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REVIEW

Nanomaterials for the Treatment of Contamination by Nosocomial Pathogens in Intensive Care Units

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Abstract: Healthcare systems worldwide face a significant challenge from nosocomial infections. These infections are associated with increased rates of disease, mortality, and healthcare expenses. Common issues with traditional treatment approaches include antibiotic resistance and inadequate pathogen targeting. Utilizing nanoparticles for the targeted administration of antimicrobial medications to infection areas has proven to enhance treatment outcomes while maintaining biocompatibility. Traditional diagnostic methods still rely on microbiological culture and susceptibility testing, while molecular technologies are seeing increased usage for rapid diagnosis. This review mainly aims to draw attention to the present state of nosocomial infections by outlining their prevalence and the ways in which nanotechnology is used to treat these illnesses. This study provides a thorough examination of the nanotherapeutic methods that have recently developed, with an emphasis on the clinical implications of different types of nanoparticles for the purpose of reducing the prevalence of nosocomial infectious diseases.

Keywords: intensive care units, nosocomial infections, nanomedicine, inorganic nanoparticles, organic nanoparticles

Introduction

Hospital-acquired infections (HAIs), also known as nosocomial infections, pose a formidable challenge in healthcare, particularly within intensive care units (ICUs). These infections, which patients contract during their hospital stay, typically appear after 48 hours of admission and are not present at the time of admission.[1] ICUs are especially prone to these infections due to the high concentration of severely ill patients and the frequent use of invasive procedures.[2] Globally, nosocomial infections impact millions of patients each year, leading to significant increases in morbidity, mortality, and healthcare costs.[3] The World Health Organization (WHO) reports that HAIs affect between 7–10% of hospitalized patients in developed countries and around 10–15% in developing countries.[4] The incidence is even higher in ICUs, with research showing that approximately 30% of ICU patients contract at least one HAI during their stay.[2] In the United States, the Centers for Disease Control and Prevention (CDC) estimates that on any given day, 1 in 31 hospital patients has at least one HAI, resulting in approximately 1.7 million infections and 99,000 related deaths annually.[5,6]

Common pathogens responsible for nosocomial infections in ICUs include *Staphylococcus aureus, P. aeruginosa, Escherichia coli*, and *Klebsiella pneumoniae*.[7] These organisms often resist multiple antibiotics, which complicates treatment and worsens patient outcomes.[8] Numerous factors can be related to contribute to the high rate of nosocomial infections in ICUs, including the severity of patients' underlying health conditions, extended hospital stays, and the use of invasive devices like central venous catheters, mechanical ventilators, and urinary catheters.[9] The frequent use of broad-spectrum antibiotics also plays a role. Pathogenic bacteria usually follow particular strategies in efflux the antibiotics or in developing into MDRs. The methods employed by MDR bacteria are represented in Figure 1. This includes increased efflux pumps, target modification, enzyme degradation, and plasmid-borne resistance genes. Structural barriers like the outer membrane and lipopolysaccharide layer, along with penicillin-binding protein (PBP) modification,

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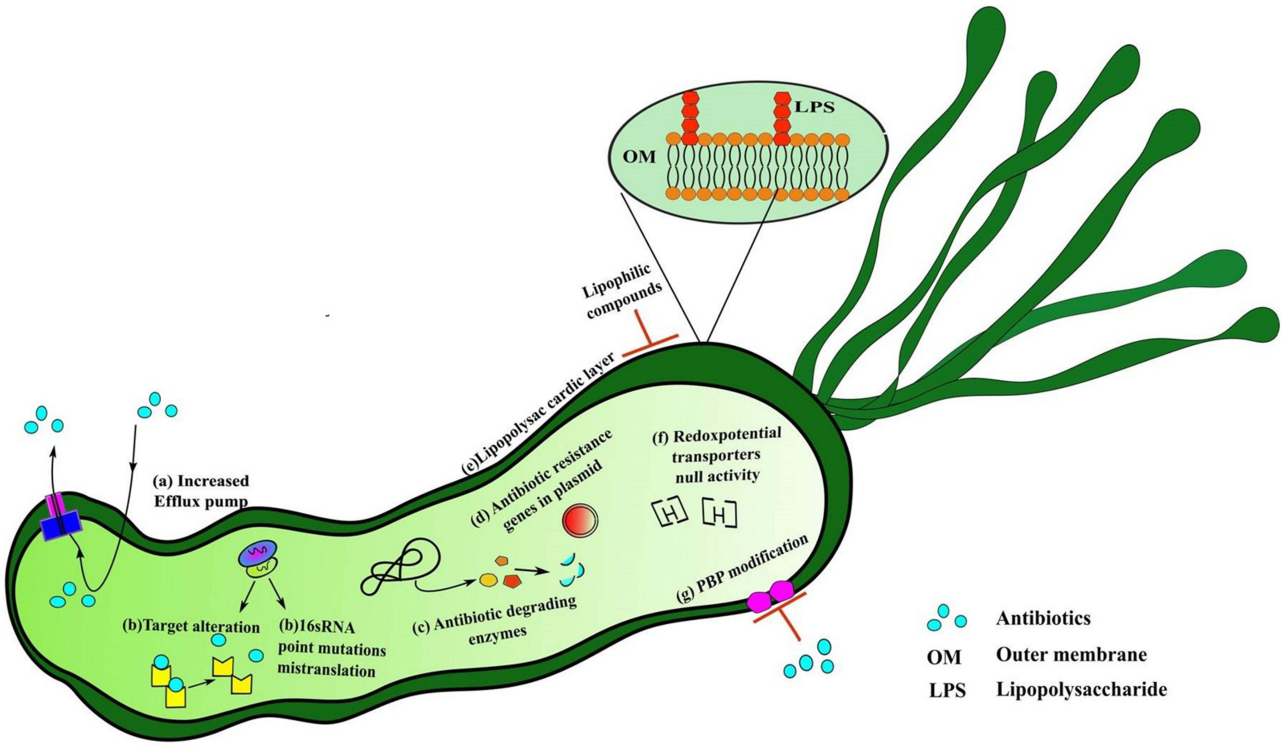

Figure 1 Multidrug resistance strategies in bacteria.

further prevent effective antibiotic action. The rise of multidrug-resistant organisms (MDROs) does add to the complexity, highlighting the need for stringent infection control measures and antimicrobial stewardship programs. Moreover, the adherence of ICU staff to infection control protocols is critical in mitigating or exacerbating the risk of HAIs.[10] A study was conducted to evaluate the incidence, risk factors, and outcomes of nosocomial infections in a combined medical and surgical ICU of a medical college hospital, involving 242 patients who had been admitted for more than 48 hours. Data collection primarily focused on the severity of illness, primary reasons for ICU admission, presence of risk factors, infections, infecting agents, length of ICU and hospital stays, and survival status. A logistic regression analysis of collected data revealed the rate of nosocomial infections was found to be 11.98% (with a 95% confidence interval of 7.89–16.07%). Pneumonia was the most common infection, accounting for 62.07% of cases, followed by urinary tract infections and bloodstream infections associated with central venous catheters. It was also reported that nosocomial infections led to a significant increase in the length of ICU and hospital stays, they did not result in a significant increase in mortality.[11]

The aim of the current review is to determine the use of nanotechnology and explore its efficacy in therapeutic management of ICU-based infections. Based on the literature that is currently accessible, this study is the first thorough comprehensive worldwide assessment that offers a conciseness of nanoparticles made specifically to fight infections that are acquired in intensive care units. In order to demonstrate nanotechnology's promise as a revolutionary solution to one of the most pressing problems in contemporary healthcare, this study will look at the field's recent developments, difficulties, and possibilities.

Risk Factors and Diagnosis of Nosocomial Infections in ICUs

The implications of nosocomial infections extend beyond individual patient health, impacting overall healthcare system efficiency and resource allocation. When look into the cause or root of Nosocomial infections (NIs) in intensive care units (ICUs), it is caused by a diverse array of pathogens. These microorganisms thrive in the hospital environment, where vulnerable patients and invasive procedures provide opportunities for infection. The pathogens responsible for NIs

in ICUs are often multidrug resistant that further complicate the treatment and developing and increasing the risk of adverse outcomes necessitating more efficient treatments. These include *Staphylococcus aureus* (*S. aureus), Pseudomonas aeruginosa* (*P. aeruginosa), Escherichia coli* (*E. coli), Klebsiella pneumonia* (*K. pneumonia), Acinetobacter baumannii* (A. baumannii), *Enterococcus species*. An overview on the most common pathogens, their risk factors and treatment options are elaborated below and listed in Table 1. *S. aureus* is a leading cause of nosocomial infections in ICUs. Methicillin-resistant *Staphylococcus aureus* (MRSA) is particularly concerning due to its resistance to many common antibiotics. MRSA is often associated with broad spectrum infections including bloodstream infections, pneumonia, surgical site infections, and soft-tissue infections, urinary tract infections (UTIs), infective endocarditis, osteomyelitis, septic arthritis. The high virulence of *S. aureus* and its ability to form biofilms on medical devices contribute to its persistence and difficulty in eradication.[12] Nosocomial staphylococci were previously unknown, but new information about their biology and transmission has emerged from genome research and molecular epidemiology.[13] It has been reported that catheterized patients are especially at risk for UTIs caused by S. aureus, which may progress to more serious conditions like bacteremia, where authors including, Muder have found that among 102 patients with

Table 1 List of Nosocomial Pathogens, Their Characteristics, Infections, Risk Factors, and Treatment Options

Pathogen	Characteristics	Types of Infection	Risk Factors	Treatment Options	Reference
Staphylococcus aureus	Gram-positive, biofilms	Bloodstream infections, Pneumonia, Surgical site infections, Soft tissue infections (UTIs), Infective endocarditis Osteomyelitis Septic arthritis Skin infections	Prolonged hospital stays Invasive procedures Immune compromised states Prior antibiotic use	Vancomycin, daptomycin, linezolid; Surgical debridement for abscesses, infected tissues; Device removal as needed	[15]
P. aeruginosa	Gram-negative, biofilms	Ventilator-associated pneumonia (VAP), UTIs, Bloodstream infections (BSIs), Skin and soft tissue infections, bone, joint, Central nervous system infections	Mechanical ventilation, Indwelling catheters Prolonged hospitalization, Immunocompromised states	Combination therapy Resistance-guided therapy	[16,17]
Escherichia coli	Gram-negative, facultative anaerobe	Catheter-associated UTIs Pneumonia Bloodstream infection, meningitis, Wound infections	Indwelling catheters Prolonged antibiotic immunocompromised states	Carbapenems, beta-lactam /beta-lactamase inhibitor combinations, Fluoroquinolone Removal of catheters or other devices	[18]
Klebsiella pneumonia	Gram-negative	Pneumonia Bloodstream infections, UTIs, Wound infections, Septicemia in premature babies	Mechanical ventilation, Indwelling catheters Antibiotic resistance Prolonged hospital stays	Carbapenems polymyxins, aminoglycosides Combination therapy for severe infections	[19]
Acinetobacter baumannii	Gram-negative, aerobic, highly resistant, survives in hospital environments	Nosocomial pneumonia, Bloodstream infections, Wound infections, Invasive procedures-related infections	Prolonged hospitalization ICU stay Mechanical ventilation Indwelling catheters	Carbapenems, sulbactam, tigecycline; combination therapy	[20]
Enterococcus species	Gram-positive, facultative anaerobe	UTIs Bloodstream infections, Wound infections, Endocarditis	Prolonged hospitalization Invasive procedures Prior antibiotic use	Linezolid, daptomycin, tigecycline; Combination therapy for VRE infections; Removal of invasive devices	[21]

Abbreviations: UTI, Urinary tract infection; BSI, Bloodstream infection; VAP, Ventilator-associated pneumonia; ICU, Intensive care unit; VRE, Vancomycin-resistant Enterococci; β-lactam, Beta-lactam antibiotics.

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S. aureus bacteriuria, 33% had UTI symptoms and 13% developed bacteremia, underscoring the potential for systemic spread.[14] The clinical presentation of *S. aureus* infections differs by site, however often includes fever and pain as common symptoms. When considering the risk factors, it includes prolonged hospitalization, invasive procedures such as catheterization, immunosuppression, and prior antibiotic use. Even-though, antibiotics like vancomycin, daptomycin, and linezolid are found to be effective, biofilm formation, and the emergence of methicillin-resistant strains are the reasons for treatment difficulties, that in turn arises for infection recurrence.[15]

P. aeruginosa is another prevalent pathogen in ICUs, known for its resistance to multiple classes of antibiotics and its ability to survive in harsh environments. This opportunistic gram-negative pathogen is commonly associated with ventilator and hospital-associated pneumonia, UTIs, and bloodstream infections. It is also associated with skin and tissue infections (including burn and wound) and also with infections at bone, joint, and central nervous system.[22] Patients requiring mechanical ventilation, those with indwelling catheters, prolonged hospital stays, or immune-compromised conditions are at particularly high risk for *P. aeruginosa* infections. These infections are often difficult to treat due to the organism's resistance to multiple antibiotic classes and its adaptive survival strategies in hostile environments. Henceforth, disease management typically involves combination antibiotic therapy and resistance-induced tailored treatment strategies.[16,17]

E. coli is a gram-negative facultative anaerobic bacterium that usually colonizes the gastrointestinal tract. These bacteria are frequently implicated in catheter-associated urinary tract infections (CAUTIs), Pneumonia in immunocompromised patients, meningitis in neonates and bloodstream infections, cholangitis from contaminated food.[23,24] The primary risk factors for *E. coli* infections include the use of indwelling catheters, prolonged antibiotic exposure, and immunocompromised conditions. Its pathogenicity is often enhanced by the formation of biofilms and the presence of virulence factors that aid in colonization and immune evasion. Treatment primarily involves antibiotics such as carbapenems, fluoroquinolones, and beta-lactam/beta-lactamase inhibitor combinations, with the choice guided by antimicrobial susceptibility patterns due to rising resistance rates.[18] *K. pneumoniae* is also often responsible for nosocomial infections like pneumonia in mechanically ventilated patients, bloodstream infections in diabetic patients, UTIs during catheterisation, Septicemia in premature babies, and wound infections.[25] Treatment options currently include antibiotics including carbapenems, polymyxins, and aminoglycosides and combination therapy is also practiced in severe infections.[19] A 5% of nosocomial pneumonia in ICU with a mortality rate of a minimum of 30% and a maximum of 70% is accounted with *A. baumannii* infections, a gram negative pathogen often encountered with an outbreak in ICU settings.[26,27] For this pathogen also, treatment include antibiotics like carbapenems, sulbactam, tigecycline and a combination therapy.[20] When looking into list of pathogens causing HAI Enterococcus species, particularly *Enterococcus faecalis* and *Enterococcus faecium*, are notable opportunistic pathogens.[28] Prolonged hospitalization, invasive procedures, prior antibiotic use have been reported as the risk factors which are always visible with their infection symptoms including UTIs, bloodstream infections, wound infections, and endocarditis. Currently Linezolid, daptomycin, tigecycline, combination therapy and removal of invasive devices are currently used as treatment options.[21] Nevertheless, Enterococci being the first Vancomycin-resistant pathogen pose a significant challenge due to their resistance to this critical antibiotic that acts against a wide range of gram-positive infections. This is often associated with higher mortality rates and limited therapeutic options. Their intrinsic resistance to many antibiotic families like (β-lactam agents and aminoglycosides) and their ability to acquire resistance genes make infections chronic to treat and control. Effective infection control measures and antibiotic stewardship are essential to managing the spread of Enterococcus in healthcare settings.[29]

Major infections caused by nosocomial pathogens and the treatment options to date are depicted in Figure 2. Prolonged hospital stays were associated with an increased risk of the most common infections, which included those of the bloodstream, pneumonia, wounds, and urinary tract. Extended days of 3–5 seem to reduce the bloodstream infection incidences. Nevertheless, medical device use (eg, catheters, mechanical ventilation, pleural drainage, and trauma involving open fractures) was identified as a risk factor for infection in a multiple regression study of various infection scenarios.[30] Infections at the site of invasive devices or surgical wounds, redness, swelling, pain, or discharge; fever, and an elevated white blood cell count are common signs of nosocomial infections. Systemic symptoms, such as tachycardia, hypotension, and altered mental status, can indicate a severe systemic infection, such as sepsis. At the onsite

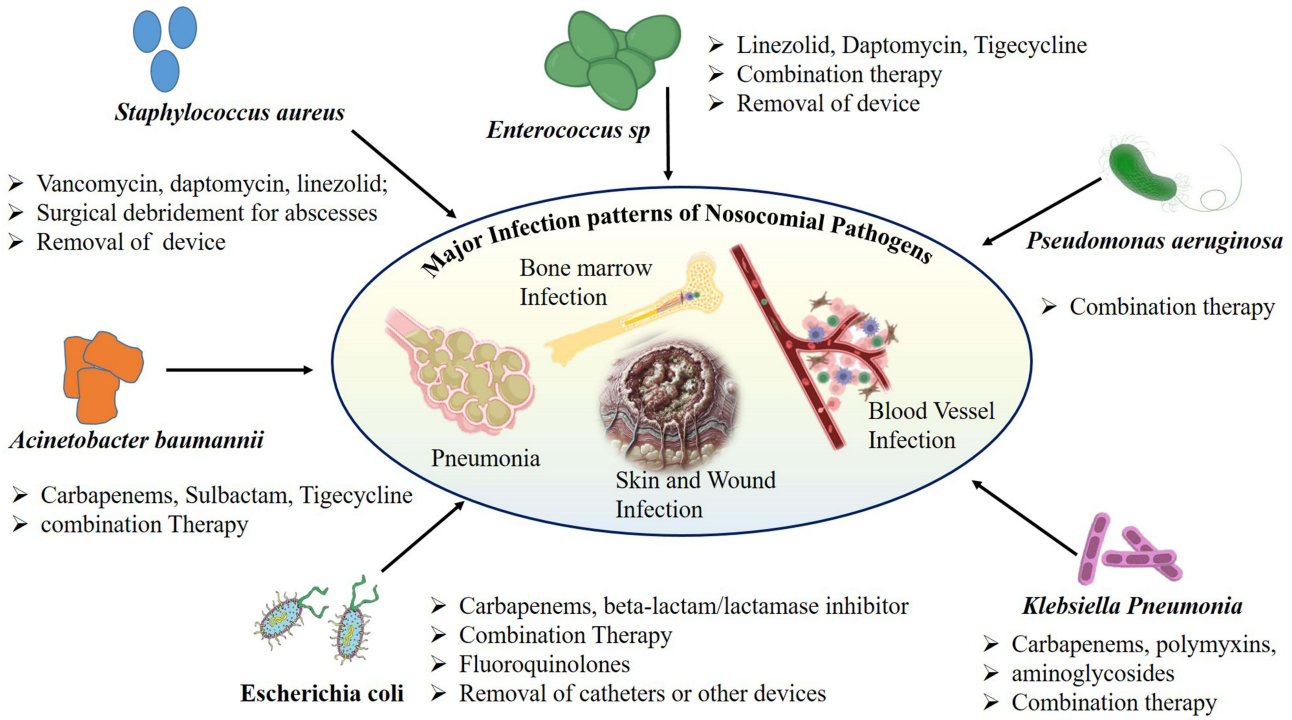

Figure 2 Various infections by Nosocomial pathogens and the treatments provided.

of symptoms, microbial culturing helps in identifying the pathogen or the infectious agent. Mostly samples like blood, urine, sputum, and tissue samples are collected from the patient.[31] Several biomarkers are also developed for the early identification of pathogens which include C-reactive protein and procalcitonin (PCT) lactate Biomarkers offer rapid, albeit indirect, evidence of infection and are useful for monitoring the effectiveness of treatment.[32] In addition to the following, a series of imaging techniques are also included in the diagnostic protocol which in turn helps in visualizing the extent and location of infections like X-rays; Computed Tomography (CT) Scans; Magnetic Resonance Imaging (MRI), and Ultrasound.[33]

Nanomaterials and the Control of Nosocomial Infections

Preventing and controlling nosocomial infections in ICUs is paramount to improve patient outcomes and reduce healthcare costs. Several strategies with proven effectiveness, including rigorous hand hygiene, the use of personal protective equipment (PPE), and the implementation of evidence-based guidelines for the care of invasive devices is of much critical. The typical systems also include ultraviolet (UV) light and hydrogen peroxide vapor systems that are increasingly used for terminal cleaning of ICU rooms, providing an additional layer of disinfection. Automated hand hygiene monitoring systems that can track compliance in real-time, providing feedback to healthcare workers and promoting adherence to hand hygiene protocols. Together with this, early detection of infection patterns and outbreaks is enabled by the use of data analytics and electronic health records (EHRs). Targeted therapies are facilitated by the use of predictive analytics to identify patients who are at high risk for HAIs. Furthermore, improvements in fast diagnostic testing make it easier to identify infections in a timely manner, which expedites and improves treatment.[34] However, the integration of nanotechnology into these strategies represents a transformative leap in infection control. Metal nanoparticles, such as silver, copper, and zinc, have been found to offer potent antibacterial properties that can significantly

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reduce microbial growth, biofilm formation, and colonization on hospital surfaces and medical equipment. Coating surfaces at hospitals and drugs with these nanomaterials addresses limitations of conventional methods, such as the risk of antibiotic resistance and also presents an enormous promise for reducing HAIs. Several studies have proved the potent antibacterial qualities of these materials in controlling or preventing microbial growth thereby addressing the drawbacks of conventional therapies.[35] The incorporation of nanoparticles, such silver, copper, or zinc, onto hospital surfaces or medical equipment might lessen the growth of biofilms and microbial colonization. To add, burgeoning sophisticated medicine delivery systems with target specificity are being made possible by nanotechnology. This in contrast to application or usage of antibiotics is of efficient as, the likelihood of antibiotic resistance is higher in conventional antibiotic treatment. Also, using tailored nanoparticles, adjoined with nanoparticles to carry the medication straight to the illness site have found to control the rise of MDR strains. Additionally, the employment of nanoscale diagnostic instruments providing faster identification is also not possible in providing better treatment while handling HAIs. The incorporation of nanotechnology into infection control strategies not only enhances the effectiveness of traditional approaches but also provides long-term solutions to safeguard against healthcare-associated infections (HAIs) and nosocomial infections, underscoring its indispensable role in modern ICU care.[36–38]

Application of Nanomedicine in Identification and Treatment of NIs in ICU

Over the past ten years, researchers have worked to find new methods for treating multi-drug-resistant (MDR) bacterial strains, especially in the post-antibiotic era. Nanotechnology has shown great potential as a key solution in this endeavor. Business Communications Company (BCC) Research estimated that the worldwide healthcare-acquired infection (HCAI) will grow from $18.9 billion in 2018 to $24.7 billion in 2023. To understand the global research trends in the application of nanoparticles for combating hospital-acquired infections (HAIs), we conducted a comprehensive bibliometric and statistical analysis of peer-reviewed scientific literature published between 2014 and 2024. To initiate it we used Databases from sources such as PubMed, and Google Scholar where, we queried using the keywords: “nanoparticles”, “nosocomial infections”, “hospital-acquired infections”, *clinical trials*, “MDR bacteria”, “antimicrobial nanomaterials”, and “nanotechnology in infection control”. Further, filters were applied like publication year, language (English), document type (original research, review articles), and relevance to HAIs. We initially retrieved approximately 16,000 articles from Google Scholar, which indexes a wide array of sources including research articles, reviews, theses, and industry repositories. To ensure quality and relevance, we cross-referenced these results with PubMed, which yielded 5624 articles focused generally on nanoparticles combating infections on peer-reviewed biomedical literature. After careful screening and cross-validation, we narrowed down the dataset to approximately 106 articles for our final analysis on nanoparticles on nosocomial infections.

Further, the 106 selected research articles were classified based on the type of nanoparticles studied inorganic and organic. We found that a total of 60 articles (approximately 56.6%) focused on inorganic nanoparticles, which included silver (15 articles; 14.2%), gold (13; 12.3%), copper (9; 8.5%), zinc oxide (17; 16.0%), and iron oxide (6; 5.7%). On the other hand, 46 articles (approximately 43.4%) addressed organic nanoparticles, with polymeric nanoparticles being the most represented (38 articles; 35.8%), followed by lipid-based nanoparticles (5; 4.7%) and dendrimers (3; 2.8%). Organic nanoparticles are often valued for their biocompatibility, biodegradability, and potential for targeted drug delivery. This distribution indicates a balanced research interest in both classes of nanoparticles, with slightly more emphasis on inorganic types due to their established antimicrobial efficacy against MDR pathogens. The statistical analysis of retrieved data is represented by using a pie chart Figure 3.

With their impressive ability to fight off microorganisms and multidrug-resistant (MDR) strains, nanomaterials show great potential as a solution for treating nosocomial infections. Numerous research studies have been published worldwide on the use of nanoparticles to combat hospital-acquired infections. One key mechanism involves the disruption of bacterial cell membranes, resulting in cell lysis and death. This effect is especially prominent with nanoparticles like silver, zinc oxide, and carbon nanotubes, as they penetrate and compromise the integrity of bacterial cell walls.[39] In addition, numerous nanomaterials can produce reactive oxygen species (ROS), leading to oxidative stress that harms essential cellular components such as DNA, proteins, and lipids. Quantum Dots (QDs), have a prominent place in this way of action. Owing to their tunable size and surface chemistry, they are able to generate specific light-activated redox

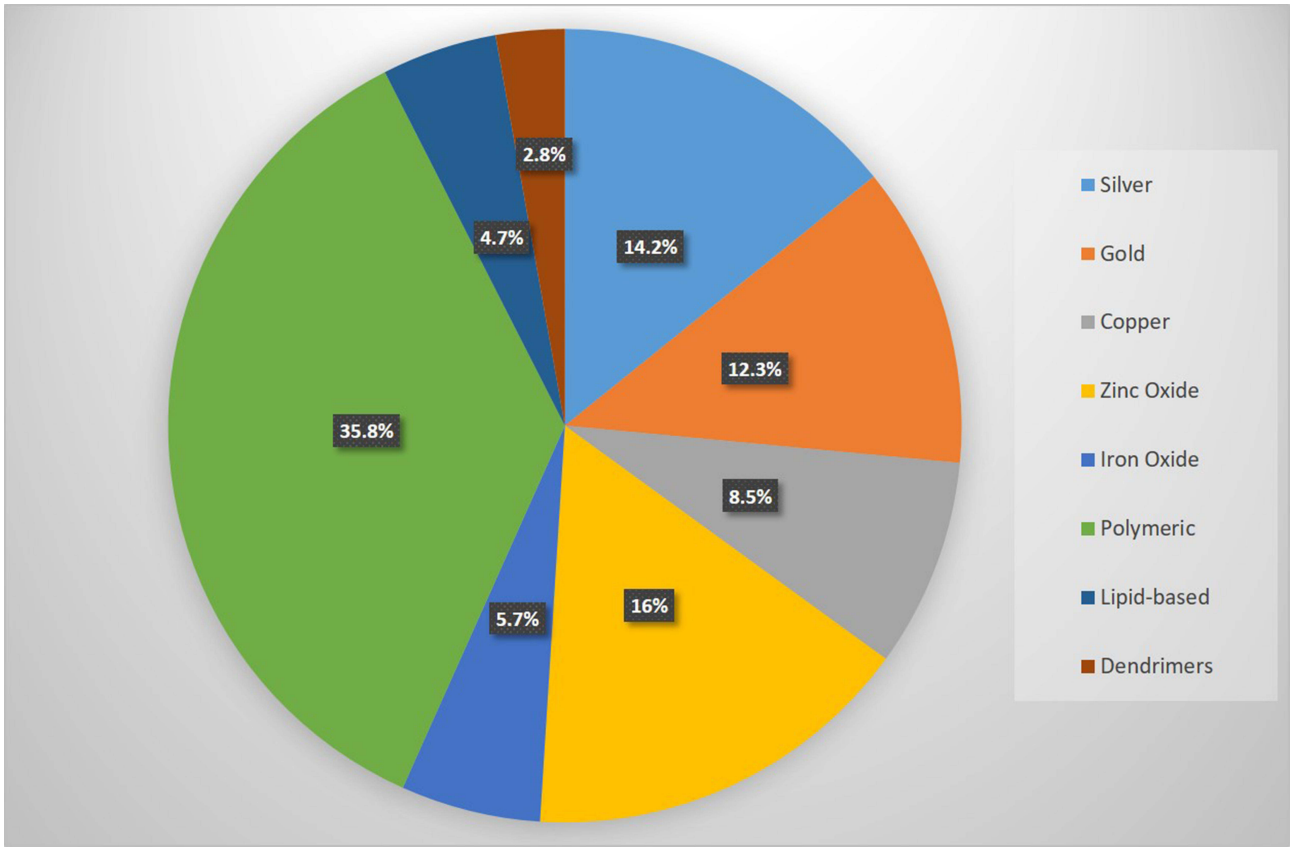

Figure 3 Percentage distribution of research articles by nanoparticle type (2014–2024) related to nosocomial infections.

species (LARS) at on exposure to light. Unlike traditional ROS mechanisms, QDs can interfere with redox balance in microbial cells, especially when engineered for size-dependent quantum confinement. Their relatively small size (2–4 nm) enables them to cross membranes, and they can be photoactivated to produce intracellular oxidative stress, making them promising tools in light-assisted antimicrobial therapy.[40] To add, certain nanomaterials can be modified with antibiotics or targeting molecules, which can improve drug delivery and help overcome bacterial resistance mechanisms: magnetic nanoparticles, like iron oxide, can disturb biofilms and bacterial structures by utilizing magnetic hyperthermia, providing an alternative and efficient method. Silica nanoparticles have demonstrated antimicrobial properties, primarily through surface functionalization, in which they can be loaded with antibiotics or metal ions (eg, silver or copper), where their porous structure allows controlled drug release. Additionally, their surface can be tailored for selective interaction with bacterial membranes, enabling both passive and active targeting which in-turn can enhance antibiotic stability and increase efficacy against resistant strains.[41] In addition, liposomes and dendrimers can encapsulate antibiotics, providing protection against enzymatic degradation and enabling precise delivery to the site of infection that in turn results in improved effectiveness of the antibiotics against multi-drug resistant bacteria.[42] These complex mechanisms demonstrate the immense potential of nanotechnology in tackling the formidable task of treating HAI, especially those caused by drug-resistant pathogens.[42] Early pathogen detection and treatment reduce nosocomial infection morbidity and death. The use of technology can prevent infections from progressing to more severe states like septicemia. It also helps hospitals establish infection control techniques to stop the spread. To prevent drug-resistant microorganisms and promote ethical antibiotic use, rapid diagnosis is essential.[43]

A study was conducted to explore the use of nanotechnology in developing a tool for early detection of pathogens. The researchers had used an ultrasensitive photonic biosensor based on a bimodal waveguide interferometer (BiMW) to quickly detect two common nosocomial bacteria: *P. aeruginosa* and Methicillin-Resistant *S. aureus* (MRSA). Using a PEGylated silane (silane-PEG-COOH), a bio-functionalization strategy was implemented to create a surface that repels

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bacteria, thus enabling specific bacterial detection. Two different biosensor assays were developed: one detecting *P. aeruginosa* using polyclonal antibodies in a direct immunoassay, and another for detecting MRSA by using aptamers that specifically target a penicillin-binding protein 2a (PBP2a). Immunoassay result were obtained in just 12 minutes and also result for the aptamer detection limit was 800 cfu/mL, showcasing its impressive speed and low detection range. This study highlights the capabilities of this biosensor as a flexible and precise tool for quickly identifying and measuring bacteria, fulfilling the necessary sensitivity criteria for diagnosing infections, as unlike traditional methods that require fluorescent or radioactive labels, this approach detects bacteria based on the physical change in the interference pattern caused by the binding of bacteria to the sensor surface. This allows for direct and real-time monitoring of bacterial presence without the need for additional labeling steps.[44] The combination of molecular beacons with gold nanoparticles has demonstrated great efficacy in both qualitative and quantitative detection of bacteria. A recent study has emphasized the creation of hybrid nanoprobes by including molecular beacon-modified gold nanoparticles which in turn showed a remarkable enhancement in the ability to detect Escherichia coli within 60min at a concentration of 100 cfu/mL. The hybrid nanoprobes possess the ability to accurately recognize synthetic DNA targets and efficiently detect them in clinical samples.[45] A recent investigation has documented the development of a nanostructured electrochemical immunosensor using zinc oxide (ZnO) as the main component. This immunosensor is capable of detecting *S. aureus*, a bacterium, in a qualitative and semi-quantitative manner. The sensor board is equipped with zinc oxide nanorods (ZnO NRs) that immobilize anti-*S. aureus* antibodies through the use of cystamine and glutaraldehyde. The immunosensor effectively identifies *S. aureus* with a low limit of detection (LoD) of around 792 CFU mL−1, allowing for the detection of *S. aureus* concentrations on human hand skin after washing.[46] Graphene is a preferred a nanomaterial due to its exceptional surface area and mechanical robustness, which are essential for the development of efficient antimicrobial coatings. The conductivity of this material enables its prospective integration into electrochemical applications. Additionally, its biocompatibility ensures safe usage in medical equipment, highlighting its versatility and efficiency in fighting microbial diseases.[47] A recent study was reported to specifically examine the process of developing and enhancing the antibacterial capabilities of coatings made from a combination of graphene, curcumin, and copper (GN@CR-Cu). The coatings were chemically synthesized by reducing Graphene oxide to graphene through either low-temperature heating or exposure to sunlight and then dispersed using X-ray photon scattering. The GN@CR-Cu coatings were found to exhibit significant antibacterial properties by contact-killing mechanism against *E. coli* and *P. aeruginosa* which was observed and confirmed through the zone inhibition method.[48] When it comes to infections caused by medical tools, nosocomial infections caused by catheter use are common. It was found that a tube wrapped in tungsten nanoparticles worked very well at killing *E. coli* and *S. aureus* in this way.[49] The general mechanisms by which various nanoparticles in combating the drug resistant bacteria are depicted in Figure 4. The antibacterial and anti-biofilm properties of the inorganic and organic nanoparticles on specific microbes and the mechanism of action are represented in Table 2. We have comprehended the nanoparticles on the basis of their types and their role in controlling nosocomial infections. On that criteria nanoparticles fall into two main categories: Inorganic and Organic nanoparticles. Inorganic nanoparticles, such as metal-based nanoparticles (eg, silver, gold, and copper nanoparticles), exhibit unique physicochemical properties, including antimicrobial activity, photocatalytic efficiency, and biocompatibility.[50] These nanoparticles are of high use in biotechnology, medicine, and environmental applications because of the ways in which they interact with biological systems, including the generation of reactive oxygen species (ROS), membrane rupture, and cellular interference. Whilst the latter, including lipid-based nanoparticles and polysaccharides, provides advantages such as targeted drug delivery, enhanced biocompatibility, and a regulated drug release. Their phospholipid and cholesterol core structures are found to enhance stability and bioavailability. The understanding on their classification is in-turn necessary for effective therapeutic approaches.[51]

Inorganic Nanoparticles

Nanoparticles are suitable for a range of biomedical applications due to their attractive features, which include biocompatibility, size adjustability, and special physicochemical, magnetic, and optical capabilities. In that category Inorganic nanoparticles are found to be non-toxic, hydrophilic, biocompatible, and very stable, making them versatile platforms for a wide range of delivery applications. There is a wide variety of inorganic nanoparticles in use. We have

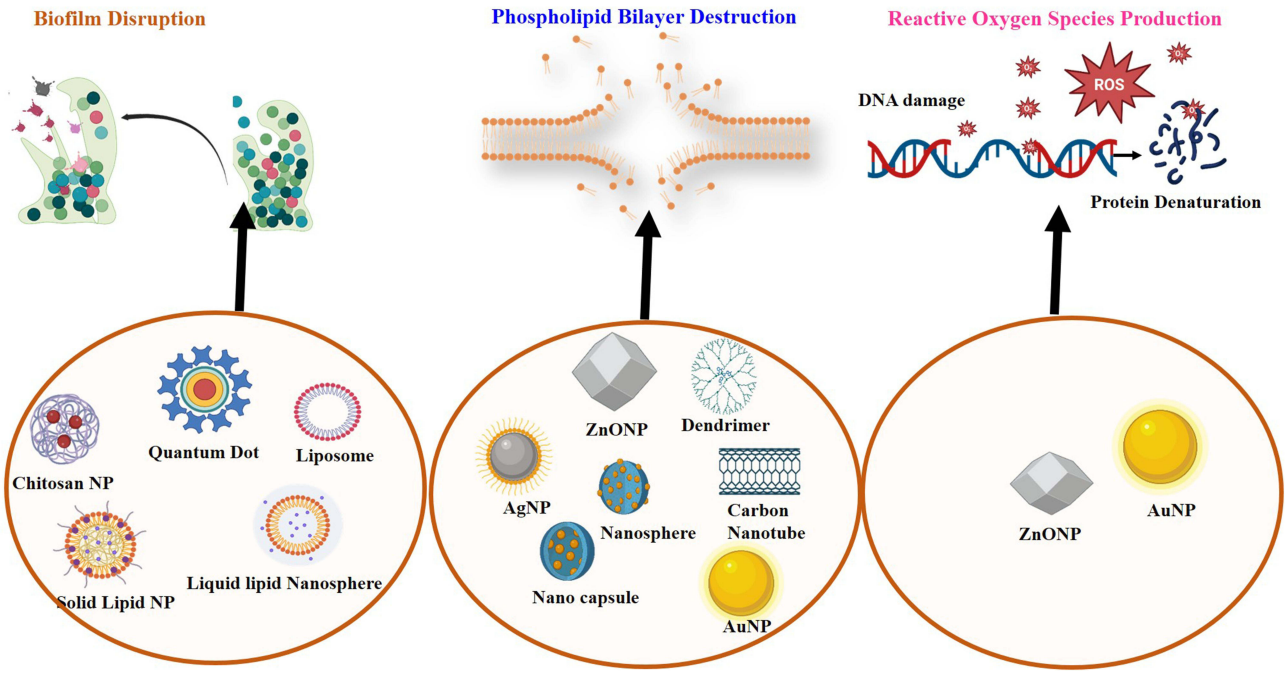

Figure 4 Range of nanoparticles and their mode of function in combating bacteria.

concentrated on inorganic nanoparticles, such as copper, silver, and gold, that are utilized to treat nosocomial infections for this review.[57,58] Metal-based NPs, such as silver (AgNPs), gold (AuNPs), and copper (CuNPs), exhibit potent bactericidal effects predominantly by generating reactive oxygen species (ROS), disrupting bacterial cell membranes, and interfering with vital cellular processes.

Table 2 List of Nanoparticles on the Basis of Their Organic and Inorganic Properties for Antibacterial and Anti-Biofilm Properties on Specific Microbes and the Mechanism of Action

Nanomaterial	Target	Mechanism of Function	Organic/ Inorganic	Specific Organism Targeted	Reference
Silver Nanoparticles	Bacterial cell	Disrupts bacterial cell membranes, inhibits DNA replication, and generates reactive oxygen species (ROS)	Inorganic	*P. aeruginosa, S. aureus, E. coli*	[52]
Gold Nanoparticles	Bacterial cells	Photothermal effects	Inorganic	*S. aureus, E. coli E. faecalis*	[53]
Iron Oxide Nanoparticles	Bacterial biofilms	Disruption of biofilms through magnetic hyperthermia	Inorganic	*S. aureus, P. aeruginosa K. pneumonia*	[54]
Chitosan Nanoparticles	Bacterial cells	Cell membrane disruption Inherent antimicrobial properties	Organic	*E. coli, S. aureus, L. monocytogenes*	[55]
Carbon Nanotubes	Bacterial cells and biofilms	Disrupts cellular structures	Inorganic	*E. coli, B. subtilis, P. aeruginosa*	[39]
Liposomes	Drug-resistant bacteria	Encapsulates antibiotics to enhance delivery and penetration, reduces drug degradation, and targets bacterial cells	Organic	*Methicillin-resistant Staphylococcus aureus (MRSA), P. aeruginosa, A. baumannii*	[42]

(*Continued*)

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Table 2 (Continued).

Nanomaterial	Target	Mechanism of Function	Organic/ Inorganic	Specific Organism Targeted	Reference
Dendrimers	Bacterial cell	Disrupts cell membranes	Organic	*E.coli, S. aureus, K. pneumonia*	[56]
Silica Nanoparticles	Bacterial cells and biofilms	Disrupts cell membranes	Inorganic	*P. aeruginosa, E. coli, S. epidermidis*	[41]
Quantum Dots	Bacterial cells	Functionalized with antibiotics. Photothermal killing of bacteria	Inorganic	*E. coli, S. aureus, S. typhimurium*	[40]

Abbreviations: ROS, Reactive oxygen species; MRSA, Methicillin-resistant *Staphylococcus aureus*.

Silver Nanoparticles (AgNPs)

AgNPs (size<100 nm) have gained popularity as therapeutic agents against microbial pathogens including bacteria and fungus due to their low environmental toxicity, high surface area-to-volume ratio, and ability to hinder biofilm formation.[59,60] AgNPs have been found to fight nosocomial infections as antibacterial agents by penetrating bacterial cell walls, forming ionic bonds with silver ions, and generating free radicals to destroy them.[52,61] A recent study carried out at Punjab-Pakistan, tertiary care hospital explores the efficiency of silver nanoparticles in combating the worrisome prevalence of carbapenem-resistant strains of MDR *P. aeruginosa*. Kirby-Bauer disc technique and PCR were employed to find high carbapenemase production and resistance genes including blaIMP-1, blaSHV, blaVIM, blaOXA, and blaTEM of the collected samples. AgNPs (5–30 nm) were synthesized utilizing *Aspergillus flavus* culture filtrate. It was found that AgNPs inhibitory zones when coupled with antibiotics like Piperacillin/tazobactam, boost the antibacterial action rather than when antibiotics were given alone.[62] Millions of people are affected annually by biofilm-based overall infections, which are major causes of morbidity and typically result in chronic nosocomial infections. When compared with free-floating bacteria, biofilm made is resistant to extreme environmental conditions, pH, and the Immune system of the host.[63] Current therapeutic practice for biofilm-associated contamination involves treating it with high-dose antibiotics and surgeries at times when necessary to minimize additional harm to the patient's health. Exopolymeric substances (EPS) in biofilms are reported to consist of polysaccharides, peptides, and nucleic acids which in-turn function as ionic resin, inhibiting the penetration of drugs like antibiotics and metal ions into biofilms and reach them. However, the antibacterial activity of (AgNPs) against the biofilm formation by nosocomial pathogen is of great interest now. A study recently reported a combined therapy and exposure of nanoparticle and antibiotic is more efficient in preventing the biofilm formation in *A. baumanii*. Their reports indicate that AgNps inhibits the bacterium at 16 μg/mL. Which is significantly lower than the MICs (1–4096 μg/mL) for traditional antibiotics, suggesting a greater potency. A synergistic interaction was found with doxycycline, tetracycline, and erythromycin. It has been reported that the nanoparticles showed significant biofilm disruption interest at minimal inhibitory attention of 2 mg/mL. Intracellular oxidative strain and thiol-group interactions and thereby affecting bacterial proteins are considered as the effective mechanism of AGNPs against the growth of bacteria.[63] Another work is fascinating where they have conducted an amalgamation and characterization of AgNPs using *A. calcoaceticus* which was successful in synthesizing extracellular silver nanoparticles through protein-mediated methods excluding nitrate reductase. The study reports that the synthesized AgNPs were able to infiltrate the inner layers of the biofilm without being absorbed by the extracellular polymeric substances (EPS), leading to the eradication of up to 98% of harmful bacteria including gram-negative and gram-positive biofilms within 24 hrs. Further, a green synthesis study analysis the spectrum of antibacterial activity of AgNPs produced from a range of plants including *Lagerstroemia indica* (*L. indica), Alstonia scholaris* and *Aglaonema multifolium* and found that among these AgNPs synthesized using *L. indica* seems to produce the highest Minimum Inhibitory Concentration (MIC) against the gram-positive and gram-negative test strains.[64] Very recently, a study was conducted on the production and efficacy assessment of green AgNPs from *Hibiscus sabdariff* measuring 58.682 nm. These AgNPs were further used in combination with the fosfomycin antibiotic to assess antimicrobial activity and synergistic patterns against a range of organisms including *Enterobacter cloacae, MRSA, K. pneumoniae*, and *E. coli* strains. The remarkable synergy observed

between AgNPs and fosfomycin underscores the potential of this combination in creating highly effective antibacterial agents to combat a range of nosocomial pathogens.[65] Various AgNP based formulations have shown promising antimicrobial properties, each with distinct advantages and limitations. After reviewing them, we were able to conclude that Hibiscus sabdariffa-synthesized AgNPs combined with fosfomycin were able to have broad-spectrum synergy against MRSA and MDR organisms. While further investigation into biofilm activity and expanded drug combinations is needed, this formulation demonstrates a strong therapeutic potential due to its biogenic origin, safety profile, and enhanced antimicrobial efficacy through combination therapy.

Gold Nanoparticles (AuNPs)

When it comes to combating germs that are resistant to many drugs, AuNPs are among the most promising metal nanoparticle choices because of their adaptable action mechanisms and possible crucial characteristics. By having the ability to synthesize them in different sizes, AuNPs provide exact manipulation of their effectiveness and characteristics. Additionally, the ability to easily modify the surface of nanoparticles to incorporate compounds such as antibiotics and extracellular or intracellular proteins due to their negative charge, as well as their biocompatibility with other metals and photothermal capabilities for heat absorption and bacteria eradication, further enhances their potential as powerful nanoparticles.[53] Especially in the photothermal bactericidal treatment, nanorod clusters and nanostars have gained much attention by disrupting biofilm and generating hypothermia to bactericidal activities.[66] Metal precursors, reducing agents, and stabilizers are the usual ingredients in the non-biological synthesis method otherwise chemical synthesis, the process most which is often used to create AuNPs. On the other hand, green synthesis, is an yet another biological method that includes extracts from bacteria, fungi, intracellular or extracellular protein, or plant extract for synthesizing AuNPs.[67,68] As the antibacterial activity of nanoparticles (NPs) is size-dependent by adjusting the substances and amounts, the production of gold nanoparticles in spherical, rod, star, and nano-capsule forms has been achievable over the last couple of years.[69] While combating the pathogen AuNPs create massive, impermanent holes as they pass through the membrane of a bacterial cell. However, when considering larger NPs between a range of 80–100 nm they have a harder time passing through bacterial cell membranes. However, a study has uncovered the mechano-bactericidal mechanism of non-translocating larger NPs, in which the results indicated that the stress in bacterial cell membranes is amplified by NP adsorption, leading to mechanical deformation, cell rupture, and eventually to cell death.[70] The high concentration of AuNPs in producing inhibitory concentration when compared to AuNPs were concerned; however, the employment of nanostars and nanorods exhibited considerable inhibition at high concentration, and also the biocompatibility was high when tested on human dermal fibroblast. Which again highlights the AuNPs characteristic efficacy in combating microbes and being compatible to oral consumption.[71] In a recent study, the effectiveness of berberine-conjugated AuNPs against methicillin-resistant *S. aureus* (MRSA) was investigated. The results showed that berberine-AuNPs were effective in eliminating MRSA by causing biofilm breakdown and cell membrane disruption. When tested on in-vivo fibroblasts in mice, the study likewise showed that all cells were viable.[72] Among the strategies compared, berberine-conjugated gold nanoparticles (AuNPs) show the most therapeutic promise, particularly for combating MRSA through combined anti-biofilm and membrane-targeted mechanisms. The in vivo efficacy, biocompatibility, and synergistic performances position them as a leading nanomaterial-based approach though further studies are needed to extend their application towards a wider range of pathogens.

Copper Nanoparticles (CuNPs)

Copper's remarkable antibacterial characteristics have long made it a popular choice for a variety of medical applications, including the treatment of wounds, sterilization of water, and the preparation of food due to their proven efficacy in contact killing.[73] In this view a study was conducted to test the antimicrobial efficacy of copper (Cu) and its alloys against various clinical isolates and reported the significant inhibition of pathogens like *MRSA, K. pneumoniae, P. aeruginosa, A. baumannii, C. albicans*, and *M. tuberculosis* at room temperature with stainless steel and PVC as controls.[74] Modern medicine uses copper's biocompatibility, antimicrobial capabilities, and malleability in medical devices, surfaces, and coatings to bring infection rates down and hygiene standards up.[75] Contact killing by copper is not a novel idea, however its use in medicine was widespread in 19th century and the advent of antibiotics subtle it later.

However, the raise of MDR necessitated different and distinctive approach to combat it. There copper again came into action. Copper being reactive, it has found to interrupt bacterial membrane and induce oxidative stresses by producing a localized release of copper ion when comes in contact with the microorganisms, leading to its death. Therefore, self-sanitizing property of copper is being envisioned to provide antimicrobial activities on contact surfaces of hospitals including door handles, touch plates, bed rails, call buttons, toilet seat and devices like intra uterine devices, and medical implants.[75] Invention of gallium-copper alloy infused antimicrobial fabric of personal protective equipment of health care workers was also a break through during COVID fight.[76] Further, CuNPs are also photocatalytic, extremely stable, and generate a large surface area, nevertheless, they are cost-effective when compared with AuNPs and AgNPs.[77] As many enzymes in microbes are copper-based, antimicrobial effects against microbial infections need a high Cu++ concentration. When given in large doses, Cu++ ions are found to generate ROS that bind with DNA and intercalate nucleic acid strands and are also found to affect amino acid synthesis in several bacteria emphasizing its efficacy in antimicrobial function by producing irreversible damages.[78] Redox synthesis commonly referred to as wet chemical synthesis is a commonly employed method for synthesis of CuNPs. Copper Sulfate, Copper Acetate, Copper chloride, and Copper Nitrate are commonly employed precursors, and Vitamin-C, polyols like Ethylene glycol are used as reducing agents for the wet chemical synthesis of CuNPs.[79,80] However, green synthesis of CuNPs combined with plant extract cell cultures of bacteria, and fungi is most acceptable as it is ecologically safe and also economically stable Even though, the methodology includes several limiting factors like temperature, pH, time, volume of reagents, and biological extract green synthesis acts as the superior method in efficient production of CuNPs.[81] Various CuNPs conjugated with plant extracts, such as *Hagenia abyssinica, Citrus medica*, and *Syzygium guineense*, have demonstrated excellent antimicrobial activity against a range of gram-positive and gram-negative bacteria, confirming the efficacy of biogenic production.[82–84] In addition to traditional methods, a contemporary approach involves using microwaves to ionize copper ions and synthesize noble metal nanoparticles (NPs) such as gold (Au), silver (Ag), palladium (Pd), and platinum (Pt). These nanoparticles are then combined with Cu_2O hetero-structures, which exhibit antimicrobial activity against a range of nosocomial pathogens.[85] So when comparing the strategies of Cu based NPs in combating infectious pathogens, the microwave-assisted synthesis of Cu_2O–noble metal hetero-structures offers the most advanced and effective solution for killing nosocomial drug-resistant pathogens. With rapid production, enhanced antimicrobial activity, and strong potential for clinical application on hospital surfaces and equipment, this method surpasses other methods in potency, as well as in its scalability and cost.

Iron Oxide Nanoparticles (IONPs)

Iron oxide nanoparticles (IONPs), major forms of IONPs include magnetite (Fe_3O_4) and its oxidized forms, maghemite (γ-Fe_2O_3) and hematite (α-Fe_2O_3)[54] categorized as one of the notable inorganic nanomaterials, have demonstrated potent anti-biofilms on bacteria, especially those formed by pathogens like *Staphylococcus aureus, P. aeruginosa*, and *Klebsiella pneumoniae*. Their effectiveness is reported to lie in their ability to generate localized heat under an alternating magnetic field, a technique known as magnetic hyperthermia—which in-turn disrupts the structural integrity of biofilms and enhances antibiotic penetration. It is further considered as a non-invasive strategy against MDR bacteria.[86,87] In a recent study, researchers have evaluated the antibacterial effect of iron-oxide nanoparticles (IONPs) against *P. aeruginosa*, a pathogen known for its biofilm-forming ability and antibiotic resistance. They synthesized different formulations of IONPs: uncoated, alginate-coated, and alginate-coated IONPs conjugated with the antibiotic tobramycin. These nanoparticles were tested on both young (3-day-old) and mature (60-day-old) *P. aeruginosa* biofilms. Results showed that alginate-coated IONPs and their drug conjugates significantly inhibited bacterial growth and biofilm formation. Importantly, this inhibition remained effective even as biofilms aged, unlike tobramycin alone, whose effectiveness found to be decreased over time. Authors hypothesize that magnetic field application further enhanced nanoparticle diffusion through mucus-like barriers since they have the ability to be guided to a selected location by an external magnetic field supporting their potential for treating chronic infections such as those found in cystic fibrosis patients.[88] A recent study was conducted with the goal of identifying a suitable formulation that could be used as a disinfectant against MDRs in hospital associated cases, especially Staphylococcus, *E.coli* and SARS-CoV-2. This was achieved by comparing cytotoxicity and biocompatibility of green-synthesized and chemically synthesized IONPs in disrupting the

microbial antioxidant defense system. Their result interestingly showed that chemically synthesized IONPs are much more effective than Green Synthesis IONPs and also their results were supported with in-vitro and in-vivo studies.[89] Further, a structurally optimized nanocomposite that merges iron oxide with mesoporous carbon, showing strong and consistent antibacterial effects across multiple bacterial strains was developed by Snehaet al, in 2024. They had used a co-precipitation method to synthesize iron oxide and mesoporous carbon–iron oxide nanostructures, where surface morphology of these nanostructures was designed to resemble grain-like textures, that could promote an enhanced interaction with bacteria. The embedded mesoporous carbon within the iron oxide matrix was reported to increase surface consistency, thereby improving bacterial contact and a broad spectrum antibacterial efficacy of iron oxide. Among the methods listed below in synthesizing IONPs, we could suggest that iron oxide–mesoporous carbon nanocomposite developed by Sneha et al is effective when compared to others. It has shown a strong and broad-spectrum antibacterial activity across multiple strains due to its optimized grain-like surface and enhanced bacterial contact. We could suggest that, it outperformed both drug-conjugated alginate-coated IONPs and chemically synthesized IONPs in disrupting biofilms and maintaining consistency. Its synthesis via co-precipitation and improved surface morphology make it highly suitable for advanced antibacterial applications.

Organic Nanoparticles (Organic NPs)

Organic-based nanoparticles, made from polysaccharides, lipids, and other organic materials, are widely used to improve the physical and chemical consistency of loaded drug molecules due to their high surface chemistry, biocompatibility, and targeted therapy versatility.[90] These nanoparticles have been shown to be promising against the inhibition of several microbial pathogens including bacteria, fungi, and viruses.[91,92]

Lipid-Based Nanoparticles

Lipid-based nanoparticles primarily include lipid molecules like fats and oils as their building block, which in turn include phospholipids, which form the structural foundation of the nanoparticle. Furthermore, cholesterol is often incorporated to stabilize the lipid bilayer and modulate its fluidity. These lipid structures can be again classified into solid and liquid lipid NPs based on their core materials. In Solid lipid NPs, the core is composed of solid lipids, where the core includes, triglycerides, fatty acids, or waxes that can encapsulate hydrophobic drugs. Similarly, the liquid lipid NPs core contains the formulation of solid and liquid lipid structures to facilitate drug loading and stability. These cores are maintained to encapsulate the hydrophobic and hydrophilic drug molecules. Production protocol is also built up by adding additives, surfactants, and stabilizers for a controlled and stable drug release. In this aspect, lipid-coated hybrid nanoparticles (LCHNPs) were produced by an emulsification method with a poly (lactic-co-glycolic acid) (PLGA) core and a dioleoyl-3-trimethylammonium propane (DOTAP) lipid shell, loaded with the antibiotic hydrophilic vancomycin. This hybrid LCHNPs were found to exhibit superior antibacterial and anti-biofilm efficacy when studied against an MRSA strain biofilm compared to free vancomycin and vancomycin-loaded PLGA nanoparticles. The study included an optimization study for the formulation of LCHNPs. They found that LCHNPs in the formulation of 45:20 of PLGA and DOTAP were efficient in delivering the maximum antibiotic without degradation and also with lesser wastage of drug during fabrication.[93] Utilization of lipid NPs through photodynamic therapy is emerging nowadays. In a recent study, liquid crystal lipid NPs were coupled with a gallium photosensitizer to produce an efficient biofilm disrupter and reach microbes and combat them through ROS production. The study was conducted against several MRSA strains and found to be efficient in developing a great inhibition and also the biocompatibility of the NP was tested on fibroblast cells.[94] Based on the discussed methodologies of lipid-based nanoparticles, LCHNPs comprising a PLGA core and DOTAP lipid shell demonstrated the highest antibacterial and antibiofilm efficacy, particularly against MRSA biofilms. Compared to free vancomycin and vancomycin-loaded PLGA alone, this hybrid system showed enhanced drug delivery efficiency, minimal degradation, and reduced drug loss during fabrication. The optimized ratio of PLGA to DOTAP further ensured a stable formulation with superior therapeutic outcomes, making it the most promising candidate among the lipid NP strategies we evaluated over here.

Polymeric Nanoparticles

Polymeric materials are used to encapsulate, entrap, dissolve, or absorb drugs or other active compounds, thereby masking their physicochemical properties and improving penetration, especially for targeted therapies. These polymeric nanoparticles, with a diameter below 1μm, are classified as nano-capsules or nano-spheres based on their composition. As in the way oil in nano-capsules creates a vesicular structure produced by interfacial polymerization, and the presence of polymeric chains in nano-spheres.[95] There are numerous methods for producing polymeric nanoparticles, including in situ polymerization or precipitation of pre-formed polymers. The interfacial polymerization of alkyl cyanoacrylates in emulsion results in nano-spheres and nano-capsules with the addition of an organic solvent and oil. Solvent extraction, which involves high-speed homogenizing the oil/water emulsion, like adding water, and evaporating the solvent, is also widely employed to generate polymeric nanoparticles.[96] Numerous studies have been reported emphasizing the efficacy of polymeric nanoparticle for the treatment of infectious pathogens. A study reported the production and assessment of hollow, calcined titanium dioxide nano-spheres ($CSTiO_2$) with a radius of approximately 345 nm and a shell thickness of 17 nm that has an electrospinning and atomic layer deposition (ALD) for the first time to combat MDR strains of *Escherichia coli* and *Staphylococcus aureus* strains. They produced calcined spherical particles with a double coating of alumina and titanium oxide, initially electrosprayed with poly(vinyl pyrrolidone) (PVP).[97] A selective biodegradable nano-sphere against *E. coli*, with an average diameter of 31 ± 6.3 nm and a zeta potential of −25.2 mV ± 1.75 mV was reported by Partho et al, in 2020. They made porous carbon nano-spheres from agro-waste garlic peels using a scalable pyrolysis method and found that these particles combat bacteria by causing membrane deformity on nano-carbon interaction. The nano-spheres developed were mesoporous, with a mean pore diameter of 15.2 nm and a total pore volume of 0.032 cm^3/g, which in turn reflects the physicochemical property needed for effective penetration of drug.[98] Another recent study has reported on a biodegradable nano-capsule development. In it, a chitosan-based nano-capsule associated with potential phytochemicals from plant-like flavonoids, quercetin and baicalein were produced and tested in vitro on the view of developing a biodegradable and biocompatible targeting agent and tested against the biofilm formation by *E. coli*. The nano-capsules were reported to provide a stable release of the flavonoids within the first 5 hours. It can be hypothesized that the indirect action of chitosan might have facilitated the effect. As chitosan and chitosan derivatives have been reported to eradicate microbes by neutralizing the negatively charged components on cell surface membrane like teichoic acids and lipopolysaccharides and there by disrupting the stability of the microbial cell membrane and electrostatic interactions that protect the cell finally leading to cell damage and death.[55]

Further, In-vitro toxicity analysis of these the encapsulated flavonoids exhibited less cytotoxicity in mammalian cells compared to their free forms, demonstrating the biocompatibility also.[99] When evaluating polymeric nanoparticles for antimicrobial therapy, we would suggest that chitosan-based systems emerge as highly promising candidates. Their natural origin, biocompatibility, and inherent antimicrobial action combined with efficient drug delivery capabilities make them a versatile and safe platform for treating drug-resistant infections and biofilms.

Dendrimers

Dendrimers are another polymeric molecule that comes under organic NPs that always stand out due to their regulated production and mono-dispersity. Flexibility during customization in size and shape during manufacturing enables the attachment of drugs, antibodies, or imaging probes to the targeted sites. Also, the lipophilic skeletons allow them to cross the cell membranes effectively. This encapsulation capability directs medications to target tissues, thereby reducing toxicity and simplifying administration. These polymeric molecules also exhibit unique intrinsic viscosity and glass transition temperature behaviors due to the lack of entanglement at higher molecular weights, which further improves their efficacy in targeted therapy.[100] Cytoplasm leakage created through electrostatic interactions in the cases of cationic and amphiphilic dendrimer NPs is their profound mechanism in combating live cells.[56] Even though these dendrimers are emerging as a prominent way to deliver drugs for antibacterial treatment even though their mechanism is unspecific in obstructing drug resistance in pathogens, as they are also found to target mammalian cell membrane also.[101] In this aspect, nitric oxide (NO)-releasing PPI dendrimers have been developed by combining NO's antibacterial properties with cationic dendrimers to reduce required concentrations and enhance biocompatibility. These hybrid NPs are found to be efficient against both gram-positive and gram-negative bacteria, including MRSA, while minimizing fibroblast

toxicity.[102] So while general dendrimers have the potential, NO-releasing PPI dendrimers outperform due to greater specificity, lower toxicity, and enhanced efficacy. It is clearly visible from the study that antimicrobial effects of nitric oxide together with the structural advantages of dendrimers, could effectively target both gram-positive and gram-negative drug-resistant strains, while minimizing toxicity to host cells. Although dendrimer NPs have been shown to be effective against microorganisms, research on this topic is restricted due to the limited specificity and has to be expanded.

Conclusions

In conclusion, by providing novel solutions that overcome the drawbacks of traditional treatments, nanoparticles like inorganic and organic types present a prominent approach towards the fight against nosocomial infections. Based on our analysis of 106 peer-reviewed articles, inorganic nanoparticles were more prominently studied (56.6%) than organic ones (43.4%) in the context of nosocomial infection control. Silver and zinc oxide were the most researched inorganic types, while polymeric nanoparticles led among organic systems. This indicates a slightly stronger research focus on the direct antimicrobial potential of inorganic nanoparticles, alongside a growing interest in biocompatible, targeted delivery platforms. Several reviewed works have shown through the processes like production of reactive oxygen species, the rupture of biofilms, and direct microbial cell injury, inorganic nanoparticles like copper, gold, and silver have shown remarkable antibacterial characteristics. These results aroused due to their adaptability, stability, and biocompatibility emphasize their crucial role in increasing the effectiveness of antibiotics and combating multidrug resistance. On the other-hand lipid-based systems, polymeric nano-spheres, and dendrimers are examples of organic nanoparticles that transport drugs in a targeted manner thereby reducing toxicity and enhancing therapeutic results. Their synergistic application with current treatment modalities, such as antibiotics and photothermal therapy, highlight their potency to transform infection management tactics. To add, advances in green synthesis and biocompatible formulations highlight an environmentally sustainable path forward, the development of hybrid systems like lipid-coated and dendrimer-based nanoparticles opens new strategies for precision medicine. The emergence of iron oxide-based hyper-thermic therapies and multi-metal hetero-structures further expand the toolbox for tackling persistent infections in high-risk hospital environments. These effects are significantly enhanced when NPs are used in combination with conventional antibiotics, as evidenced by statistical data from recent studies that reported synergistic inhibition zones, minimum inhibitory concentrations (MICs), and up to 98% bacterial biofilm reduction when compared to antibiotics alone. For instance, AgNPs synthesized by biological methods have demonstrated an MIC value as low as 16 μg/mL, that significantly outperformed the efficacy of traditional antibiotics. Moreover, during combinatorial treatments with other antibiotics had consistently shown a robust effect of these materials in producing enhanced antibacterial zones and greater biofilm disruption, with quantitative findings further strengthening their efficacy. Even though, significant progress has been made, we recommend further research is essential to optimize the nanoparticle synthesis, enhancement of its specificity, and nullifying their cytotoxic effects through in-vitro and in-vivo approaches alongside clinical trials. The integration of nanoparticles into clinical practice, supported by stringent safety evaluations and regulatory frameworks, will definitely hold immense promise in reducing the burden of conventional therapy for nosocomial infections and thereby improving patient outcomes in healthcare settings.

Disclosure

The authors report no conflict of interest in this work.

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