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Application of Chemically and Physically Synthesized Metal Nanoparticles to *Staphylococcus aureus*

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Author's contribution

The sole author designed, analysed, interpreted and prepared the manuscript.

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Review Article

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ABSTRACT

The infections caused by *S. aureus* have emerged as a grave challenge to human health worldwide. Further, conventional antibiotic therapies for *S. aureus*-mediated infections are gradually becoming ineffective due to the emergence of drug-resistant strains like methicillin-resistant *Staphylococcus aureus* (MRSA). In search of alternative novel therapeutic strategies against *S. aureus*, the use of metal nanoparticles is proliferating. Among different synthesis methods of metal nanoparticles, chemical and physical methods are the most common. Despite reports of metal nanoparticles' efficacy against drug-resistant *S. aureus* strains, contemporary reports that the bacteria can evolve resistance to nanoparticles are a significant source of concern. There is also the issue of metal nanoparticle toxicity, which affects a variety of organisms. The clinical translatability of published research conclusions is another major hurdle in nanotherapeutics research. More research is needed to make nanoparticle-based treatments a viable and long-term therapy for infections caused by *S. aureus*. The present review provides an overview of the therapeutic application of physicochemically synthesized nanoparticles (electron beam, mechanical grinding, milling, spray pyrolysis, vapour phase synthesis, electrolysis, photochemical, solutions and gels, wound healing, anticancer, antioxidant, biosensing, cosmetics, antimicrobial, human health care and water treatment) of various metals (transition metals, post-transition metals, alkaline earth metals, rare earth metals, etc.) against various *S. aureus* strains.

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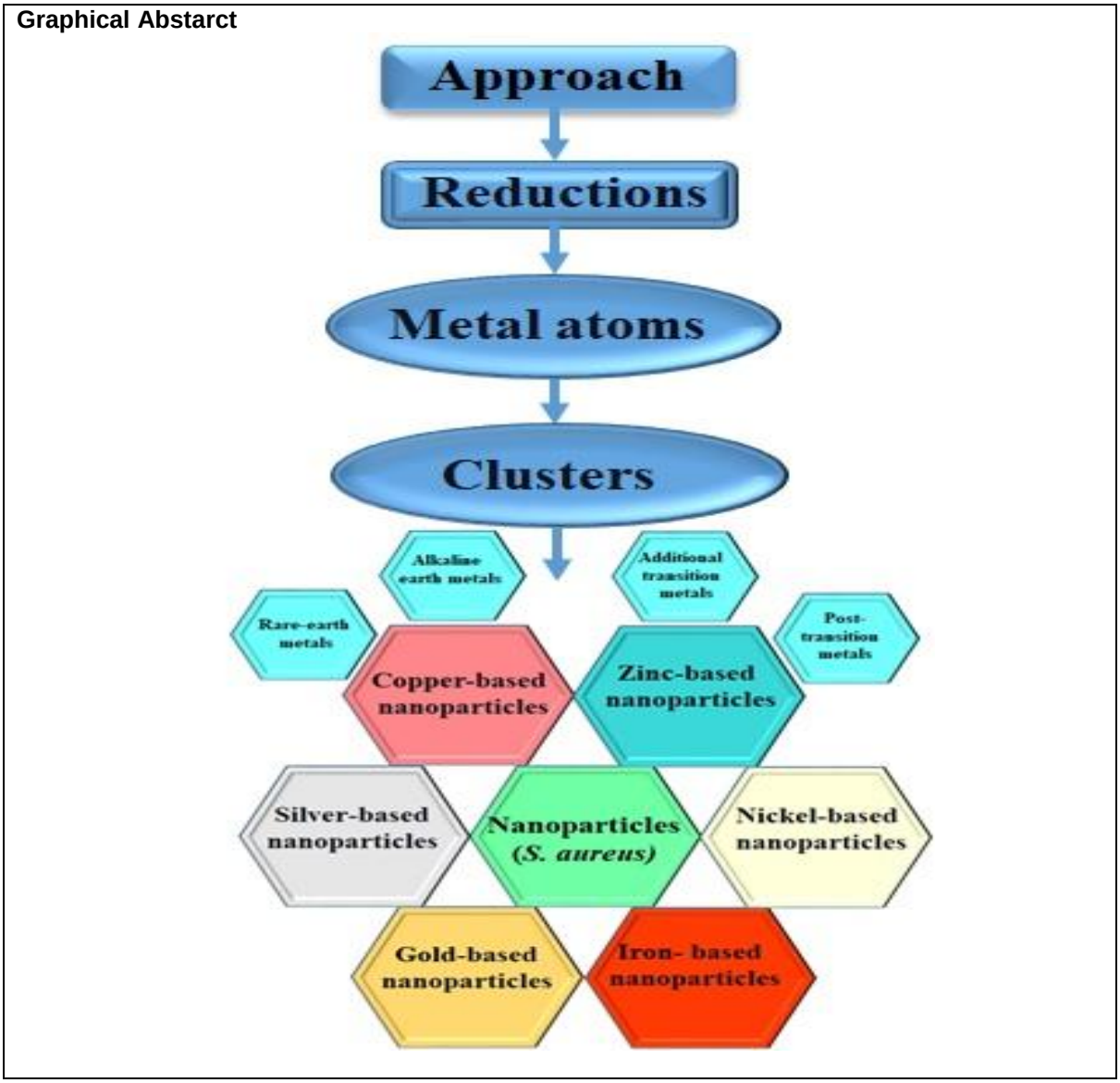
Graphical Abstarct



Keywords: Nanoparticles; chemical synthesis; physical synthesis; Staphylococcus aureus; MRSA; antibacterial.

ABBREVIATION

MRSA : Methicillin-resistant Staphylococcus aureus,
AgNPs : Silver nanoparticles,
ZnO NPs : Zinc oxide nanoparticles,
AuNPs : Gold nanoparticles,
MBC : Maximum bactericidal concentration,
DMF : Dimethylformamide,
PAA : Polyacrylic acid,
TBO : Toluidine blue O,
CTAB : Cetyl trimethyl ammonium bromide,
NiO NPs : Nickel oxide nanoparticles,
ROS : Reactive oxygen species,
PdNPs : Palladium nanoparticles
MIC : Minimum inhibitory concentration

1. INTRODUCTION

Staphylococcus aureus (*S. aureus*) is a gram-positive bacterium that belongs to *Staphylococcus* and was first isolated by surgeon Alexander Ogston from human pus in 1880. It is a standard part of the body's microbiota, commonly found in the upper respiratory tract and skin. It is one of the most frequent causes of skin and soft tissue infections that generally start as a minor boil or abscesses but may lead to severe life-threatening blood, muscle, and bone infections. Moreover, it may

spread to the other vital internal organs such as the brain, lungs, hearts, etc [1,2]. Endocarditis, meningitis, osteomyelitis, pyomyositis, necrotizing fasciitis, impetigo, etc., are some significant diseases caused by *S. Aureus* [3,2]. It is the most commonly isolated bacterial strain from hospitalized patients in the United States from 1998 to 2005 [4] and the second most cause for nosocomial infections related deaths in the United States [5]. *S. aureus* can also form biofilm by colonizing both host tissue and artificial surfaces like medical implants.

The biofilm-forming ability of *S. aureus* is an important virulence factor that provides resistance against antibiotics, allows bacterial persistence in host tissues, and helps the bacteria overcome host defense [6]. The severity of *S. aureus*-associated infections is further exacerbated by the emergence of antibiotic-resistant strains such as methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Staphylococcus aureus*, vancomycin-intermediate *Staphylococcus aureus*, and delafloxacin-resistant *Staphylococcus aureus* — a newly isolated strain from hospitals in Brooklyn, New York, USA [7]. Importantly, *S. aureus* has created a considerable economic burden on society and healthcare institutions due to the need for treatment and hospitalization [8,9]. The current antimicrobial approaches against *S. aureus* are plagued with multiple problems, such as human toxicity, bacterial resistance, and inadequacy against bacterial biofilms [10,11].

The World Health Organization [12] emphasized that methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Staphylococcus aureus*, vancomycin-intermediate *Staphylococcus aureus* are among the high-priority multi-drug resistant organisms that demand coordinated efforts in the research and development of new antibiotics and novel therapeutic approaches.

Nanomedicine is one such novel approach that has been exploited by numerous studies to combat *S. aureus*. Nanomedicine is a fast-growing multidisciplinary field combining material science, chemical science, pharmacological science, and biological science. It is the application of nanotechnology in medicine, serving clinical roles in screening, diagnosis, management, and therapy of diseases [13-16]. Over conventional medicine, nanomedicines offer better solubility and bioavailability, fewer side effects, and a lower likelihood of development of resistance by the biological system against them [17,18]. Further, nanomedicines, particularly nanoparticles (NPs), have been explored and, in some cases, approved. By the concerned agencies after successful clinical trials for treating various medical conditions. Such as cancer, infectious diseases, renal diseases, immune disorders, endocrine and exocrine disorders, neurodegenerative disorders, diabetes, and cardiovascular diseases [19-22]. Nanoparticles are structures with a size range from 1 to 100 nm (although some studies include molecules up to 1000 nm with specific properties under the definition of nanoparticles) and play a leading role in nanomedicine [23,24]. In this review paper, we have discussed the use of metal nanoparticles synthesized by chemical and physical methods for inhibiting the growth of *S. aureus*. Further, the review mainly focuses on the therapeutic use of monometallic nanoparticles against *S. aureus* infection.

2. CHEMICAL AND PHYSICAL SYNTHESIS OF NANOPARTICLES

Depending on the starting material used in the reaction, nanoparticles can be synthesized by either a top-down or bottom-up approach. The physical method represents top-down strategy, whereas the chemical method can be applied in both top-down and bottom-up strategies of nanoparticles synthesis [25-28]. Physical methods include the preparation of nano-sized structures by breaking-down bulk materials. Mechanical ball milling, electrospraying, physical vapor deposition (sputtering, electron beam evaporation, pulsed laser deposition), inert gas condensation, melt mixing, laser pyrolysis, and flash spray pyrolysis are some of the most frequently used physical methods for the fabrication of nanoparticles [26].

The chemical synthesis of nanoparticles generally involves the reduction of metal ions in aqueous or non-aqueous solutions into their metallic form in the presence of a reducing agent and stabilizing agent. Such as polyvinyl alcohol (PVA), polyvinyl pyrrolidone (PVP), sodium dodecyl sulfate (SDS), dodecanoic acid (DDA), surfactin, etc., which prevent aggregation of nanoparticles [29]. The common reducing agents used in the chemical synthesis are ascorbic acid, dimethylformamide (DMF), ethylene glycol, hydrazine hydrate, sodium borohydride (NaBH4), sodium citrate, polyols, etc [30,29]. Sol-gel method, microwave-assisted synthesis,

sonochemical synthesis, microemulsion method, hydrothermal and solvothermal methods, polyol synthesis. The chemical reduction method, chemical vapor deposition technique, and supercritical fluid precipitation method are the most routinely used chemical methods for synthesizing nanoparticles [31]. The metallic nanoparticles synthesized via physical and chemical methods have shown promising results in controlling *S. aureus* growth (Fig. 1).

This review catalogs the antibacterial application of metal (gold, silver, copper, zinc, iron, and other transition metals; post-transition metals; rare-earth metals; alkaline earth metals) nanoparticles fabricated through either chemical or physical methods against *S. aureus* infection (Fig. 2).

3. SILVER-BASED NANOPARTICLES

Silver has been known to humanity for its antibacterial property for hundreds of years. Many silver-based nanoparticles have been prepared by chemical or physical methods to kill *S. aureus.* Hwang and group [32] reported that chemically synthesized spherical-shaped silver nanoparticles (AgNPs) have a mean size of 3 nm. In combination with antibiotics (ampicillin, chloramphenicol, and kanamycin), inhibit the growth of and biofilm formation by *S. aureus*. Guzman et al. [30] synthesized AgNPs with a size between 10 and 20 nm from the chemical reduction of aqueous silver nitrate solution in the presence of reducing agents hydrazine hydrate and sodium citrate, and stabilizer SDS. The authors reported excellent antibacterial activity for the AgNPs against both *S. aureus* and drug-resistant strain MRSA.

Further, according to the authors, the silver ions released by AgNPs and the affinity of silver with sulfur and phosphorus groups present in the bacterial cell membrane were responsible for the bactericidal effect of AgNPs against *S. aureus* and MRSA [30]. Chudobova and group [33] synthesized silver phosphate nanoparticles having a size between 200 and 300 nm via a chemical method. The silver phosphate nanoparticles inhibited the growth of *S. aureus*, with the minimum inhibitory concentration (MIC) and total inhibitory concentration of 10 µM and 300 µM, respectively [33]. AgNPs fabricated in a microwave-assisted method in the presence of ascorbic acid as reluctant and starch as stabilizers exhibited antibacterial properties against *S. aureus* in disk diffusion assay [34]. Wady and group [35] synthesized AgNPs in a chemical reduction method that utilized sodium borohydride as a reductant and PVA as a stabilizing agent. The authors reported the bacteriostatic and bactericidal effect of AgNPs on *S. aureus* and MRSA planktonic cells. Ayala-Núñez and group [36] found that the size of AgNPs affects its antibacterial property against *S. aureus*. The authors used AgNPs in three different sizes: 10 nm, 30-40 nm, and 100 nm. The smallest-sized AgNPs (10 nm) had the highest antibacterial activity against MRSA. They were non-toxic to the HeLa cells, whereas AgNPs with large sizes (30-40 nm and 100 nm) had a moderate effect on MRSA and had a toxic effect on HeLa cells [36].

Similar to the size, the shape of AgNPs also affects their antibacterial activity against *S. aureus*. For example, Gao et al. [37] synthesized spherical-shaped AgNPs in a chemical reduction method with L-ascorbic acid as the reluctant and PVP as the surface modifier. The authors demonstrated superior antibacterial activity for spherical-shaped AgNPs than triangle-shaped nanoplates versus *S. aureus*.

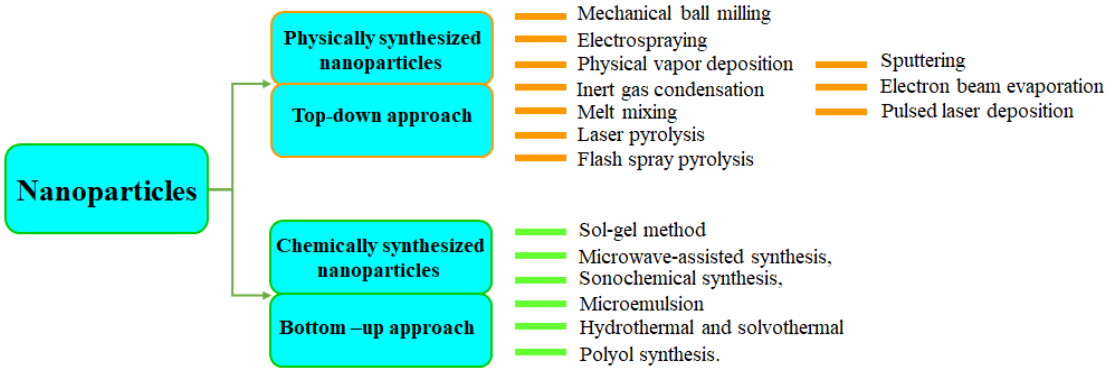


Fig. 1. Schematic illustration of the various mechanisms of nanoparticles against *Staphylococcus aureus*

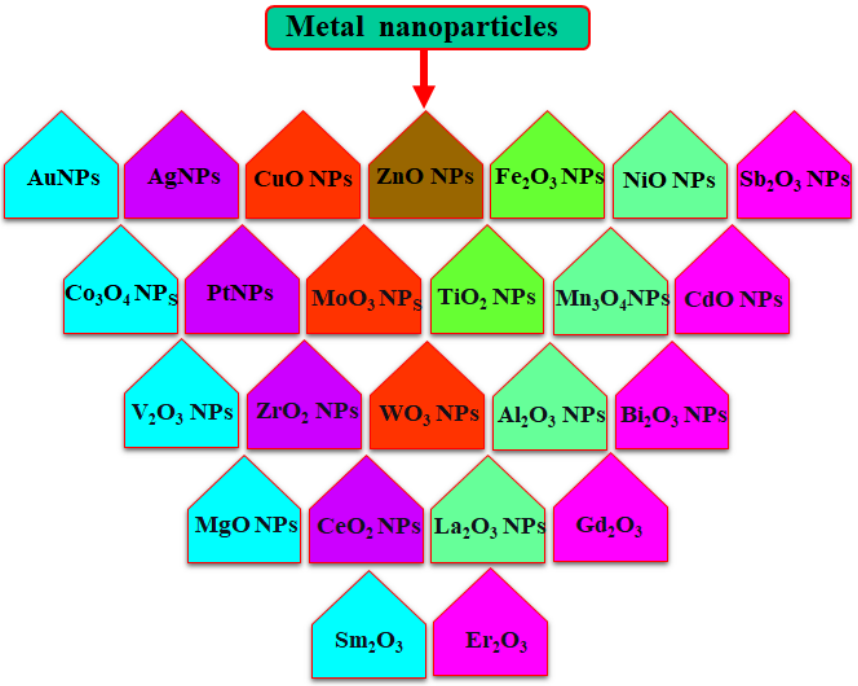


Fig. 2. Graphic representation of the various antibacterial metal nanoparticles against *Staphylococcus aureus*

Bankier and group [38] showed the antibacterial effect of rod-shaped AgNPs prepared from thermal plasma techniques against *S. aureus*. Actis et al. [39] prepared, through two different chemical methods (a novel thermal method and polyol process), AgNPs in three different geometries: spherical with size 34.10±3.18 nm, triangular with size 28.80±4.89 nm, and cuboid with size 75.29±7.15 nm. The authors did not find any significant effect of shape on the antibacterial activity of AgNPs against *S. aureus*; however, MRSA showed higher susceptibility to cuboid-shaped AgNPs than either to spherical- or triangular-shaped AgNPs [39]. AgNPs can also be used to prepare surfaces to prevent the growth of *S. aureus* strains. In one such study, AgNPs coated on glass surfaces inhibited biofilm formation by clinically isolated strains MRSA and methicillin-sensitive *S. aureus* (MSSA) [40].

Similarly, Piçarra and groups [41] coated glass, polystyrene, and steel surfaces with AgNPs and noted good antibacterial activity for the coated surfaces against *S. aureus*. Combining AgNPs with antibiotics, drugs, blue light, or other chemical groups can increase AgNPs' antibacterial efficacy versus *S. aureus*. For example, Akram et al. [42] found that the triple combination of AgNPs (15-20 nm) blue light (460 nm and 250 mW for one hour). Moreover, different antibiotics (amoxicillin, azithromycin, clarithromycin, linezolid, and vancomycin) more effectively killed clinical MRSA isolates in comparison with the double combination of AgNPs and antibiotics or AgNPs and blue light. Cavassin et al. [43] synthesized citrate-, chitosan-, and PVA-functionalized spherical AgNPs, respectively, and reported antibacterial activity for the functionalized AgNPs against oxacillin-resistant *Staphylococcus aureus*. Similarly, in another study, PEG-functionalized AgNPs of 14 nm exhibited the most miniature MIC (3.31±0.03 µg/mL) and thus the highest bactericidal activity compared with the T80-functionalized AgNPs of 45 nm size and SDS-functionalized AgNPs of 54 nm size against *S. aureus* [44].

AgNPs functionalized with antibiotics such as ampicillin [45]. vancomycin [46-48]. cephradine [49] rifampicin [50] have been effectively utilized as antibacterial agents against *S. aureus* and MRSA. Li and group (2011) studied the mechanism of AgNPs against *S. aureus* and reported that AgNPs damage the cell membrane integrity, interfere with healthy cell metabolism, and condense the bacterial DNA.

4. GOLD-BASED NANOPARTICLES

Like silver, gold is another metal whose nanoparticles are extensively explored for its

antibacterial properties against *S. aureus.* Shamaila et al. [51] in a chemical method using $NaBH_4$ as a reducing agent, synthesized gold nanoparticles (AuNPs) in two size ranges: 7-34 nm and 30-40 nm. Both types of AuNPs exhibited antibacterial activities against *S. aureus*, with MIC values of 3.92 µg/mL and 3.98 µg/mL for AuNPs with sizes 7-34 nm and size 30-40 nm, respectively.

On the other hand, some studies found no or deficient antibacterial activity against *S. aureus* for naked AuNPs that is AuNPs without any surface modification [52,53]. Conjugation of AuNPs with antibiotics such as gentamicin [54] amoxicillin [55] ampicillin [56] vancomycin [57] streptomycin, and kanamycin [58,59] etc. have been shown to improve the antibacterial efficacy of both AuNPs and antibiotics against *S. aureus*. Darabpour's group [60] attached methylene blue dye to the surface of AuNPs and used the conjugated AuNPs in photodynamic antimicrobial chemotherapy to deactivate the MRSA biofilm. Kuo et al. [61] prepared gold nanorods coated with polyacrylic acid (PAA) and conjugated with toluidine blue O (TBO).

The modified gold nanorods in the presence of 633 nm HeNe laser caused photothermal deactivation of MRSA [61]. In two separate studies, antibiotic-loaded, antibody-conjugated, polymer-coated gold nano-constructs were combined with photothermal heating to kill *S. aureus* [62,63]. AuNPs conjugated with vascular endothelial growth factor A165 (VEGF-A165) and (11-mercaptoundecyl)-N, N, N-trimethylammonium (11-MTA) cation showed wound healing property on MRSA-induced wounds in diabetic mice [64]. AuNPs have also been used in therapeutic systems devised to inhibit MRSA biofilm formation [65-67]. The shape of AuNPs affects its antibacterial properties against *S. aureus*. In one such exciting study, authors found flower-shaped AuNPs (40.6±2.2 nm) to have more potent antibacterial activity than sphere- and star-shaped AuNPs towards *S. aureus* [69].

In a similar study, the maximum antibacterial activity toward *S. aureus was* shown by gold nanocubes (zone of inhibition of 16.5 mm) followed by gold nanospheres (zone of inhibition of 13.5 mm) and gold nanostars (zone of inhibition of 12.5 mm) [70]. Similarly, other studies reported the therapeutic potential of gold nanorods with various surface modifications against *S. aureus* [71,72].

5. IRON- BASED NANOPARTICLES

Iron nanoparticles have emerged as a promising antibacterial agent because of their superpara magnetic properties and biocompatibility [73,74]. Another advantage of magnetic nanoparticles is that they can be retrieved after being used in the treatment [75]. The commonly used iron oxide nanoparticles for antibacterial properties are α-Fe_2O_3 (hematite), γ- Fe_2O_3 (maghemite), and Fe_3O_4 (magnetite). Tran et al. [76] synthesized PVA-coated iron oxide nanoparticles (mixture of γ-Fe_2O_3 and Fe_3O_4) using a matrix-mediated method. The PVA-coated iron nanoparticles had the size of 9±4 nm and arrested the growth of *S. aureus* in the live/dead assay [77]. Rhombohedral-shaped Fe_2O_3 NPs with an average size of 35.16±1.47 nm were bactericidal against *S. aureus* at a maximum bactericidal concentration (MBC) value of 80±1.5 µg/mL [78]. Ravikumar and group [78] found a zone of inhibition in agar well diffusion assay for Fe_2O_3 NPs (size, 9-11 nm) against *S. aureus*. Hematite NPs (50-110 nm) synthesized by pulsed laser ablation method in dimethylformamide (DMF) and SDS solutions showed excellent antibacterial activity toward *S. aureus* [79]. Similarly, Fe_3O_4 NPs (9.7 nm) synthesized by flame spray pyrolysis method displayed antibacterial activity against *S. aureus*, with MBC value between 10 and 100 µg/mL [80]. In another study, spherical magnetite NPs (50–100 nm) coated with oleic acid showed excellent anti-biofilm activity against *S. aureus* [81]. Similarly, EDTA-Na3-functionalized magnetite NPs were found to have biofilm removing ability against MRSA [82]. Kim's group [83] conjugated magnetite NPs with anti-*S. aureus* protein-A antibody. Under the influence of heat generated by the high-amplitude, high-frequency, alternating magnetic field, the conjugated magnetite NPs effectively killed *S. aureus*. They promoted wound healing in *S. aureus*-infected mouse model [83]. Iron oxide nanoparticles can also be used as a drug delivery vehicle to treat *S. aureus-associated* infections [84]. For example, Manna and group [82]. used amine-functionalized, biocide-coated, non-spherical Fe_3O_4 NPs of varied shapes (cubic, disk-like, hexagonal, rectangular, and rod-like) to deactivate MRSA bacteria entirely in only two hours. Very recently, Nickel and group [83] synthesized magnetic nanoparticles (a mixture of Fe_3O_4 and γ-Fe_2O_3) of distinct shapes (spherical, cubic, and tetrapod) via thermal decomposition of iron oleate. The researchers used magnetic nanoparticles to transport biocidal agent cetyl trimethyl

ammonium bromide (CTAB) within the extracellular matrix of the bacterial cells to eradicate MRSA biofilms [84].

6. NICKEL-BASED NANOPARTICLES

Nickel-based nanoparticles have also been studied for their antibacterial activities toward *S. aureus*. Pang et al. [85] synthesized nickel oxide (NiO) nanotubes and nanoflowers from the precursor bis (dimethylglyoximato) nickel (II) and $NiCl_2$, respectively. The NiO nanotubes exhibited more potent antibacterial activity with a MIC value of 6.25 µg/mL than NiO nanoflowers having a MIC value of 50 µg/mL against *S. aureus*. Baek and An [86] compared the antibacterial activities of nickel oxide nanoparticles (NiO NPs), copper oxide nanoparticles (CuO NPs), zinc oxide nanoparticles (ZnO NPs), and antimony trioxide nanoparticles (Sb_2O_3 NPs) against *S. aureus*. All tested metal oxide nanoparticles showed antibacterial activities against *S. aureus*, and the order of their antibacterial activities was as follows: CuO NPs > NiO NPs > ZnO NPs > Sb_2O_3 NPs [86] .Similarly, in another comparative study, Argueta-Figueroa and group [87] reported that. In contrast, copper NPs exerted a bactericidal effect on *S. aureus*; nickel NPs only showed a bacteriostatic effect on the bacteria. Mirhosseini and group [88] synthesized nickel nanoparticles (NiNPs) and nickel hydroxide nanoparticles ($Ni(OH)_2$ NPs) of 5 nm and 75 nm size, respectively, by chemical reduction method. NiNPs exhibited higher antibacterial activity with the MIC and MBC values of 0.81 mg/mL and 1.62 mg/mL than $Ni(OH)_2$ NPs for which the MIC and MBC values were 6.5 mg/mL and 13 mg/mL [88].

7. COPPER--BASED NANOPARTICLES

Nanoparticles of copper metal have also emerged as potent nanotherapeutics against infectious diseases caused by microbes, especially *S. aureus*. Copper-based nanoparticles synthesized through various chemical and physical methods, such as flame spray pyrolysis method [80]. sol-gel method [89] mechanical milling [90]. pulsed laser ablation method [91] chemical reducing method [87] hydrothermal technique [92] have been found to possess antibacterial activity against *S. aureus* strains. Kruk and coworkers [93] presented the effectiveness of monodispersed copper NPs (50 nm) synthesized by reducing copper salt with hydrazine in the aqueous SDS solution against MRSA. Spherical-shaped copper oxide nanoparticles (CuO NPs) with a size range from 5 to 10 nm were synthesized through the electrochemical reduction method. The nanoparticles showed good antibacterial activity against *S. aureus* [93] Azam et al. [77] revealed that CuO NPs restrict *S. aureus* growth in size- and concentration-dependent manner. CuO NPs exhibited higher antibacterial activity for Gram-positive bacteria than for Gram-negative bacteria. Ren et al. [94] used thermal plasm technology to prepare CuO NPs. The CuO NPs were active against MRSA and other *S. aureus* strains, with MBC values ranging from 100 µg/mL to 2500 µg/mL [94]. Chatterjee and coworkers [95] prepared spherical-shaped copper NPs with 56.2 nm size by reducing CuCl2 in the presence of gelatin as a stabilizer. The copper NPs inhibited the growth of *S. aureus,* with the MIC and MBC values of 4.5 and 9 µg/mL, respectively. Usman et al. [96] synthesized copper NPs (2–350 nm) via chemical method using chitosan polymer as a stabilizer and reported the antibacterial activity of copper NPs toward MRSA. Nanoparticles of various oxide phases of copper (Cu, CuO, and Cu2O) were synthesized at different pH (3, 5, 7, 9, and 11) in a low-temperature chemical reduction method by Moshalagae Motlatle et al. [97]. The researchers reported a difference in the bactericidal property of the tested nanoparticles against *S. aureus*. The highest zone of inhibition in disk diffusion assay was shown by copper nanoparticles formed at pH 7 [97]. Further, the authors suggested that the difference was due to the pH that affected surface charges on copper nanoparticles [97]. Copper-based nanoparticles have also been shown to inhibit biofilm formation and act against resistant *S. aureus* strains [98,99].

8. ZINC-BASED NANOPARTICLES

Zinc-based nanomaterials are additional nanotherapeutics that many studies have used against *S. aureus* infection. For instance, Baek and An [86] reported inhibition of *S. aureus* growth by zinc oxide nanoparticles (ZnO NPs) having a size range of 50 to 70 nm. Similarly, ZnO NPs of tiny size (3 nm) exhibited bacteriostatic and bactericidal activities toward *S. aureus*, with the MIC and MBC values of 0.5 mg/mL and 8 mg/mL, respectively [100]. In a comparative antibacterial study against *S. aureus*, hexagonal-shaped ZnO NPs (19.89±1.43 nm) showed maximum antibacterial activity followed by CuO NPs (29.11±1.61 nm), and the minor antibacterial activity was shown by Fe_2O_3 NPs (35.16±1.47 nm) [77]. Pati and coworkers

synthesized spherical shaped ZnO NPs of 500 nm size via wet chemical methods using zinc nitrate and sodium hydroxide as precursors and soluble starch as a stabilizing agent. The authors reported that ZnO NPs perturbed biofilm formation by both *S. aureus* and MRSA and substantially reduced the *S. aureus* bacterial load and inflammation in *vivo* skin infection mice model [101].

Similarly, in another study, ZnO NPs reduced the bacterial load and promoted wound healing in an experimental mice model infected with *S. aureus* [102]. In Jesline et al.'s [103] study, ZnO NPs of size less than 100 nm showed good antibacterial activity against biofilm-forming and non-biofilm forming MRSA strains. Salina and group [104] reported that the antibacterial activity of ZnO NPs against *S. aureus* is pH and temperature-dependent. The authors observed that ZnO nanofluid formed by dissolving zinc oxide NPs in glycerol and ammonium citrate inhibited the growth of *S. aureus* in a concentration-dependent manner, and temperature increase and acidic pH can further improve the antibacterial effect of ZnO nanofluid on *S. aureus* [104]. ZnO NPs (20.4 nm) synthesized by flame spray pyrolysis method showed antibacterial activity against *S. aureus,* with MBC value between 1-10 µg/mL [80].

Similarly, very small-sized (3 nm) ZnO NPs synthesized via the sol-gel method exhibited a prominent antibacterial effect at the exponential phase of *S. aureus*. Reyes-Torres et al. [105] synthesized spherical ZnO NPs of 15 nm size using the mixture of $LiNO_3$/$NaNO_3$ as inorganic media and found the nanoparticles, alone and with the antibiotic ampicillin, to be effective against *S. aureus*. In a new study, Kadiyala et al. [106] showed the concentration-dependent killing of *S. aureus* by spherical and hexagonal shape ZnO NPs. The researchers found that the antibacterial activity of ZnO NPs against MRSA is not mediated by reactive oxygen species (ROS), as commonly reported, but by the regulation of energy metabolism pathways. Such as carbohydrate metabolism, amino acid biosynthesis, and pyrimidine biosynthesis pathway. Further, the authors also proposed that the changes in the energy metabolism of the bacteria could be due to the biomimetic role played by ZnO NPs in the bacterial cells [106]. In another new study, Choi and coworkers [107] synthesized novel caffeic acid-conjugated ZnO nanoparticles that inhibited the growth of both *S. aureus* and MRSA. Patra et al. [108] reported the microwave-assisted synthesis of ZnO NPs with hexagonal shape and size distribution of 18-20 nm. The authors further conjugated ZnO NPs with antibiotic ciprofloxacin and found an excellent antibacterial activity for the conjugated nanoparticles against the clinically isolated multidrug-resistant strain of *S. aureus* [108]. De Souza et al. [109] utilized the sonochemical method to synthesize rod-shaped ZnO NPs, with a length of 145.1 nm and a diameter of 97.2 nm that showed a zone of inhibition in agar well against *S. aureus*. Horky et al. [110] investigated the efficacy against *S. aureus* and MRSA of zinc phosphate-based NPs that were prepared using different precursors: $(NH_4)_2HPO_4$, $Na_2HPO_4{\cdot}7H_2O$, $Na_4P_2O_7$, and $Na_5P_3O_{10}$. Zinc phosphate-based NPs exhibited better antibacterial activity against *S. aureus* with IC_{50} value ranging between 0.5 and 1.6 mmol/L, whereas against MRSA, the nanoparticles were less potent with IC50 value ranging from 1.2 to 4.7 mmol/L [110].

9. ADDITIONAL TRANSITION METALS

Physicochemically synthesized nanoparticles of transition metals other than silver, gold, iron, nickel, copper, and zinc have been less studied as antibacterial agents against *S. aureus*. Transition metals include titanium, palladium, cobalt, molybdenum, cadmium, vanadium, manganese, tungsten, zirconium, and platinum.

Ghosh et al. [111] in a pyrolysis method using two different cobalt precursors, a coordination polymer and a dinuclear complex, synthesized two types of cobalt oxide nanoparticles (Co_3O_4 NP_S): square-shaped with a smaller size range of 10-25 nm and hexagonal-shaped with a more extensive size range of 100-150 nm. Both types of Co_3O_4 NP_S displayed bacteriostatic and bactericidal activity toward *S. aureus.* The MIC and MBC values were 128 µg/mL for square-shaped Co_3O_4 NP_S and 64 µg/mL and 128 µg/mL, respectively, for hexagonal-shaped Co_3O_4 NP_S [111]. Similarly, Co_3O_4 NP_S of 11.5 nm size synthesized by flame spray pyrolysis method showed antibacterial activity against *S. aureus*, with an MBC value of 100 µg/ml [80]. In a recent report, researchers fabricated cobalt nanosuspension from three different cobalt-based metallosurfactants -CoCTAC (bishexadecyltrimethylammonium cobalt tetrachloride), CoDDA (bis-dodecyl amine cobalt dichloride). Furthermore, CoHEXA (bishexadecylamine cobalt dichloride)-via microemulsion method without using any

reducing agents and reported antimicrobial activities against *S. aureus* for all the three cobalt-based nanosuspension [112].

Konieczny et al. [113] demonstrated size-dependent inhibition of *S. aureus* growth by using a colony-reduction assay using PVP-coated platinum nanoparticles NPs (PtNPs). Similarly, small-sized pectin-capped PtNPs (2-5 nm) fabricated via chemical reduction method displayed excellent bacteriostatic effect at the MIC value of 31.2 µg/ml toward *S. aureus* [114]. Platinum nanoparticles disintegrate the cytoplasmic membrane and cell wall of *S. aureus* and induce leakage of intracellular components [115].

Recently, transition metal molybdenum has also generated interest due to its limited toxicity to humans, biodegradability, and fast elimination from the body [116]. Irregularly shaped molybdenum oxide nanoparticles (MoO_3 NP_S) of 46 nm size prepared via electrochemical reduction method were reported to be efficient in killing *S. aureus* in agar well diffusion assay [117]. Similarly, MoO_3 NP_S synthesized in a one-step thermal decomposition method using ammonium heptamolybdate tetrahydrate as precursor inhibited the growth of both MSSA and MRSA at MIC value of 700 µg/ml [118]. Desai and coworkers [119] reported antibacterial action against *S. aureus* of MoO_3 NP_S nanocrystals having hexagonal rods with sea urchin-like morphology prepared through the chemical bath deposition technique. The coating of MoO_3 NP_S on the glass surface also exhibited good antibacterial activity against *S. aureus* [41].

Titanium nanoparticles have also been explored for their antibacterial properties against *S. aureus* [120,80]. The titanium nanoparticles are mainly utilized as an antibacterial coating on implants to keep them safe from infection after surgery [121]. Roy and group [120] synthesized titanium dioxide NPs (TiO_2 NPs) via the sol-gel method using citric acid as a reducing agent and α-Dextrose saturated solution as a surfactant. The researchers observed that TiO_2 NPs could enhance the effectiveness of common antibiotics (β-lactam, cephalosporins, aminoglycosides, glycopeptides, fluoroquinolones, azalides, macrolides, lincosamides, and sulphonamides) against MRSA [120]. Jesline's group reported the efficacy of commercially synthesized TiO_2 NPs (<50 nm) against biofilm-forming MRSA strains. TiO_2 NPs (12.2 nm) synthesized by flame spray pyrolysis method showed antibacterial activity against *S. aureus*, with an MBC value of >100 µg/Ml [80]. TiO_2 is commonly found in three different phases: anatase, brookite, and rutile. Nanoparticles of all the three-phase variants have been studied as antibacterial agents versus *S. aureus*. Haq et al. [122] prepared TiO_2 NPs via the chemical precipitation method at room temperature and investigated the effect of temperature on the antibacterial activity of the nanoparticles against *S. aureus*. Researchers found that TiO_2 NPs at 120°C consisted of anatase phase with tetragonal morphology and were toxic for *S. aureus*, whereas TiO_2 NPs at 900°C contained only rutile phase with tetragonal geometry and exhibited no antibacterial activity against the bacteria [122]. On the contrary, Fei and group [123] found that cotton fabrics treated with rutile phase TiO_2 nanocrystals of less than 10 nm size prepared at room temperature showed bactericidal activity toward *S. aureus*. Similarly, in another study, thin films of anatase TiO_2 NPs on glass and titanium surfaces in the presence of UV light showed photocatalytic bactericidal activity against *S. aureus* [124]. The biphasic brookite-anatase TiO_2 NPs in combination with UV light showed better antibacterial activity than either TiO_2 NPs or UV light alone against the drug-resistant strain of *S. aureus* [125].

Palladium is another transition metal whose nanoparticles have been exploited for their antibacterial activity toward *S. aureus*. Adams et al. [126] fabricated spherical palladium nanoparticles (PdNPs) from the precursor palladium acetate via a modified pyrolysis reaction. The researchers obtained PdNPs in three sizes (2.0±0.1 nm, 2.5±0.2 nm, and 3.1±0.2 nm) and found that PdNPs at a concentration as low as 10-9 M could kill *S. aureus*. Moreover, the small-sized PdNPs (2.0±0.1 nm) were more toxic than the PdNPs with sizes of 2.5±0.2 nm and 3.1±0.2 nm to *S. aureus*. Similarly, PdNPs having a size of 15.1 nm synthesized by flame spray pyrolysis method showed antibacterial activity against *S. aureus*, with MBC value in the range between 10 and 100 µg/mL [80]. Recently in a fascinating study, authors reported the shape dependence of PdNPs on its antibacterial activity toward drug-resistant *S. aureus* [127]. The authors used the hydrothermal method to prepare cube-shaped and octahedron-shaped PdNPs. The cube-shaped PdNPs were more effective than octahedron-shaped PdNPs in killing drug-resistant *S. aureus*. Further, according to Fang et al. [127] oxidase- and peroxidase-like properties of PdNPs generate reactive oxygen species that damage *S. aureus*.

Azhir et al. [128] investigated the effect of hausmannite manganese oxide nanoparticles (Mn_3O_4 NPs) (10–30 nm) prepared via precipitation method on *S. aureus*. The Mn_3O_4 NPs inhibited *S. aureus* concentration-dependent with MIC and MBC values of 625 and 1250 µg/ml [128]. Aurora and group (2015) utilized the flame spray pyrolysis method to synthesize Mn_3O_4 NPs (15.2 nm), which showed antibacterial activity against *S. aureus* with MBC value 10-100 µg/ml. Cherian et al. [129] using the co-precipitation method, fabricated spherical-shaped manganese dioxide nanoparticles (Mn_3O_4 NPs) have sizes 40.5–70 nm and found the nanoparticles toxic to *S. aureus*.

Nanoparticles of cadmium oxide, another transition metal, were synthesized by Salehi and group [130] using a chemical method including cadmium sulfate as a precursor and CTAB as the surfactant. Cadmium oxide NPs (CdO NPS) inhibited the growth of *S. aureus* in a concentration-dependent manner, and at 20 µg/ml, it ultimately killed *S. aureus* within 25-30 hours [130]. Similarly, Nandhini and group [131] used the precipitation method to synthesize CdO NPs, effective against *S. aureus*. Abd et al. [132] prepared a thin film of CdO NPs with (50–110 nm) antibacterial property against *S. aureus*. Rectangle shape CdO NPs prepared in a microwave-assisted hydrothermal method inhibited *S. aureus growth* in agar well diffusion assay [133].

Vanadium is another transition metal whose nanoparticles have been utilized against *S. aureus*. For instance, via a hydrothermal method, Natalio et al. [134] prepared vanadium pentoxide nanowires (V_2O_5 NWs) of 300 nm length and 20 nm width. The nanowires of V_2O_5 were found to mimic the role of enzyme vanadium haloperoxidases and cause significant reduction (96%) in *S. aureus* growth [134]. Wang and coworkers [135]. prepared metallic vanadium NPs, V_2O_3 NPs, VO_2 NPs, and V_2O NP_S films by depositing them on quartz glass via the magnetron sputtering method. All nanofilms proved to be effective against MRSA and were further found to be non-toxic to mammalian cells, thus holding promises for therapeutic application in controlling implant-related infection caused by *S. aureus* [136].

Zirconium nanoparticles represent another transition metal-based approach against *S. aureus, although* multiple studies on the antibacterial effect of zirconium-based nanoparticles toward *S. aureus* have shown contradictory results. For example, Ravikumar et al. [78] did not find any anti-*S. aureus* activity for commercial zirconium dioxide nanoparticles (ZrO_2 NPs) with less than 100 nm size either in well diffusion assay or broth dilution assay. Similarly, neither Jangra et al. found any antibacterial activity against *S. aureus* for ZrO_2 NPs of two size ranges (5–30 nm and 15-20 nm), both synthesized by hydrothermal method. On the other hand, in the study of Fathima and group [137] chemically-synthesized spherical-shaped ZrO_2 NPs (15–21 nm) showed antibacterial activity versus *S. aureus* in disc diffusion assay. Similarly, agglomerated ZrO_2 NPs of 30 nm size synthesized by the sol-gel method exhibited good antibacterial activity on *S. aureus* [138]. Thakare and group [139] utilized the sol-gel method to fabricate tetragonal ZrO_2 NPs (35–60 nm). The nanoparticles were capable of arresting the growth of *S. aureus* bacteria [139].

Nanoparticles of transition metal tungsten can be effective against *S. aureus*. Aruoja et al. [80] reported the efficacy of tungsten trioxide nanoparticles (WO_3 NPs) of 10.6 nm size synthesized by flame spray pyrolysis method against *S. aureus*, with an MBC value of more than 100 µg/mL ([80]. Similarly, in another study, tungsten nanoparticles (SNPs) (8.1±2.8 nm) at the MIC value of 1500 µg/mL inhibited the growth of *S. aureus* in direct spotting method and cup diffusion method [140]. Bankier et al. [38] did not find any antibacterial effect for tungsten carbide nanoparticles (250 nm, hexagonal) on *S. aureus* in flow cytometry dead assay. A recent study showed that tungsten oxide (WO_3-x) nanodots could inhibit *S. aureus* in a concentration- and a time-dependent fashion [141].

10. POST-TRANSITION METALS

Few studies have explored physicochemically synthesized nanoparticles of pure post-transition metals such as aluminum, bismuth, and tin against *S. aureus*.

Ravikumar et al. [78] prepared aluminum oxide nanoparticles (Al_2O_3 NPs) and found antibacterial activity for the nanoparticles against *S. aureus* only in well diffusion assay but not in broth dilution assay. Aruoja et al. [80] used the flame spray pyrolysis method to synthesize Al_2O_3 NPs of (11.4 nm) that showed anti-*S. aureus* antibacterial activity with an MBC value of

more than 100 µg/ml. Similarly, spherical Al_2O_3 NPs (9.5 nm) arrested the growth and reproduction of clinically-isolated *S. aureus* strains, MRSA, and MSSA [142].

Campos and group [143] compared antibacterial activities of bismuth sulfide nanoparticles (Bi2S3 NPs), metallic bismuth nanoparticles (BiNPs), bismuth oxide nanoparticles (Bi_2O_3 NPs), and silver nanoparticles (AgNPs) on *S. aureus*. In the study, both BiNPs and Bi2O3 NPs showed suitable antibacterial activities, whereas Bi_2S_3 NPs exhibited minor antibacterial activity [143]. Kadhim [144] using laser ablation techniques, synthesized spherical-shaped BiNPs, and reported their effectiveness against *S. aureus*. Very recently, Vazquez-Munoz and coworkers [145] synthesized PVP-coated BiNPs with sizes ranging from 1.7 nm to 44.4 nm via a chemical reduction method. The nanoparticles exhibited excellent antibacterial activity against planktonic *S. aureus* cells at the MIC value of 1 µg/ml, and they also inhibited biofilm formation by *S. aureus* [145]. Amininezhad and group [146] prepared spherical-shaped tin oxide nanoparticles (SnO_2 NPs) by the solvothermal method and showed their antibacterial potential toward *S. aureus*. Similarly, Kumar et al. [147,148] also showed tetragonal rutile nanocrystals of SnO_2 to have bactericidal activity on *S. aureus* bacteria.

11. ALKALINE EARTH METALS

Alkaline earth metals like calcium and magnesium at a nanoscale size have been found to possess the ability to kill *S. aureus*. For example, magnesium oxide nanoparticles (MgO NPs) (13.6 nm) synthesized by flame spray pyrolysis method showed antibacterial activity against *S. aureus* at the MBC value of more than 100 µg/mL [80]. On the contrary, in Ravikumar et al. [78] study, MgO NPs of less than 50 nm size did not show any activity against *S. aureus* in healthy diffusion or broth dilution method. In another study, Bindhu et al. [149] reported the synthesis of well-dispersed spherical nanoparticles of magnesium oxide through a wet chemical reaction method. The magnesium oxide nanoparticles displayed antibacterial properties toward *S. aureus* [149]. Similarly, in the study of Nguyen et al. [150] MgO NPs (size 23±5 nm) exhibited bacteriostatic and bactericidal activities against *S. aureus* and MRSA. The MIC and MBC were 0.7 and 1.4 mg/ml against *S. aureus;* and 1.0 and 1.4 mg/ml against MRSA [150]. In other studies, magnesium oxide nanoparticles were prepared from the wet chemical method [150,152] and microwave-assisted synthesis [153] were found to control the growth of *S. aureus*.

12. RARE-EARTH METALS

Rare earth metals-based nanoparticles are gaining widespread importance in biomedical applications because of their low toxicity and high chemical and thermal stability [154]. Limited studies have utilized pure rare-earth metals nanoparticles to destroy *S. aureus.* Studies have used them as a dopant to improve upon the various properties of other metal nanoparticles [155].

The studies on cerium oxide nanoparticles (CeO_2 NPs) as an antibacterial agent against *S. aureus* have shown conflicting results. Ravishankar et al. [156] synthesized spherical-shaped CeO_2 NPs by solution combustion technique using ceric ammonium nitrate as an oxidizer and ethylenediaminetetraacetic acid (EDTA) as fuel at a high temperature of 450°C. The researchers did not find any activity for CeO_2 NPs up to the concentration of 1000 µg/50 µl against *S. aureus* either in agar well diffusion assay or in broth dilution assay. On the other hand, Ravikumar et al. [78] reported inhibition of *S. aureus* by commercially available CeO_2 NPs in agar healthy diffusion test. However, the authors did not find any antibacterial activity of CeO_2 NPs in the broth dilution method. In another interesting study, Masadeh and group [157] reported that the spherical-shaped CeO_2 NPs have a size in the range from 25 to 50 nm significantly reduced antibacterial activity of the antibiotic ciprofloxacin against MSSA and MRSA. The MIC values for ciprofloxacin against MRSA and MSSA planktonic culture were 0.10±0.04 and 0.40±0.20 µg/mL. However, in the presence of CeO_2 NPs, the MIC values increased many folds indicating a decrease in efficacy of the antibiotic against both MRSA and MSSA [157].

Balusamy et al. [158] in a comparative study, reported that spherical lanthanum oxide nanoparticles (La_2O_3 NPs) of size 100 nm showed antibacterial activity against *S. aureus*, whereas La_2O_3 bulk material having a size of 1 µm was not effective against the bacteria. In another study, Dědková and group [159] prepared nanoparticles of gadolinium oxide (Gd_2O_3), samarium oxide (Sm_2O_3), and erbium oxide (Er_2O_3) in a simple thermal decomposition reaction and observed that all tested rare earth metals nanoparticles could inhibit the growth of *S. aureus* [160-167].

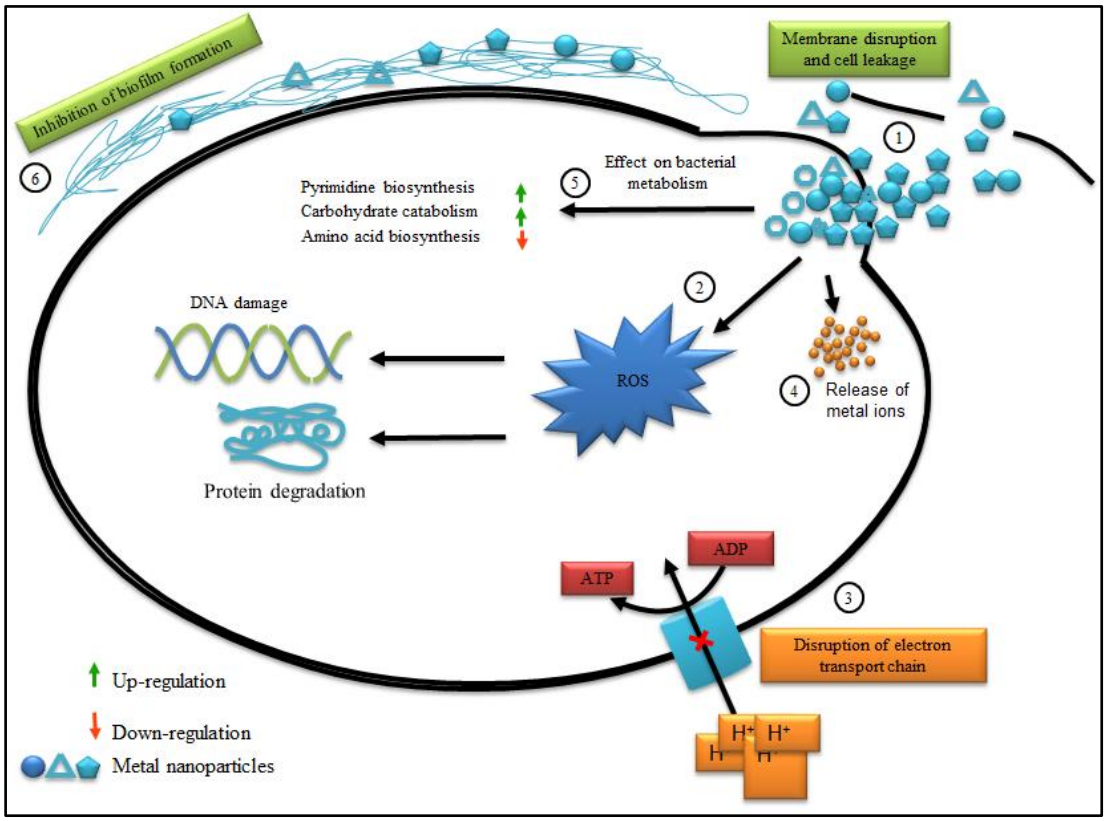


Fig. 3. Schematic representation of the various antibacterial mechanisms of metal nanoparticles against *Staphylococcus aureus*

These include (1) disruption of bacterial membrane and leakage of intracellular content, (2) reactive oxygen species (ROS) generation that cause break in DNA, protein degradation, etc. (3) disruption of electron transport chain, (4) release by certain meta nanoparticles of metal ions that further wreak havoc inside the cell, (5) alteration in the bacterial metabolic pathway, (6) inhibition of biofilm formation

13. CONCLUSION

Staphylococcus aureus causes various infections responsible for a significant number of deaths worldwide. The emergence of many drug-resistant strains of *S. aureus* has made treating the associated infections very difficult. The failure of conventional antibiotics has led to novel therapeutic approaches, such as nanosize structures. In this review, we have highlighted the application of metal nanoparticles prepared through chemical and physical methods against *S. aureus* strains. Large metal nanoparticles can be synthesized through diverse chemical and physical methods. Although research in nanoparticle-based therapeutics for infectious diseases is growing at a breakneck pace, it is still far behind the use of nanoparticles for cancer therapy. Similarly, despite reports of the effectiveness of metal nanoparticles against *S. aureus'* drug-resistant strains, the recent reports that the bacteria can develop resistance against nanoparticles are a significant concern. Additionally, there is the issue of metal nanoparticle toxicity to multiple organs such as kidney, brain, muscle, bone, skin, liver, heart, spleen, etc. The other major challenge in nanotherapeutics research is the clinical translatability of published research findings. Therefore, there is opportunity for further research to make nanoparticles-based therapeutics a viable and long-term solution for *S. aureus*-associated infections.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Author has declared that no competing interests exist.

REFERENCES

1. McCaig LF, McDonald LC, Mandal S, Jernigan DB. *Staphylococcus aureus*-associated skin and soft tissue infections in ambulatory care. Emerging infectious diseases. 2006;12(11):1715–1723. Available:https://doi.org/10.3201/eid1211.060190
2. David MZ, Daum RS. Treatment of *Staphylococcus aureus* Infections. In: Bagnoli F., Rappuoli R., Grandi G. (eds) *Staphylococcus aureus.* Current Topics in Microbiology and Immunology, vol 409. Springer, Cham. 2017;325-383. Available:https://doi.org/10.1007/82_2017_42
3. Lowy FD. *Staphylococcus aureus* infections. The New England Journal of Medicine. 1998;339(8):520–532. https://doi.org/10.1056/NEJM199808203390806
4. Styers D, Sheehan DJ, Hogan P, Sahm DF. Laboratory-based surveillance of current antimicrobial resistance patterns and trends among Staphylococcus aureus: 2005 status in the United States. Annals of Clinical Microbiology and Antimicrobials. 2006;5:2. Available:https://doi.org/10.1186/1476-0711-5-2
5. Magill SS, Edwards JR, Bamberg W, Beldavs ZG, Dumyati G, Kainer MA, Lynfield R, Maloney M, McAllister-Hollod, L, Nadle J, Ray SM, Thompson DL, Wilson LE, Fridkin SK, Emerging Infections Program Healthcare-Associated Infections and Antimicrobial Use Prevalence Survey Team. Multistate point-prevalence survey of health care-associated infections. The New England Journal of Medicine. 2014; 370(13):1198–1208. Available:https://doi.org/10.1056/NEJMoa1306801
6. Oliveira M, Bexiga R, Nunes SF, Carneiro C, Cavaco LM, Bernardo F, Vilela CL. Biofilm-forming ability profiling of *Staphylococcus aureus* and *Staphylococcus epidermidis* mastitis isolates. Veterinary Microbiology. 2006; 118(1):133–140. Available:https://doi.org/10.1016/j.vetmic.2006.07.008
7. Iregui A, Khan Z, Malik S, Landman, D, Quale J. Emergence of delafloxacin-resistant *staphylococcus aureus* in brooklyn, New York. Clinical Infectious Diseases. 2020;70(8):1758-1760. Available:https://doi.org/10.1093/cid/ciz787
8. Suaya JA, Mera RM, Cassidy A, O'Hara, P, Amrine-Madsen H, Burstin S, Miller LG. Incidence and cost of hospitalizations associated with *Staphylococcus aureus* skin and soft tissue infections in the United States from 2001 through 2009. BMC Infectious Diseases. 2014;14:296. Available:https://doi.org/10.1186/1471-2334-14-296
9. Lee BY, Singh A, David MZ, Bartsch, SM, Slayton RB, Huang SS, Zimmer SM, Potter MA, Macal, CM, Lauderdale D. S., Miller LG, Daum RS. The economic burden of community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA). Clinical microbiology and infection: The official publication of the European Society of Clinical Microbiology and Infectious Diseases. 2014;19(6):528–536 Available:https://doi.org/10.1111/j.1469-0691.2012.03914.x
10. Church D, Elsayed S, Reid O, Winston B, Lindsay R. Burn wound infections. Clinical Microbiology Reviews. 2006;19(2):403–434. Available:https://doi.org/10.1128/CMR.19.2.403-434.2006
11. Monroe D. Looking for chinks in the armor of bacterial biofilms. Plos Biology. 2007; 5(11):2458–2461. Available:https://doi.org/10.1371/journal.pbio.0050307
12. World Health Organization. Prioritization of pathogens to guide discovery, research and development of new antibiotics for drug-resistant bacterial infections, including tuberculosis; 2017. Available:https://www.who.int/medicines/areas/rational_use/prioritization-of-pathogens/en/
13. Freitas RA. What is nanomedicine? Nanomedicine: Nanotechnology, Biology and Medicine. 2005;1(1):2–9. Available:https://doi.org/10.1016/j.nano.2004.11.003
14. Fülöp Z, Kurkov SV, Nielsen TT, Larsen KL, Loftsson T. Self-assembly of cyclodextrins: formation of cyclodextrin polymer based nanoparticles. Journal of Drug Delivery Science and Technology. 2012;22(3):215–221. Available:https://doi.org/10.1016/S1773-2247(12)50032-8

15. Moghimi SM, Hunter AC, Murray JC. Nanomedicine: current status and future prospects. The FASEB Journal. 2005; 19(3):311-330.
Available:https://doi.org/10.1096/fj.04-2747rev
16. Riehemann K, Schneider SW, Luger TA, Godin B, Ferrari M, Fuchs H. Nano-medicine—Challenge and Perspectives. Angewandte Chemie International Edition. 2009;48(5):872–897.
Available:https://doi.org/10.1002/anie.200802585
17. Hock SC, Ying YM, Wah CL. A review of the current scientific and regulatory status of nanomedicines and the challenges ahead. PDA Journal of Pharmaceutical Science and Technology. 2011;65(2):177–195.
18. Stankic S, Suman S, Haque F, Vidic J. Pure and multi metal oxide nanoparticles: synthesis, antibacterial and cytotoxic properties. Journal of Nanobiotechnology. 2016;14(1):1-20.
Available:https://doi.org/10.1186/s12951-016-0225-6
19. Kabanov AV, Gendelman HE. Nano-medicine in the diagnosis and therapy of neurodegenerative disorders. Progress in Polymer Science. 2016;32(8):1054–1082.
Available:https://doi.org/10.1016/j.progpolymsci.2007.05.014
20. Etheridge ML, Campbell SA, Erdman AG., Haynes CL, Wolf SM, McCullough J.The big picture on nanomedicine: the state of investigational and approved nanomedicine products. Nanomedicine: Nanotechnology, Biology and Medicine. 2013;9(1):1–14.
Available:https://doi.org/10.1016/j.nano.2012.05.013
21. Lee Chung B, Toth MJ, Kamaly N, Sei YJ, Becraft J, Mulder WJ, Fayad ZA, Farokhzad, OC, Kim Y, Langer R. Nanomedicines for endothelial disorders. Nano Today. 2015;10(6):759–776.
Available:https://doi.org/10.1016/j.nantod.2015.11.009
22. Noorlander CW, Kooi MW, Oomen AG, Park MVDZ, Vandebriel RJ, Geertsma RE. Horizon scan of nanomedicinal products. Nanomedicine. 2015;10(10):1599–1608.
Available:https://doi.org/10.2217/nnm.15.21
23. Kim BYS, Rutka JT, Chan WCW. Nanomedicine. New England Journal of Medicine. 2010;363(25):2434–2443.
Available:https://doi.org/10.1056/nejmra0912273
24. Hawthorne GH, Bernuci MP, Bortolanza M, Issy AC, Del-Bel E. Clinical developments in antimicrobial nanomedicine: Toward novel solutions. Nanostructures for Antimicrobial Therapy: Nanostructures in Therapeutic Medicine Series. 2017;653–668.
Available:https://doi.org/10.1016/B978-0-323-46152-8.00029-9
25. Yu HD, Regulacio MD, Ye E, Han MY. Chemical routes to top-down nano-fabrication. Chemical Society Reviews. 2017;42(14):6006-6018.
Available:https://doi.org/10.1039/c3cs60113g
26. Dhand C, Dwived N, Loh XJ, Ying A. NJ, Verma NK, Beuerman RW, Lakshminarayanan R, Ramakrishna S. Methods and strategies for the synthesis of diverse nanoparticles and their applications: a comprehensive overview. RSC Advances. 2015;5(127).
Available:https://doi.org/10.1039/C5RA19388E
27. Reverberi AP, Kuznetsov NT, Meshalkin VP, Salerno M, Fabiano B. Systematical analysis of chemical methods in metal nanoparticles synthesis. Theoretical Foundations of Chemical Engineering. 2016;50(1):59-66.
Available:https://doi.org/10.1134/S0040579516010127
28. Jamkhande PG, Ghule NW, Bamer AH, Kalaskar MG. Metal nanoparticles synthesis: An overview on methods of preparation, advantages and disadvantages, and applications. Journal of Drug Delivery Science and Technology. 2019;53:101174.
Available:https://doi.org/10.1016/j.jddst.2019.101174
29. Iravani S, Korbekandi H, Mirmohammadi SV, Zolfaghari B. Synthesis of silver nanoparticles: chemical, physical and biological methods. Research in Pharmaceutical Sciences. 2014;9(6):385–406.
30. Guzman M, Dille J, Godet S. Synthesis and antibacterial activity of silver nanoparticles against gram-positive and gram-negative bacteria. Nanomedicine: Nanotechnology, Biology and Medicine. 2012;8(1):37–45.
Available:https://doi.org/10.1016/j.nano.2011.05.007

31. Ealias AM, Saravanakumar MP. A review on the classification, characterisation, synthesis of nanoparticles and their application. IOP Conference Series: Materials Science and Engineering. 2017; 263(3):032019. Available:https://doi.org/10.1088/1757-899x/263/3/032019
32. Hwang I-s, Hwang JH, Choi H, Kim K-J, Lee DG. Synergistic effects between silver nanoparticles and antibiotics and the mechanisms involved. Journal of Medical Microbiology. 2017;61(12):1719–1726. Available:https://doi.org/10.1099/jmm.0.047100-0
33. Chudobova D, Cihalova K., Dostalova, S., Ruttkay-Nedecky, B., Merlos Rodrigo, M. A, Tmejova K, Kopel P, Nejdl L, Kudr, J, Gumulec J, Krizkova S, Kynicky, J., Kizek R, Adam V. Comparison of the effects of silver phosphate and selenium nanoparticles on *Staphylococcus aureus* growth reveals potential for selenium particles to prevent infection. FEMS Microbiology Letters. 2014;351(2):195–201. Available:https://doi.org/10.1111/1574-6968.12353
34. Valodkar, M., Modi, S., Pal, A., & Thakore, S. (2011). Synthesis and anti-bacterial activity of Cu, Ag and Cu–Ag alloy nanoparticles: A green approach. Materials Research Bulletin, 46(3), 384–389. https://doi.org/10.1016/j.materresbull.2010.12.001
35. Wady AF, Machado AL, Foggi CC, Zamperini CA, Zucolotto V, Moffa EB, Vergani CE. Effect of a silver nanoparticles Solution on *Staphylococcus aureus* and *Candida* spp. Journal of Nanomaterials; 2014. Available:https://doi.org/10.1155/2014/545279
36. Ayala-Núñez, N. V., Lara Villegas, H. H., del Carmen Ixtepan Turrent, L., & Rodríguez Padilla, C. (2009). Silver nanoparticles toxicity and bactericidal effect against methicillin-resistant *Staphylococcus aureus*: nanoscale does matter. NanoBiotechnology, 5(1-4), 2–9. Available:https://doi.org/10.1007/s12030-009-9029-1
37. Gao M, Sun L, Wang Z, Zhao Y. Controlled synthesis of Ag nanoparticles with different morphologies and their antibacterial properties. Materials Science and Engineering: C. 2013;33(1):397–404. Available:https://doi.org/10.1016/j.msec.2012.09.005
38. Bankier C, Matharu RK, Cheong YK, Ren GG, Cloutman-Green E, Ciric L. Synergistic antibacterial effects of metallic nanoparticle combinations. Scientific Reports. 2013;9(16074):1–8. Available:https://doi.org/10.1038/s41598-019-52473-2
39. Actis L, Srinivasan, A, Lopez-Ribot, J. L., Ramasubramanian AK, Ong JL. Effect of silver nanoparticle geometry on methicillin susceptible and resistant *Staphylococcus aureus*, and osteoblast viability. Journal of Materials Science: Materials in Medicine. 2015;26(7). Available:https://doi.org/10.1007/s10856-015-5538-8
40. Ansari M, Khan H, Khan A, Cameotra S, Alzohairy M. Anti-biofilm efficacy of silver nanoparticles against MRSA and MRSE isolated from wounds in a tertiary care hospital. Indian Journal of Medical Microbiology. 2015;33(1):101-109. Available:https://doi.org/10.4103/0255-0857.148402
41. Piçarra S, Lopes, E., Almeida, P. L., de Lencastre H, Aires-de-Sousa, M. Novel coating containing molybdenum oxide nanoparticles to reduce *Staphylococcus aureus* contamination on inanimate surfaces. Plos One. 2019;14(3): e0213151. Available:https://doi.org/10.1371/journal.pone.0213151
42. Akram FE, El-Tayeb T, Abou-Aisha K, El-Azizi M. A combination of silver nanoparticles and visible blue light enhances the antibacterial efficacy of ineffective antibiotics against methicillin-resistant *Staphylococcus aureus* (MRSA). Annals of Clinical Microbiology and Antimicrobials. 2016;15(1):48. Available:https://doi.org/10.1186/s12941-016-0164-y
43. Cavassin, E. D., de Figueiredo, L. F. P., Otoch JP, Seckler, M. M., de Oliveira, R. A., Franco, FF., Marangoni, V. S., Zucolotto V., Levin, ASS., Costa, S. F. Comparison of methods to detect the in vitro activity of silver nanoparticles (AgNP) against multidrug resistant bacteria. Journal of Nanobiotechnology. 2016;13(1). Available:https://doi.org/10.1186/s12951-015-0120-6
44. Bhattacharya D, Samanta S, Mukherjee, A, Santra CR, Ghosh, AN, Niyogi SK, Karmakar P. Antibacterial activities of

polyethylene glycol, tween 80 and sodium dodecyl sulphate coated silver nanoparticles in normal and multi-drug resistant bacteria. Journal of Nanoscience and Nanotechnology. 2016;12(3):2513–2521.
Available:https://doi.org/10.1166/jnn.2012.6148

45. Brown AN, Smith K, Samuels TA, Lu, J, Obare SO, Scott, ME. Nanoparticles functionalized with ampicillin destroy multiple-antibiotic-resistant isolates of *Pseudomonas aeruginosa* and *Enterobacter aerogenes* and methicillin-resistant *Staphylococcus aureus*. Applied and Environmental Microbiology. 2012; 78(8):2768-2774.
Available:https://doi.org/10.1128/AEM.06513-11
46. Hur YE, Park Y. Vancomycin-functionalized gold and silver nanoparticles as an antibacterial nanoplatform against methicillin-resistant *Staphylococcus aureus*. Journal of Nanoscience and Nanotechnology. 2016;16(6):6393–6399.
Available:https://doi.org/10.1166/jnn.2016.12393
47. Esmaeillou M, Zarrini G, Rezaee MA. Vancomycin capped with silver nanoparticles as an antibacterial agent against multi-drug resistance bacteria. Advanced pharmaceutical bulletin. 2017; 7(3):479-483.
Available:https://doi.org/10.15171/apb.2017.058
48. Kaur A, Preet S, Kumar V, Kumar R, Kumar R. Synergetic effect of vancomycin loaded silver nanoparticles for enhanced antibacterial activity. Colloids and Surfaces B: Biointerfaces. 2019; 176:62-69.
Available:https://doi.org/10.1016/j.colsurfb.2018.12.043
49. Masri A., Anwar, A., Ahmed, D., Siddiqui, R., Raza Shah, M, Khan N. Silver nanoparticle conjugation-enhanced antibacterial efficacy of clinically approved drugs cephradine and vildagliptin. Antibiotics, 7(4):100.
Available:https://doi.org/10.3390/antibiotics7040100
50. Farooq, U., Ahmad, T., Khan, A., Sarwar, R., Shafiq, J., Raza, Y., Ahmed, A., Ullah, S., Rehman, N.U, Al-Harrasi, A. Rifampicin conjugated silver nanoparticles: a new arena for development of antibiofilm potential against methicillin resistant *Staphylococcus aureus* and *Klebsiella pneumoniae*. International Journal of Nanomedicine. 2019;14:3983–3993.
https://doi.org/10.2147/IJN.S198194
51. Shamaila, S., Zafar, N., Riaz, S., Sharif, R., Nazir, J, Naseem, S. Gold nanoparticles: An efficient antimicrobial agent against enteric bacterial human pathogen. Nanomaterials. 2016;6(4):71.
Available:https://doi.org/10.3390/nano6040071
52. Li WR, Xie, X. B., Shi, Q. S., Duan, S. S., Ouyang, Y. S, Chen Y. Ben. Antibacterial effect of silver nanoparticles on *Staphylococcus aureus*. BioMetals. 2011; 24(1):135–141.
Available:https://doi.org/10.1007/s10534-010-9381-6
53. Rai A, Prabhune A, Perry CC. Antibiotic mediated synthesis of gold nanoparticles with potent antimicrobial activity and their application in antimicrobial coatings. Journal of Materials Chemistry. 2011; 20(32):6789–6798.
Available:https://doi.org/10.1039/c0jm00817f
54. Yang X, Zhang L, Jiang, X. Aminosaccharide–gold nanoparticle assemblies as narrow-spectrum antibiotics against methicillin-resistant *Staphylococcus aureus*. Nano Research. 2018;11(12):6237–6243.
Available:https://doi.org/10.1007/s12274-018-2143-4
55. Ahangari A, Salouti M, Heidari Z., Kazemizadeh AR, Safari AA. Development of gentamicin-gold nanospheres for antimicrobial drug delivery to *Staphylococcal* infected foci. Drug Delivery. 2013;20(1):34–39.
Available:https://doi.org/10.3109/10717544.2012.746402
56. Kalita S, Kandimalla, R, Sharma KK, Kataki AC, Deka, M, Kotoky, J. Amoxicillin functionalized gold nanoparticles reverts MRSA resistance. Materials Science and Engineering: C. 2016;61:720–727.
Available:https://doi.org/10.1016/j.msec.2015.12.078
57. Fan, Y., Pauer, A. C., Gonzales, A. A, Fenniri, H. Enhanced antibiotic activity of ampicillin conjugated to gold nanoparticles on PEGylated rosette nanotubes. International Journal of Nanomedicine. 2019;14:7281–7289.
Available:https://doi.org/10.2147/IJN.S209756

58. Gu H, Ho PL, Tong E, Wang L, Xu B. Presenting vancomycin on nanoparticles to enhance antimicrobial activities. Nano Letters. 2019;3(9):1261–1263.
Available:https://doi.org/10.1021/nl034396z
59. Saha B, Bhattacharya J, Mukherjee A., Ghosh A, Santra, C, Dasgupta, AK, Karmakar, P. In vitro structural and functional evaluation of gold nanoparticles conjugated antibiotics. Nanoscale Research Letters, 2(12):614–622.
Available:https://doi.org/10.1007/s11671-007-9104-2
60. Darabpour, E., Kashef, N., Amini, S. M., Kharrazi, S, Djavid, G. E. Fast and effective photodynamic inactivation of 4-day-old biofilm of methicillin-resistant *Staphylococcus aureus* using methylene blue-conjugated gold nanoparticles. Journal of Drug Delivery Science and Technology. 2017;37:134–140.
Available:https://doi.org/10.1016/j.jddst.2016.12.007
61. Kuo W-S, Chang, C-N, Chang Y-T, Yeh, C-S. Antimicrobial gold nanorods with dual-modality photodynamic inactivation and hyperthermia. Chemical Communications. 2009;(32):4853–4855.
Available:https://doi.org/10.1039/B907274H
62. Meeker DG, Jenkins SV, Miller EK, Beenken KE, Loughran AJ, Powless, A., Muldoon TJ, Galanzha, EI, Zharov VP, Smeltzer MS, Chen, J. Synergistic photothermal and antibiotic killing of biofilm-associated *Staphylococcus aureus* using targeted antibiotic-loaded gold nanoconstructs. ACS Infectious Diseases. 2016;2(4):241–250.
Available:https://doi.org/10.1021/acsinfecdis.5b00117
63. Meeker, DG., Wang, T, Harrington, WN., Zharov, VP., Johnson, S.A, Jenkins, SV., Oyibo, SE., Walker, C. M., Mills, W. B., Shirtliff, ME, Beenken, KE. Versatility of targeted antibiotic-loaded gold nanoconstructs for the treatment of biofilm-associated bacterial infections. International Journal of Hyperthermia. 2018;34(2):209-219.
Available:https://doi.org/10.1080/02656736.2017.1392047
64. Wei, SC, Chang, L., Huang CC, Chang, HT. Dual-functional gold nanoparticles with antimicrobial and proangiogenic activities improve the healing of multidrug-resistant bacteria-infected wounds in diabetic mice. Biomaterials science. 2019;7(11:4482-4490.
Available:https://doi.org/10.1039/c9bm00772e
65. Hu, D., Li, H., Wang, B., Ye, Z., Lei, W., Jia, F., Jin, Q., Ren, K.F, Ji, J. Surface-adaptive gold nanoparticles with effective adherence and enhanced photothermal ablation of methicillin-resistant *Staphylococcus aureus* biofilm. ACS Nano. 2017;11(9):9330–9339.
Available:https://doi.org/10.1021/acsnano.7b04731
66. Ramasamy, M, Lee, J.-H, Lee, J. Development of gold nanoparticles coated with silica containing the antibiofilm drug cinnamaldehyde and their effects on pathogenic bacteria. International Journal of Nanomedicine. 2017;12:2813–2828.
https://doi.org/10.2147/IJN.S132784
67. Mizdal CR., Stefanello, S. T., Da Costa Flores, V., Agertt, VA, Bonez PC, Rossi GG., da Silva TC, Soares FAA, de Lourenço Marques L, de Campos MMA. The antibacterial and anti-biofilm activity of gold-complexed sulfonamides against methicillin-resistant *Staphylococcus aureus*. Microbial Pathogenesis. 2018;123: 440–448.
Available:https://doi.org/10.1016/j.micpath.2018.08.002
68. Xie, Y., Liu, Y., Yang, J., Liu, Y., Hu, F., Zhu, K., & Jiang, X. Gold nanoclusters for targeting methicillin-resistant *Staphylococcus aureus* in vivo. Angewandte Chemie International Edition. 2018;57(15):3958–3962.
Available:https://doi.org/10.1002/anie.201712878
69. Penders, J, Stolzoff, M., Hickey, DJ., Andersson, M, Webster, TJ. Shape-dependent antibacterial effects of non-cytotoxic gold nanoparticles. International Journal of Nanomedicine. 2017L12:2457–2468.
Available:https://doi.org/10.2147/IJN.S124442
70. Hameed, S, Wang, Y, Zhao, L., Xie, L, Ying Y. Shape-dependent significant physical mutilation and antibacterial mechanisms of gold nanoparticles against foodborne bacterial pathogens (*Escherichia coli*, *Pseudomonas aeruginosa* and *Staphylococcus aureus*) at lower concentrations. Materials Science and Engineering: C. 2020;108:110338.

Available:https://doi.org/10.1016/j.msec.2019.110338
71. Pissuwan, D., Cortie, CH., Valenzuela, S. M, Cortie, MB. Functionalised gold nanoparticles for controlling pathogenic bacteria. Trends in Biotechnology. 2010;28(4):207–213. Available:https://doi.org/10.1016/j.tibtech.2009.12.004
72. Bermúdez-Jiménez, C., Romney, M. G., Roa-Flores, S. A., Martínez-Castañón, G., & Bach, H. (2019). Hydrogel-embedded gold nanorods activated by plasmonic photothermy with potent antimicrobial activity. Nanomedicine: Nanotechnology, Biology and Medicine, 22, 102093. https://doi.org/10.1016/j.nano.2019.102093
73. Berry, C. C., & Curtis, A. S. G. (2003). Functionalisation of magnetic nanoparticles for applications in biomedicine. Journal of Physics D: Applied Physics, 36(13), R198-R206. https://doi.org/10.1088/0022-3727/36/13/203
74. Mahmoudi, M., Sahraian, M. A., Shokrgozar, M. A., & Laurent, S. (2011). Superparamagnetic Iron Oxide Nanoparticles: Promises for Diagnosis and Treatment of Multiple Sclerosis. ACS Chemical Neuroscience, 2(3), 118–140. https://doi.org/10.1021/cn100100e
75. Manna, P. K., Nickel, R., Wroczynskyj, Y., Yathindranath, V., Li, J., Liu, S., Thliveris, J. A., Klonisch, T., Miller, D. W., and van Lierop, J. (2018). Simple, hackable, size-selective, amine-functionalized Fe-oxide nanoparticles for biomedical applications. Langmuir, 34(8), 2748–2757. https://doi.org/10.1021/acs.langmuir.7b02822
76. Tran, N., Mir, A., Mallik, D., Sinha, A., Nayar, S., & Webster, T. J. (2010). Bactericidal effect of iron oxide nanoparticles on *Staphylococcus aureus*. International Journal of Nanomedicine, 5, 277-283. https://doi.org/10.2147/ijn.s9220
77. Azam, A., Ahmed, A. S., Oves, M., Khan, M. S., Habib, S. S., & Memic, A. (2012). Antimicrobial activity of metal oxide nanoparticles against Gram-positive and Gram-negative bacteria: a comparative study. International Journal of Nanomedicine, 7, 6003–6009. https://doi.org/10.2147/IJN.S35347
78. Ravikumar S, Gokulakrishnan R, Boomi P. In vitro antibacterial activity of the metal oxide nanoparticles against urinary tract infectious bacterial pathogens. Asian Pacific Journal of Tropical Disease. 2012;2(2):85–89. https://doi.org/10.1016/s2222-1808(12)60022-x
79. Ismail RA, Sulaiman GM, Abdulrahman, SA, Marzoog TR. Antibacterial activity of magnetic iron oxide nanoparticles synthesized by laser ablation in liquid. Materials Science and Engineering: C. 2015;53:286–297. Available:https://doi.org/10.1016/j.msec.2015.04.047
80. Aruoja, V., Pokhrel, S., Sihtmäe, M., Mortimer, M., Mädler, L, Kahru, A.Toxicity of 12 metal-based nanoparticles to algae, bacteria and protozoa. Environmental Science: Nano. 2015;2(6):630–644. Available:https://doi.org/10.1039/c5en00057b
81. Velusamy, P., Chia-Hung, S., Shritama, A., Kumar, G. V., Jeyanthi, V, Pandian, K. Synthesis of oleic acid coated iron oxide nanoparticles and its role in anti-biofilm activity against clinical isolates of bacterial pathogens. Journal of the Taiwan Institute of Chemical Engineers. 2016;59:450–456. Available:https://doi.org/10.1016/j.jtice.2015.07.018
82. Manna, P. K., Nickel, R., Li, J., Wroczynskyj, Y., Liu, S., & van Lierop, J. (2019). EDTA-Na_3 functionalized Fe_3O_4 nanoparticles: Grafting density control for MRSA eradication. Dalton Transactions, 48(19), 6588–6595. Available:https://doi.org/10.1039/c8dt05152f
83. Kim, M.-H., Yamayoshi, I., Mathew, S., Lin, H., Nayfach, J, Simon SI. Magnetic nanoparticle targeted hyperthermia of cutaneous *Staphylococcus aureus* infection. Annals of Biomedical Engineering. 2013;41(3):598–609. https://doi.org/10.1007/s10439-012-0698-x
84. Nickel, R., Kazemian, M. R., Wroczynskyj, Y., Liu S, van Lierop J. Exploiting shape-selected iron oxide nanoparticles for the destruction of robust bacterial biofilms -- active transport of biocides via surface charge and magnetic field control. Nanoscale; 2020. https://doi.org/10.1039/c9nr09484a
85. Pang, H., Lu, Q., Li, Y, Gao, F. Facile synthesis of nickel oxide nanotubes and their antibacterial, electrochemical and magnetic properties. Chemical Communications. 2009;(48):7542.

https://doi.org/10.1039/b914898a

86. Baek, Y.-W, An, Y.-J. Microbial toxicity of metal oxide nanoparticles (CuO, NiO, ZnO, and Sb_2O_3) to *Escherichia coli*, *Bacillus subtilis*, and *Streptococcus aureus*. Science of The Total Environment, 2011;409(8):1603–1608. Available:https://doi.org/10.1016/j.scitotenv.2011.01.014
87. Argueta-Figueroa L., Morales-Luckie R. A., Scougall-Vilchis RJ, Olea-Mejía OF. Synthesis, characterization and antibacterial activity of copper, nickel and bimetallic Cu–Ni nanoparticles for potential use in dental materials. Progress in Natural Science: Materials International. 2014; 24(4):321–328. Available:https://doi.org/10.1016/j.pnsc.2014.07.002
88. Mirhosseini, M., Kheiri Hafshejani, B., Dashtestani, F, Hakimian, F, Haghirosadat, BF. Antibacterial activity of nickel and nickel hydroxide nanoparticles against multidrug resistance K. pneumonia and E. coli isolated urinary tract. Nanomedicine Journal. 2018;5(1):19–26. Available:https://doi.org/10.22038/nmj.2018.05.004
89. Dadi, R., Rabah, A., Traore, M., Mielcarek, C, Kanaev, A. Antibacterial activity of ZnO and CuO nanoparticles against gram positive and gram negative strains. Materials Science and Engineering: C. 2019;104:109968. Available:https://doi.org/10.1016/j.msec.2019.109968
90. Moniri Javadhesari, S., Alipour, S., Mohammadnejad, S., Akbarpour, MR. Antibacterial activity of ultra-small copper oxide (II) nanoparticles synthesized by mechanochemical processing against *S. aureus* and E. coli. Materials Science and Engineering C. 2019;105:110011. Available:https://doi.org/10.1016/j.msec.2019.110011
91. Swarnkar, R. K., Pandey, J. K., Soumya, K. K., Dwivedi, P., Sundaram, S., Prasad, S Gopal R. Enhanced antibacterial activity of copper/copper oxide nanowires prepared by pulsed laser ablation in water medium. Applied Physics A. 2016;122(7). Available:https://doi.org/10.1007/s00339-016-0232-3
92. Giannousi, K., Lafazanis, K., Arvanitidis, J., Pantazaki, A, Dendrinou-Samara, C. Hydrothermal synthesis of copper based nanoparticles: antimicrobial screening and interaction with DNA. Journal of Inorganic Biochemistry. 2014;133:24-32. Available:http://doi.org/10.1016/j.jinorgbio.2013.12.009
93. Kruk, T., Szczepanowicz, K., Stefańska, J., Socha RP, Warszyński P. Synthesis and antimicrobial activity of monodisperse copper nanoparticles. Colloids and surfaces B: Biointerfaces, 128, 17-22. Available:https://doi.org/10.1016/j.colsurfb.2015.02.009
94. Jadhav, S., Gaikwad, S., Nimse, M, Rajbhoj, A. Copper oxide nanoparticles: synthesis, characterization and their antibacterial activity. Journal of Cluster Science. 2011;22(2):121–129. Available:https://doi.org/10.1007/s10876-011-0349-7
95. Ren, G., Hu, D, Cheng, EW., Vargas-Reus, MA., Reip P, Allaker, RP. Characterisation of copper oxide nanoparticles for antimicrobial applications. International journal of antimicrobial agents. 2009;33(6):587-590. Available:https://doi.org/10.1016/j.ijantimicag.2008.12.004
96. Chatterjee, AK, Sarkar RK, Chattopadhyay, AP, Aich, P., Chakraborty, R, Basu, T. A simple robust method for synthesis of metallic copper nanoparticles of high antibacterial potency against *E. coli*. Nanotechnology. 2012;23(8):085103. Available:https://doi.org/10.1088/0957-4484/23/8/085103
97. Usman, MS, Zowalaty MEE., Shameli, K, Zainuddin N, Salama M, Ibrahim NA. Synthesis, characterization, and antimicrobial properties of copper nanoparticles. International Journal of Nanomedicine. 2011;8:4467-4479. Available:https://doi.org/10.2147/IJN.S50837
98. Moshalagae Motlatle A, Kesavan Pillai S, Rudolf Scriba M, Sinha Ray, S. Chemical synthesis, characterization and evaluation of antimicrobial properties of Cu and its oxide nanoparticles. Journal of Nanoparticle Research. 2016;18(10):1–10. Available:https://doi.org/10.1007/s11051-016-3614-8
99. Agarwala M, Choudhury B, Yadav RNS. Comparative study of antibiofilm activity of copper oxide and iron oxide nanoparticles against multidrug resistant biofilm forming uropathogens. Indian Journal of Microbiology. 2004;54(3):365-368.

Available:https://doi.org/10.1007/s12088-014-0462-z

100. Singh A, Ahmed, A, Prasad KN, Khanduja S., Singh SK., Srivastava JK, Gajbhiye, NS. Antibiofilm and membrane-damaging potential of cuprous oxide nanoparticles against *Staphylococcus aureus* with reduced susceptibility to vancomycin. Antimicrobial agents and chemotherapy, 2015;59(11):6882-6890. Available:https://doi.org/10.1128/AAC.01440-15
101. Emami-Karvani Z, Chehrazi P. Antibacterial activity of ZnO nanoparticle on Gram-positive and Gram-negative bacteria. African Journal of Microbiology Research. 2011;5(12):1368–1373. Available:https://doi.org/10.5897/AJMR10.159
102. Pati R., Mehta, R. K., Mohanty, S., Padhi, A., Sengupta, M., Vaseeharan, B., Goswami, C, Sonawane A. Topical application of zinc oxide nanoparticles reduces bacterial skin infection in mice and exhibits antibacterial activity by inducing oxidative stress response and cell membrane disintegration in macrophages. Nanomedicine: nanotechnology, biology, and Medicine. 2014;10(6):1195–12,08. Available:https://doi.org/10.1016/j.nano.2014.02.012
103. Daghdari, G. S., Ahmadi, M., Dastmalchi Saei, H., & Tehrani, A. A. (2017). The effect of ZnO nanoparticles on bacterial load of experimental infectious wounds contaminated with *Staphylococcus aureus* in mice. Nanomedicine Journal. 2017; 4(4):232–236. Available:https://doi.org/10.22038/nmj.2017.04.005
104. Jesline A, John NP, Narayanan PM, Vani C, Murugan S. Antimicrobial activity of zinc and titanium dioxide nanoparticles against biofilm-producing methicillin-resistant *Staphylococcus aureus*. Applied Nanoscience. 2015;5(2):157–162. https://doi.org/10.1007/s13204-014-0301-x
105. Saliani M, Jalal R, Goharshadi EK. Effects of pH and temperature on antibacterial activity of zinc oxide nanofluid against *Escherichia coli* O157: H7 and *Staphylococcus aureus*. Jundishapur Journal of Microbiology. 2015;8(2):e17115. Available:https://doi.org/10.5812/jjm.17115
106. Reyes-Torres, MA, Mendoza-Mendoza, E., Miranda-Hernández, ÁM., Pérez-Díaz, MA., López-Carrizales, M., Peralta-Rodríguez RD, Sánchez-Sánchez R, Martinez-Gutierrez F. Synthesis of CuO and ZnO nanoparticles by a novel green route: Antimicrobial activity, cytotoxic effects and their synergism with ampicillin. Ceramics International; 2019. Available:https://doi.org/10.1016/j.ceramint.2019.08.171
107. Kadiyala U, Turali-Emre ES, Bahng JH, Kotov NA, Van Epps JS. Unexpected insights into antibacterial activity of zinc oxide nanoparticles against methicillin resistant *Staphylococcus aureus* (MRSA). Nanoscale. 2017;10(10):4927–4939. Available:https://doi.org/10.1039/C7NR08499D
108. Choi K-H, Nam KC, Lee S-Y, Cho G, Jung, J-S, Kim H-J, Park BJ. Antioxidant potential and antibacterial efficiency of caffeic acid-functionalized ZnO nanoparticles. Nanomaterials. 2017;7(6): 148. Available:https://doi.org/10.3390/nano7060148
109. Patra P., Mitra, S., Debnath, N., Pramanik, P, Goswami A. Ciprofloxacin conjugated zinc oxide nanoparticle: A camouflage towards multidrug resistant bacteria. Bulletin of Materials Science. 2014;37(2): 199–206. Available:https://doi.org/10.1007/s12034-014-0637-6
110. De Souza RC, Haberbeck, LU, Riella HG, Ribeiro DHB, Carciofi BAM. Antibacterial activity of zinc oxide nanoparticles synthesized by solochemical process. Brazilian Journal of Chemical Engineering. 2019;36(2):885–893. Available:https://doi.org/10.1590/0104-6632.20190362s20180027
111. Horky P, Skalickova, S., Urbankova, L., Baholet, D, Kociova, S., Bytesnikova, Z., Kabourkova, E, Lackova, Z., Cernei, N., Gagic, M, Milosavljevic V. Zinc phosphate-based nanoparticles as a novel antibacterial agent: in vivo study on rats after dietary exposure. Journal of Animal Science and Biotechnology. 2019;10(1):17. Available:https://doi.org/10.1186/s40104-019-0319-8
112. Ghosh T, Dash SK, Chakraborty P, Guha, A., Kawaguchi, K., Roy S., Chattopadhyay, T, Das D. Preparation of antiferromagnetic Co_3O_4 nanoparticles from two different precursors by pyrolytic method: in vitro antimicrobial activity. RSC Advances. 2014;4(29):15022–15029.

Available:https://doi.org/10.1039/C3RA47769J

113. Dogra, V., Kaur, G., Jindal, S., Kumar, R., Kumar S, Singhal NK. Bactericidal effects of metallosurfactants based cobalt oxide/hydroxide nanoparticles against *Staphylococcus aureus*. Science of The Total Environmen; 2019. Available:https://doi.org/10.1016/j.scitotenv.2019.05.078
114. Konieczny P, Goralczyk AG, Szmyd R, Skalniak L, Koziel J, Filon, FL, Crosera M, Cierniak A, Zuba-Surma EK, Borowczyk, J, Laczna, E. Effects triggered by platinum nanoparticles on primary keratinocytes. International Journal of Nanomedicine. 2013;8:3963–3975. Available:https://doi.org/10.2147/IJN.S49612
115. Ayaz Ahmed KB., Raman, T, Anbazhagan V. Platinum nanoparticles inhibit bacteria proliferation and rescue zebrafish from bacterial infection. RSC Advances. 2010; 6(50):44415–44424. Available:https://doi.org/10.1039/c6ra03732a
116. Chwalibog A, Sawosz E, Hotowy A, Szeliga J, Mitura S, Mitura K, Grodzik M, Orlowski P, Sokolowska A. Visualization of interaction between inorganic nanoparticles and bacteria or fungi. International Journal of Nano-medicine. 2010;5:1085–1094. Available:https://doi.org/10.2147/IJN.S13532
117. Hao J, Song G, Liu T, Yi X, Yang K, Cheng L, Liu Z. In vivo long-term biodistribution, excretion, and toxicology of PEGylated transition-metal dichalcogenides MS_2 (M = Mo, W, Ti) nanosheets. Advanced Science. 2018;4(1): 1600160. Available:https://doi.org/10.1002/advs.201600160
118. Dighore N, Jadhav S, Anandgaonker P, Gaikwad S, Rajbhoj A. Molybdenum oxide nanoparticles as antimicrobial agents. Journal of Cluster Science. 2017;28(1): 109-118. Available:https://doi.org/10.1007/s10876-016-1048-1
119. Lopes E, Piçarra, S., Almeida, P. L., de Lencastre H, Aires-de-Sousa, M. Bactericidal efficacy of molybdenum oxide nanoparticles against antimicrobial-resistant pathogens. Journal of Medical Microbiology. 2018;67(8):1042–1046. Available:https://doi.org/10.1099/jmm.0.000789
120. Desai N, Mali S, Kondalkar V, Mane R, Hong C, Bhosale, P. Chemically grown MoO_3 nanorods for antibacterial activity study. Journal of Nanomedicine & Nanotechnology. 2015;6(6):1. Available:https://doi.org/10.4172/2157-7439.1000338
121. Roy AS, Parveen A, Koppalkar AR, Ambika Prasad MVN. Effect of nano titanium dioxide with different antibiotics against methicillin resistant *Staphylococcus aureus*. Journal of Biomaterial Nanobiotechnology. 2010;1(1):37–41. Available:https://doi.org/10.4236/jbnb.2010.11005
122. Orapiriyakul W, Young PS, Damiati L, Tsimbouri PM. Antibacterial surface modification of titanium implants in orthopaedics. Journal of Tissue Engineering. 2018;9:204173141878983. Available:https://doi.org/10.1177/2041731418789838
123. Haq S., Rehman, W, Waseem, M., Javed, R., Mahfooz-ur-Rehman, & Shahid, M. Effect of heating on the structural and optical properties of TiO_2 nanoparticles: antibacterial activity. Applied Nanoscience. 2018;8(1-2):11–18. Available:https://doi.org/10.1007/s13204-018-0647-6
124. Fei B, Deng Z, Xin JH, Zhang Y, Pang, G. Room temperature synthesis of rutile nanorods and their applications on cloth. Nanotechnology. 2006;17(8):1927–1931. Available:https://doi.org/10.1088/0957-4484/17/8/021
125. Shiraishi K, Koseki H, Tsurumoto, T, Baba K, Naito, M, Nakayama, K, Shindo H. Antibacterial metal implant with a TiO_2-conferred photocatalytic bactericidal effect against *Staphylococcus aureus*. Surface and Interface Analysis. 2009;41(1):17–22. Available:https://doi.org/10.1002/sia.2965
126. Shah RR, Kaewgun S, Lee BI, Tzeng T-RJ. The antibacterial effects of biphasic brookite-anatase titanium dioxide nanoparticles on multiple-drug-resistant *Staphylococcus aureus*. Journal of Biomedical Nanotechnology. 2008;4(3): 339–348. Available:https://doi.org/10.1166/jbn.2008.324
127. Adams CP, Walker KA, Obare SO, Docherty KM. Size-dependent antimicrobial effects of novel palladium

nanoparticles. Plos One. 2015;9(1): e85981.
Available:https://doi.org/10.1371/journal.pone.0085981

128. Fang G, Li, W., Shen, X, Perez-Aguilar, J. M, Chong, Y., Gao, X., Chai, Z., Chen, C., Ge C, Zhou R. Differential Pd-nanocrystal facets demonstrate distinct antibacterial activity against Gram-positive and Gram-negative bacteria. Nature communications. 2018;9(1):1-9.
Available:https://doi.org/10.1038/s41467-017-02502-3
129. Azhir, E., Etefagh, R., Shahtahmasebi, N., Mashreghi M, Pordeli P. Preparation, characterization and antibacterial activity of manganese oxide nanoparticles. Physical Chemistry Research. 2015;3(3):197–204.
Available:https://doi.org/10.22036/pcr.2015.9329
130. Cherian, E., Rajan, A, Baskar, G. Synthesis of manganese dioxide nanoparticles using co-precipitation method and its antimicrobial activity. International Journal of Modern Science and Technology. 2016;1:17-22.
131. Salehi B, Mehrabian S, Ahmadi M. Investigation of antibacterial effect of cadmium oxide nanoparticles on *Staphylococcus aureus* bacteria. Journal of Nanobiotechnology. 2014;12:26.
Available:https://doi.org/10.1186/s12951-014-0026-8
132. Nandhini, M., Monika, M., Prakash, V., Pawar J, Henry, R. Synthesis and characterization of cadmium oxide nanoparticles for antibacterial activity. In Proceedings of the 3rd International Conference on Communication and Electronics Systems, ICCES. 2018;195–197.
Available:https://doi.org/10.1109/CESYS.2018.8724000
133. Abd AN, Al Marjani MF, Kadham ZA. Synthesis of CdO NPS for antimicrobial activity. International Journal of Thin Film Science and Technology. 2018;7(1):43-47.
Available:https://doi.org/10.18576/ijtfst/070106
134. Karthik K, Dhanuskodi S, Gobinath C, Prabukumar S, Sivaramakrishnan S. Multifunctional properties of CdO nanostructures synthesised through microwave assisted hydrothermal method. Materials Research Innovations. 2019; 23(5):310-318.
Available:https://doi.org/10.1080/14328917.2018.1475443
135. Natalio, F., André, R., Hartog AF, Stoll, B., Jochum KP, Wever R, Tremel, W. Vanadium pentoxide nanoparticles mimic vanadium haloperoxidases and thwart biofilm formation. Nature Nanotechnology. 2012;7(8):530–535.
Available:https://doi.org/10.1038/nnano.2012.91
136. Wang J, Zhou H, Guo G, Cheng, T., Peng X, Mao X, Li J, Zhang X. A functionalized surface modification with vanadium nanoparticles of various valences against implant-associated bloodstream infection. International Journal of Nanomedicine. 2017;12:3121-3136.
Available:https://doi.org/10.2147/ijn.s129459
137. Wang L, Hu, C, Shao L. The antimicrobial activity of nanoparticles: present situation and prospects for the future. International Journal of Nanomedicine. 2017b;12:1227–1249.
Available:https://doi.org/10.2147/ijn.s121956
138. Fathima JB., Pugazhendhi, A, Venis, R. Synthesis and characterization of ZrO_2 nanoparticles-antimicrobial activity and their prospective role in dental care. Microbial Pathogenesis. 2017;110:245–251.
Available:https://doi.org/10.1016/j.micpath.2017.06.039
139. Sultana, S., Rafiuddin, Khan, MZ, Shahadat, M. Development of ZnO and ZrO_2 nanoparticles: Their photocatalytic and bactericidal activity. Journal of Environmental Chemical Engineering. 2015;3(2):886–891.
Available:https://doi.org/10.1016/j.jece.2015.02.024
140. Thakare VG, Joshi, P. A., Godse, RR., Bhatkar VB., Wadegaokar, PA, Omanwar SK. Evaluation of biological activities of nanocrystalline tetragonal zirconia synthesized via sol-gel method. International Journal of Pharmacy and Pharmaceutical Sciences. 2016;8(6):125–131.
141. Syed MA, Manzoor U., Shah, I, Bukhari SHA. Antibacterial effects of Tungsten nanoparticles on the Escherichia coli strains isolated from catheterized urinary tract infection (UTI) cases and *Staphylococcus aureus*. New Microbiologica. 2010;33(4):329–335.

142. Duan, G., Chen, L., Jing, Z., De Luna, P., Wen, L, Zhang, L., Zhao, L., Xu, J., Li, Z., Yang Z, Zhou R. Robust Antibacterial Activity of Tungsten Oxide (WO_{3-x}) Nanodots. Chemical Research in Toxicology. 2019;32(7):1357–1366. Available:https://doi.org/10.1021/acs.chemrestox.8b00399
143. Ansari, MA., Khan, HM., Khan AA., Pal R, Cameotra, SS. Antibacterial potential of Al_2O_3 nanoparticles against multidrug resistance strains of *Staphylococcus aureus* isolated from skin exudates. Journal of Nanoparticle Research. 2013; 15(10):1970. Available:https://doi.org/10.1007/s11051-013-1970-1
144. Campos, V., Almaguer-Flores, A., Velasco-Arias, D., Díaz, D, Rodil SE. Bismuth and silver nanoparticles as antimicrobial agent over subgingival bacterial and nosocomial strains. Journal of Materials Science and Engineering A. 2018;8(7-8):142-146. Available:https://doi.org/10.17265/2161-6213/2018.7-8.002
145. Kadhim A. Analytical characterization and antimicrobial activity of bismuth nanoparticles synthesized using laser ablation technique. Engineering and Technology Journal, 36(1 Part C); 2018. https://dx.doi.org/10.30684/etj.36.1C.11
146. Vazquez-Munoz, R., Arellano-Jimenez, J, Lopez-Ribot JL. Bismuth nanoparticles obtained by a facile synthesis method exhibit antimicrobial activity against *Staphylococcus aureus* and Candida albicans. bioRxiv preprint; 2020. Available:https://doi.org/10.1101/2020.06.05.137109
147. Amininezhad SM, Rezvani A, Amouheidari, M, Amininejad SM, Rakhshani S. The antibacterial activity of SnO_2 nanoparticles against *Escherichia coli* and *Staphylococcus aureus*. Zahedan Journal of Research in Medical Sciences. 2015;17(9):e1053. Available:https://doi.org/10.17795/zjrms-1053
148. Kumar, S., Kumar, M., Thakur, A., and Patial S. Water treatment using photocatalytic and antimicrobial activities of tin oxide nanoparticles. Indian Journal of Chemical Technology. 2017;24(4):435-440. Available:http://nopr.niscair.res.in/handle/123456789/42562
149. Kumar, V., Sharma, N, Maitra, S. S. In vitro and in vivo toxicity assessment of nanoparticles. International Nano Letters. 2017;7(4):243–256. Available:https://doi.org/10.1007/s40089-017-0221-3
150. Bindhu MR., Umadevi, M., Kavin Micheal, M., Arasu, MV, Abdullah Al-Dhabi, N. Structural, morphological and optical properties of MgO nanoparticles for antibacterial applications. Materials Letters. 2016;166:19–22. Available:https://doi.org/10.1016/j.matlet.2015.12.020
151. Nguyen N-YT, Grelling, N, Wetteland, CL, Rosario R, Liu H. Antimicrobial activities and mechanisms of magnesium oxide nanoparticles (nMgO) against pathogenic bacteria, yeasts, and biofilms. Scientific Reports. 2018;8(16260):1–23. Available:https://doi.org/10.1038/s41598-018-34567-5
152. Sundrarajan M, Suresh J, Gandhi RR. A comparative study on antibacterial properties of MgO nanoparticles prepared under different calcination temperature. Digest journal of nanomaterials and biostructures, 7(3):983-989.
153. Krishnamoorthy K., Manivannan, G., Kim, SJ, Jeyasubramanian, K, Premanathan, M. Antibacterial activity of MgO nanoparticles based on lipid peroxidation by oxygen vacancy. Journal of Nanoparticle Research. 2012;14(9):1063. https://doi.org/10.1007/s11051-012-1063-6
154. Makhluf S, Dror R, Nitzan Y, Abramovich Y, Jelinek R, Gedanken A. Microwave-assisted synthesis of nanocrystalline MgO and its use as a bacteriocide. Advanced Functional Materials. 2005;15(10):1708-1715. Available:https://doi.org/10.1002/adfm.200500029
155. Escudero A, Becerro AI, Carrillo-Carrión, C, Núñez, NO, Zyuzin, MV., Laguna M, González-Mancebo, D, Ocaña M, Parak WJ. Rare earth based nanostructured materials: synthesis, functionalization, properties and bioimaging and biosensing applications. Nanophotonics. 2017;6(5): 881-921. Available:https://doi.org/10.1515/nanoph-2017-0007
156. Daksh D, Agrawal YK. Rare Earth-Doped Zinc Oxide Nanostructures: A Review. Reviews in Nanoscience and Nanotechnology. 2016;5(1):1–27. Available:https://doi.org/10.1166/rnn.2016.1071

157. Ravishankar TN, Ramakrishnappa T, Nagaraju G, Rajanaika H. Synthesis and Characterization of CeO2Nanoparticles via Solution Combustion Method for Photocatalytic and Antibacterial Activity Studies. Chemistry Open. 2015;4(2):146–154.
Available:https://doi.org/10.1002/open.201402046
158. Masadeh MM., Karasneh, GA, Al-Akhras, MA, Albiss BA, Aljarah, KM, Al-azzam Sayer I, Alzoubi KH. Cerium oxide and iron oxide nanoparticles abolish the antibacterial activity of ciprofloxacin against gram positive and gram negative biofilm bacteria. Cytotechnology. 2017; 67(3):427–435.
Available:https://doi.org/10.1007/s10616-014-9701-8
159. Balusamy B, Kandhasamy YG, Senthamizhan A, Chandrasekaran G, Subramanian MS, Kumaravel TS. Characterization and bacterial toxicity of lanthanum oxide bulk and nanoparticles. Journal of Rare Earths. 2015;30(12):1298–1302.
Available:https://doi.org/10.1016/s1002-0721(12)60224-5
160. Dědková K, Kuzníková Ľ, Pavelek L, Matějová K, Kupková J, Barabaszová KČ, Váňa R, Burda J, Vlček J, Cvejn D, Kukutschová J. Daylight induced antibacterial activity of gadolinium oxide, samarium oxide and erbium oxide nanoparticles and their aquatic toxicity. Materials Chemistry and Physics. 2015; 197:226-235.
Available:https://doi.org/10.1016/j.matchemphys.2017.05.039
161. Jangra, SL., Stalin, K., Dilbaghi, N., Kumar, S., Tawale, J., Singh, SP, Pasricha, R. Antimicrobial activity of zirconia (Zro_2) nanoparticles and zirconium complexes. Journal of Nanoscience and Nanotechnology. 2012;12(9):7105–7112.
Available:https://doi.org/10.1166/jnn.2012.6574
162. Ajdary M, Moosavi MA, Rahmati M, Falahati M, Mahboubi M, Mandegary A, Jangjoo S, Mohammadinejad R, Varma, RS. Health concerns of various nanoparticles: A review of their in vitro and in vivo toxicity. Nanomaterials. 2018;8(9): 634.
Available:https://doi.org/10.3390/nano8090634
163. Anselmo AC, Mitragotri S. A review of clinical translation of inorganic nanoparticles. AAPS Journal. 2015;17(5): 1041–1054.
Available:https://doi.org/10.1208/s12248-015-9780-2
164. Elbehiry A, Al-Dubaib, M., Marzouk, E, Moussa I. Antibacterial effects and resistance induction of silver and gold nanoparticles against *Staphylococcus aureus* -induced mastitis and the potential toxicity in rats. Microbiology Open. 2018; 8(4):e00698.
Available:https://doi.org/10.1002/mbo3.698
165. Panáček, A., Kvítek, L., Smékalová, M., Večeřová, R., Kolář, M, Röderová, M., Dyčka, F, Šebela, M, Prucek, R., Tomanec, O, Zbořil R. Bacterial resistance to silver nanoparticles and how to overcome it. Nature Nanotechnology. 2017;13(1):65–71.
Available:https://doi.org/10.1038/s41565-017-0013-y
166. Satalkar P, Elger BS, Hunziker P, Shaw D. Challenges of clinical translation in nanomedicine: A qualitative study. Nanomedicine: Nanotechnology, Biology and Medicine. 2017;12(4):893–900.
Available:https://doi.org/10.1016/j.nano.2015.12.376
167. Shreffler JW, Pullan JE, Dailey KM, Mallik S, Brooks AE. Overcoming hurdles in nanoparticle clinical translation: the influence of experimental design and surface modification. International Journal of Molecular Sciences. 2019;20(23):6056.
Available:https://doi.org/10.3390/ijms20236056

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