about their safety for medical use, necessitating further research to optimize their synthesis and reduce potential side effects. Similarly, while SiO_2-NPs are generally regarded as biocompatible, their functionalization to achieve desired antibacterial properties must be carefully balanced to maintain mechanical integrity, particularly when used in composite materials (Metryka et al., 2021; Karaman et al., 2020).

CaO-NPs and SiO_2-NPs show promising future applications in infection control. They could be introduced into medical devices, wound dressings, and surface coatings to prevent bacterial growth and biofilm formation. These NPs may also enhance drug delivery and targeting bacterial infections more effectively. Their use in antimicrobial coatings for implants and catheters could reduce healthcare-associated infections, while integration into personal protective equipment (PPE) may provide additional protection against pathogens. Beyond healthcare, CaO-NPs and SiO_2-NPs could play a role in environmental applications, such as water treatment and air filtration, helping to combat waterborne diseases and improve indoor air quality. As research progresses, these NPs hold great potential for both public health and environmental sustainability (Kokkarachedu et al., 2024; Mondal et al., 2024).

Looking forward, the development of novel nano-antibacterial agents that combine the strengths of CaO-NPs and SiO_2-NPs, or integrate them with existing antibiotics, could offer new strategies for overcoming bacterial resistance and enhancing treatment efficacy. Continued multidisciplinary research will be crucial in overcoming the current limitations and optimizing the design, synthesis, and application of these NPs for a broad range of antibacterial and environmental applications (AlMatar et al., 2018; Bharti, 2024; Uddin et al., 2021).

Conclusion

This review highlights the potential of CaO-NPs and SiO_2-NPs as promising alternatives to conventional antibiotics. These NPs exhibit diverse mechanisms, including ROS generation and enhanced drug delivery, offering a multifaceted approach to infection control. Their potential applications extend beyond clinical settings, with significant potential in consumer products and environmental decontamination.

The next step in extending the antibacterial effects of NPs, particularly for clinical applications, involves addressing several key challenges, such as enhancing their efficacy, ensuring biocompatibility, and overcoming current limitations. Preclinical studies are essential to evaluate the biocompatibility, bioactivity, and immunological effects of NPs. Key assessments include their interactions with immune cells, cytotoxicity, cell viability, and the formation of hydroxyapatite layers in simulated body fluid, indicating bioactivity. Protein adsorption is also crucial for their interaction with biological systems. These studies provide critical insights to optimize the safety and effectiveness of NPs, laying the groundwork for their clinical applications.

CaO-NPs and SiO_2-NPs have shown potential in clinical infection control due to their antibacterial properties. Challenges include NP stability, biocompatibility, toxicity concerns, and optimizing delivery systems. Recent studies emphasize the effectiveness of CaO-NPs and SiO_2-NPs in water purification and medical device coatings, where they show strong antibacterial activity against both Gram-positive and Gram-negative bacteria. Integrating these NPs into existing antimicrobial strategies could improve infection prevention and treatment.

Additionally, the synergistic potential of CaO-NPs and SiO_2-NPs with antibiotics positions them as crucial tools in combating drug-resistant infections. Their ability to enhance the efficacy of current antimicrobial therapies underscores the need for ongoing research and development. By refining their use, these NPS could become vital components of advanced antimicrobial strategies, offering new hope in the battle against resistant pathogens. Furthermore, nanoparticle-antibiotic formulations have shown potential in improving drug delivery, overcoming antibiotic resistance, and reducing side effects. However, the transition from laboratory research to clinical application requires rigorous testing, including preclinical studies and multiple clinical trials. While some NP-antibiotic formulations are progressing through preclinical stages, there is limited information on their advancement to human clinical trials. Despite the complexities of drug development and regulatory approval processes, it is realistic that innovative NP-antibiotic formulations may enter clinical trials soon.

Authors' contributions

HA, MAA, and *LAY* collaboratively contributed to the conceptualization, design, and implementation of the systematic review described herein. All authors critically evaluated and refined the manuscript, providing intellectual contributions to ensure the coherence and integrity of the final review article. *HA* played a pivotal role in the initial conceptualization and design, including the selection of studies, refinement of inclusion and exclusion criteria, synthesis and interpretation of results, and Writing – Original Draft Preparation of the manuscript. *MAA* played the leadership role in executing the systematic review, encompassing the development of the review protocol, ensuring methodological rigor and relevance to the research question, overseeing the screening process, and contributing to manuscript drafting and review. *LAY* undertook the role of assessing study quality and risk of bias in the selected articles, resolving discrepancies, and ensuring the accuracy of the extracted data.

Compliance with ethics guidelines

This article is based on previously conducted studies. It does not contain any new studies with human participants or animals performed by any of the authors.

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Conflict of interest

The authors have no conflict of interest to declare and collectively affirm their commitment to the accuracy and reliability of the systematic review presented in this article.

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