


## How do material characteristics and antimicrobial mechanisms affect microbial control and water disinfection performance of metal nanoparticles?

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### ABSTRACT

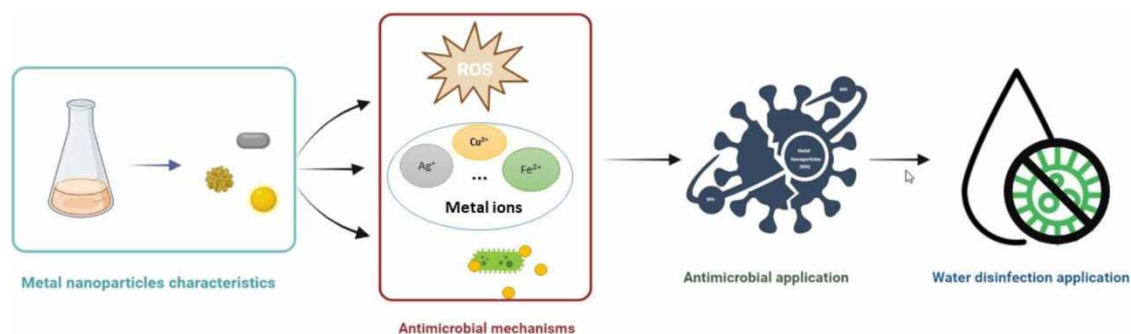
Nanotechnology has been rapidly developing in the past decade, and metal nanomaterials have shown promising improvement in microbial control. Metal nanoparticles have been applied in medical settings for adequate disease spread control and to overcome the challenges of multidrug-resistant microorganisms. Recently, the demand for safe water supply has increased, requiring higher sanitation of the water treatment technology as well as being environmentally sustainable. However, the employed water disinfection technologies cannot meet the elevated demand due to limitations including chemical byproducts, immobility, energy consumption, etc. Metal nanomaterials are considered to be an alternative disinfection technology considering their high efficiency, mobility, and stability. A significant amount of research has been carried out on enhancing the antimicrobial efficiency of metal nanomaterials and determining the underlying antimicrobial mechanisms. This paper provides an overview of emerging metal nanomaterials development, including the synthesis method, material characteristics, disinfection performance, environmental factors, potential mechanism, limitations, and future opportunities in the water disinfection process.

**Key words:** antimicrobial mechanism, bacteria, drinking water, metal nanoparticles, water disinfection

### HIGHLIGHTS

- Antimicrobial mechanisms are governed by microbe–metal nanoparticles interactions.
- Synthesis methods and material characteristics impact microbial control performance.
- Demonstrations via experimental study and simulation support its applicability.
- Nanoscale metal materials have multi-tasking ability versus conventional treatments.
- Limitations of possible toxicity, cost, and manufacturing call for further research.

### GRAPHICAL ABSTRACT



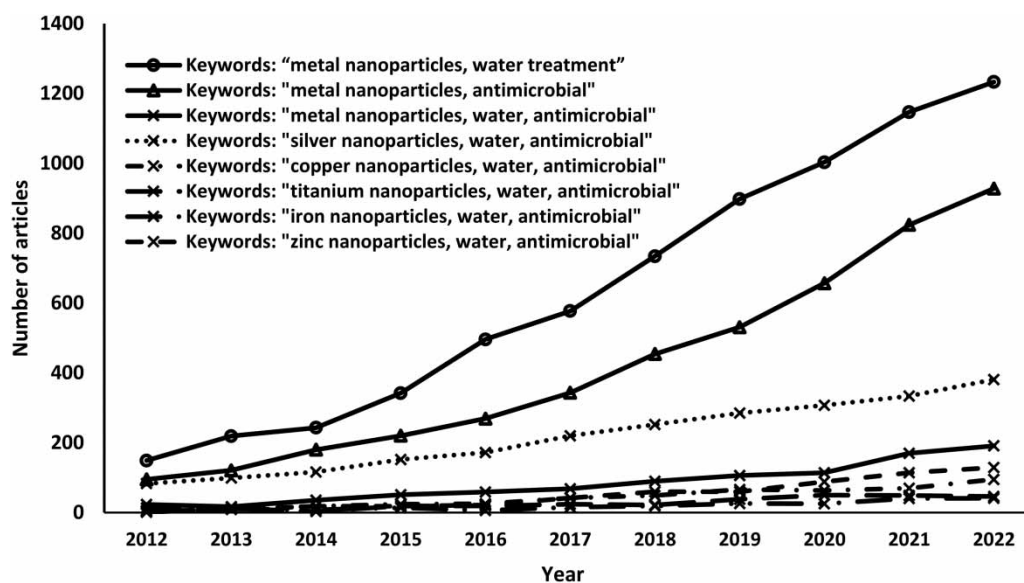
## 1. INTRODUCTION

Illness associated with inadequate water sanitation has been a heavy global health burden. The development of sand filtration and chlorination provides an effective way to end waterborne epidemics in developed countries. However, many rural areas and developing urban regions still do not have access to centralized water treatment

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plants due to their remote locations, lack of funds, and operational difficulties. It has been reported that over two billion people are consuming feces-contaminated drinking water sources and causing over 485,000 deaths each year (Rodgers & Vaughan 2002). It is imperative to provide reliable drinking water sources and effective wastewater management strategies to those in urban and rural areas who do not have a safe drinking water supply to minimize the health risks and infectious diseases associated with waterborne pathogens. The currently employed water disinfection technology mainly includes sand filtration, chlorination, UV disinfection, ozonation, etc. The challenges faced with these developed techniques are currently raising concerns, such as the formation of carcinogenic disinfection byproducts (DBPs) using chlorination and ozonation technologies; moreover, the energy consumption and influent turbidity limitations associated with the performance of UV irradiation limited its application in remote or developing locations (Liu & Zhang 2006; Du *et al.* 2017). The high capital cost or accessibility is another challenge to providing centralized water treatment systems for such areas. Therefore, there is still an essential need for an alternative disinfection technology that can achieve effective performance while being mobile, broad-spectrum, eco-friendly, energy-saving, simple to run, and economically viable.

Metal materials are considered alternative antimicrobial agents, which can be traced back to the 8th century when people used silver to prevent disease transmission (Gnanadhas *et al.* 2013). The US Environmental Protection Agency (US EPA) has also recognized copper as an effective antimicrobial material that could be applied in facilities with high sanitary requirements, such as hospitals (Molteni *et al.* 2010; Colin *et al.* 2018; Vincent *et al.* 2018). Furthermore, researchers found that utilizing metal nanoparticles in the recent global pandemic can effectively control COVID-19 spread on different mediums (Behbudi 2021; Chintagunta *et al.* 2021). Therefore, metal materials have the potential to be developed as point-of-use water treatment systems to improve safe water accessibility. It is also known that the metal materials are inert in a water environment and eliminate the risk of generating toxic DBPs compared to the conventional water disinfection technology (Li *et al.* 2008). Among different metal material forms, metal nanoparticles are expected to be an effective form of metal materials in water disinfection applications considering their large specific surface area and high reactivity, which provide more active sites for their interactions with microbes. Thus, there is an increasing trend in investigating various metal nanoparticles using different synthesized technologies to inactivate broad-spectrum pathogens. According to the quantitative analysis of the publication trend on metal nanoparticles applied in antimicrobial applications and water treatment using the Web of Science database, there has been a significant increase in scientific publications in the recent 10 years, as shown in Figure 1. Furthermore, compared to various types of metal nanomaterials, silver nanoparticles are a leading metal nanomaterial applied in the antimicrobial application and water treatment application. The numbers of the sole study on silver nanoparticles even surpass the number of multi-metal nanoparticles studies. It is envisioned that functional metal nanoparticles can build effective, robust, safe, economically viable, and point-of-use systems to enhance water safety for remote location



**Figure 1** | Year-wise research documents of metal nanoparticles antimicrobial application.

residents like Indigenous communities and developing country residents. It may also be an alternative emergency response technology following catastrophic events to ensure a safe water supply.

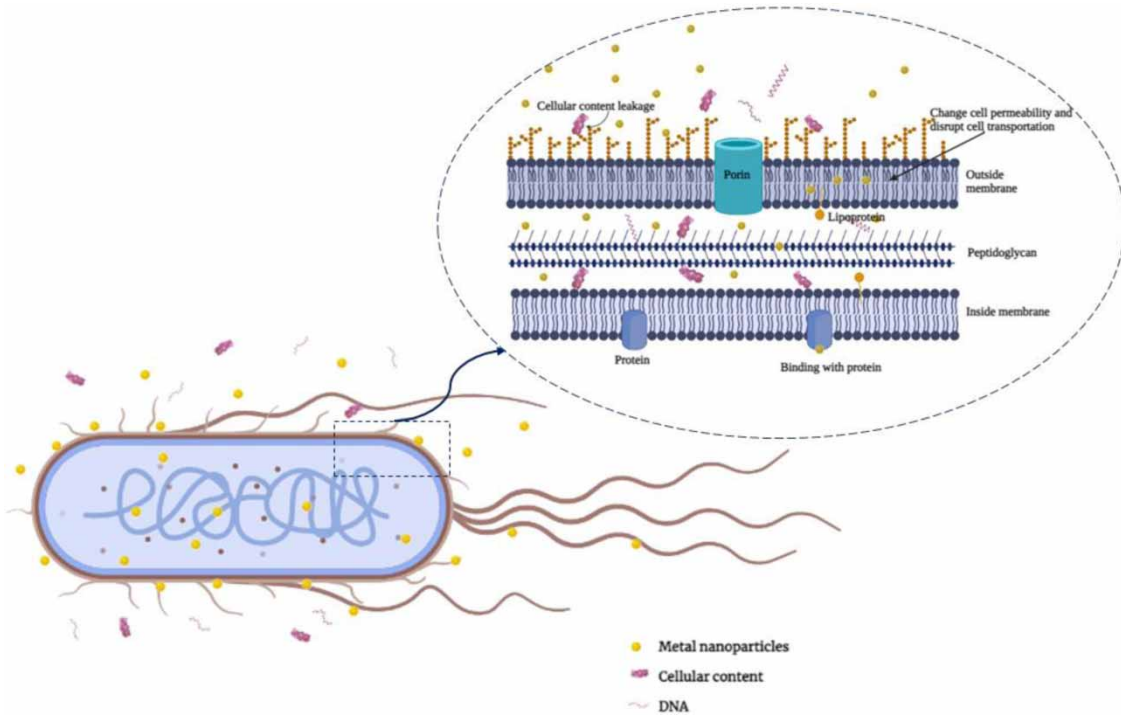
Although metal nanomaterials have been widely studied in recent years, there is no comprehensive review on how metal nanomaterials characteristics may impact the antimicrobial mechanisms and there is a lack of comparison on water disinfection performance of different metal nanomaterials at different scales and conditions. This review paper first discusses the potential antimicrobial mechanisms of metal nanoparticles to facilitate the understanding of the possible interaction between microbes and metal nanoparticles in the following sections. The synthesis methods, material characteristics, and microbial control performance of different metal types are reviewed in this study to further demonstrate the capability of each metal type on antimicrobial activities. The potential dominant antimicrobial mechanism of different metal nanoparticles and how their antimicrobial performance is impacted by material characteristics are elaborated. The performance and applicability of the metal nanoparticles applied in water disinfection are also focused on for the first time in this paper, including studies in both laboratory bench and simulation scales. This review paper aims to reveal the state of the art of antimicrobial research with metal nanomaterials and discusses the feasibility of applying metal nanomaterials in water disinfection with the understanding of the potential antimicrobial mechanisms. This review paper identified the potential of applying metal nanomaterials in water disinfection and also pointed out challenges of further development for researchers to tackle.

## 2. BACTERIOSTATIC MECHANISM OF METAL MATERIALS

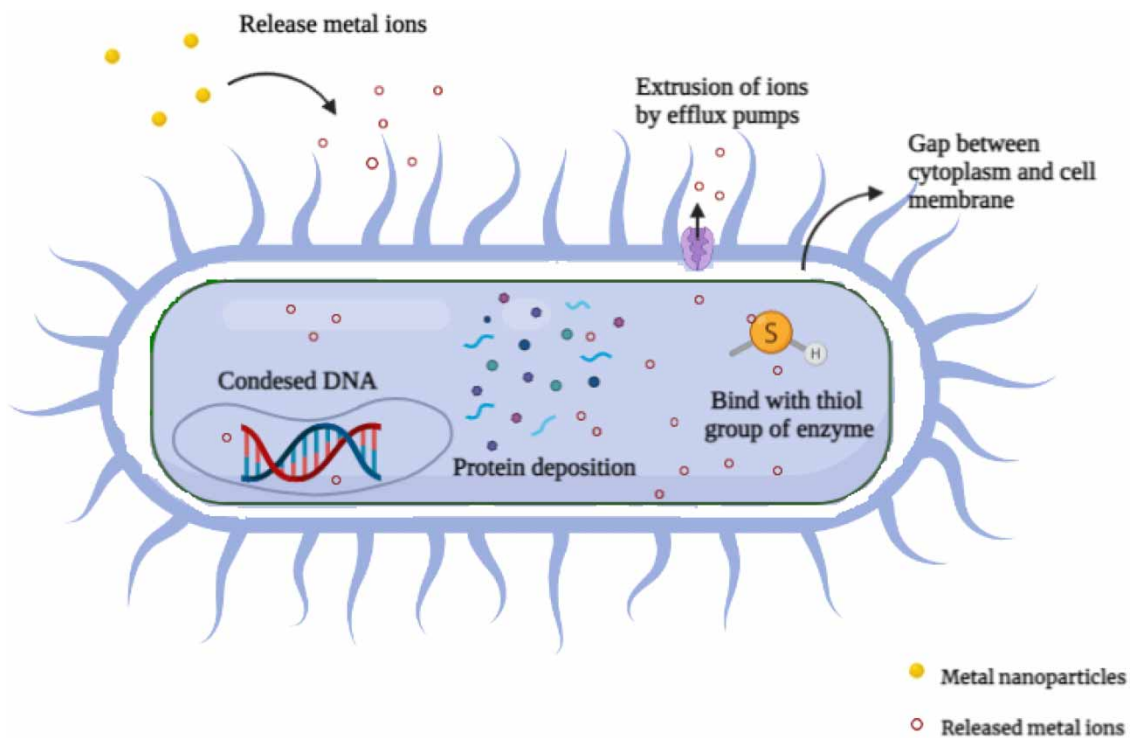
Metal materials are considered alternative antimicrobial agents and have attracted intense research interest worldwide (Miao *et al.* 2019; Falinski *et al.* 2020; Chong & Ge 2021). Research has been carried out on the bacteriostatic mechanisms underlying the antimicrobial activities of metal materials to understand the antimicrobial potential of metal nanoparticles. Although the bacteriostatic mechanism of metal nanoparticles has been investigated during the past decade, controversy still exists. In the process of exploring the antimicrobial mechanisms of metal materials, three main mechanisms were identified: contact-killing effect, liberated metal ions effect, and ROS effect. In this section, the author reviewed each potential antimicrobial mechanism of metal materials and illustrated how the metal material may interact with the cells and how they may inactivate microorganisms. The current findings are grouped into three as per the proposed antimicrobial mechanisms followed by a visualized summary for each mechanism.

**Mechanism A:** One of the most acknowledged mechanisms is the contact-killing effect of the metal nanoparticles as demonstrated in Figure 2. Several studies visualized the interaction between metal nanoparticles and bacteria and showed that the intrusive metal nanoparticles entered inside the bacteria or attached (Sondi & Salopek-Sondi 2004; Morones *et al.* 2005; Vincent *et al.* 2018). It has been indicated that the metal nanoparticles may interact with the cell membrane and peptidoglycan layers, which changed cell permeability or respiration, disrupted cell transportation activities and eventually led to cellular content leakage and cell death (Vincent *et al.* 2018). Gold *et al.* reported that metal-based nanoparticles could interact with the phospholipid layer and bind to cytosolic proteins, which eventually cause cell lysis or death (Gold *et al.* 2018). The antimicrobial mechanism of metal nanoparticles may vary while targeting different microorganisms as per recent studies. For example, in another study, nAg was attached to the special surface protein of HIV, which is responsible for binding with its host cell (Elechiguerra *et al.* 2005). That was considered due to the interaction between nAg and the proteins' disulfide groups.

**Mechanism B:** The second mechanism was based on the effect of liberated metal ions from metal nanoparticles (Figure 3; Frei *et al.* 2023). Feng *et al.* (2000) investigated the silver ions treatment of *Escherichia coli* and *Staphylococcus aureus*. They found that it could cause the internal structural change of bacteria for both Gram-negative and Gram-positive cells. 10 µg/ml AgNO<sub>3</sub> was incubated with the bacteria cells to compare the cell morphology with untreated cells. It was clear that after the treatment of silver ions, the DNA molecules were significantly condensed, and the author also reported an apparent gap between the cytoplasm and cell membrane. Comparatively, the untreated cells had uniform electron density. The morphological change was concluded as the self-protection activities of cells. The interference between silver ions and cells led to cell protein deposition to inhibit ions' entrance into the cytoplasm. Therefore, DNA replication was inhibited and condensed. Another study tested the antibacterial efficiency of silver ions and copper ions on Gram-negative cells (Sicairos-Ruelas *et al.* 2019). The antibacterial properties of silver ions were further validated; on the contrary, copper ions were less effective



**Figure 2** | Potential antimicrobial mechanism of metal nanoparticles in bacterial cells – the contact-killing effect.



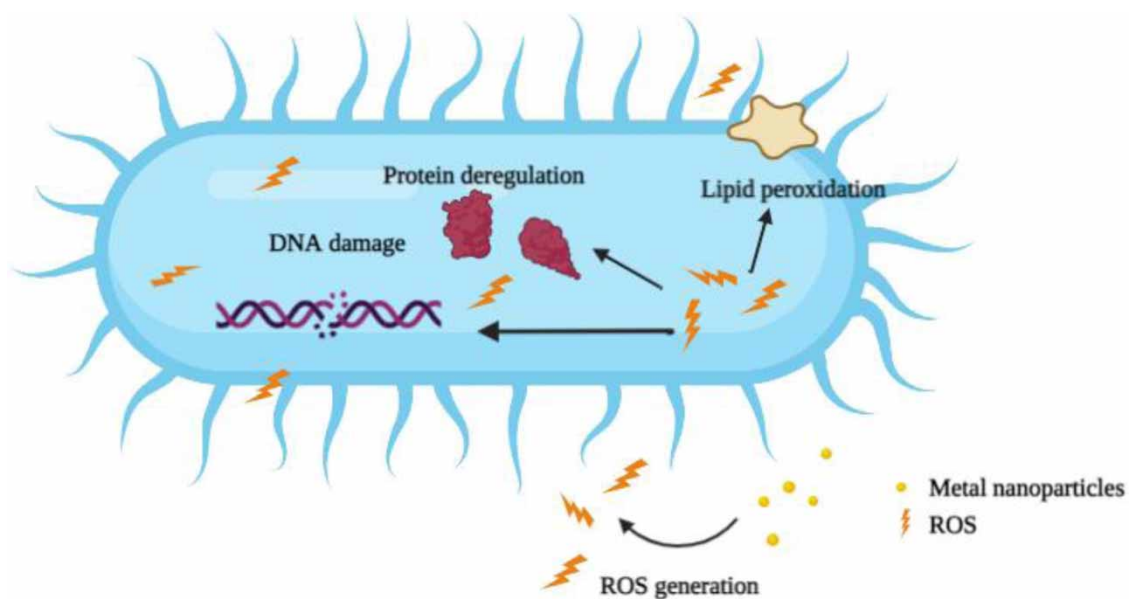
**Figure 3** | Potential antimicrobial mechanism of metal nanoparticles in bacterial cells – the effect of the released ions.

in inactivating some bacteria strains under even a higher concentration. The studies agreed the self-protection activities of the cells might lead to cell death. Some bacteria strains may be less sensitive to the toxicity of copper ions, whereas copper was either extruded by efflux pumps or blocked from the cell membrane. Ge *et al.* studied how the bacteria uptake silver ions in the presence of magnesium ions and discovered that



magnesium ions decreased the antimicrobial activity of silver ions. The presence of magnesium also decreased the intracellular silver mass. That further demonstrated that antimicrobial efficiency is closely related to the mass of intracellular silver ions (Ge *et al.* 2011). In the study of Applerot *et al.* (2012), the antibacterial performances of copper ions and nCu were compared by treating *E. coli*. nCu exhibited an effective bactericidal efficiency; comparatively, no significant antibacterial activity was observed with the treatment of copper ions only. That study gave evidence that leached metal ions toxicity may not be the only mechanism underlying the excellent antimicrobial performance of metal nanoparticles. Another study shared a different stance on the copper ions effect, suggesting that the bacteria inactivation was achieved by interactions between copper ions and cell elements (Park *et al.* 2012). They reported that cupric ions could permeate cell porins and will be reduced to cuprous ions by intracellular reactive oxygen species (ROS). Cuprous ions then interacted with the thiol group to physically disrupt cells, which eventually contributed to the effective antimicrobial performance of copper ions. The researchers compared the bactericidal efficacy of different treatment groups to investigate the toxicity of copper ions, including copper species with chelating agents, reductants, or ROS scavengers, respectively. According to the results, the addition of copper ions and chelating agents completely hindered the inactivation of bacteria. Furthermore, chemical reductants reduced cupric ions to cuprous ions, and the antimicrobial activities were significantly enhanced. Based on that, the result illustrated that cuprous ion is the dominant species of inactivating bacterial cells.

Mechanism C: Interestingly, many other studies reported a different antimicrobial mechanism: metal-induced ROS effects (Li *et al.* 2008; Applerot *et al.* 2012; Moschini *et al.* 2013; Kruk *et al.* 2015; Mukherjee *et al.* 2023). ROS is metabolism of oxygen generated during bacteria growth, and under natural circumstances, cells can detoxify ROS spontaneously by enzymes (Cabiscol Català *et al.* 2000; Fedorova *et al.* 2010). An abundance of studies indicated that metal materials could accelerate ROS generation as catalyzes. Most of the studies stated that the antimicrobial activities of metal were a result of the DNA lesion and protein damage caused by the overloaded ROS. Some studies proved the generation of ROS with the addition of metal nanoparticles using electron spin resonance microscopy (Kim *et al.* 2007; Applerot *et al.* 2012). Applerot *et al.* (2012) reported that the copper nanoparticle could catalyze ROS production, and the concentration of intracellular ROS was quantified, which was positively related to the size of the copper nanoparticles, contact time, and concentration of nanoparticles. It has been indicated that ROS formation could lead to cell protein deregulation, lipid peroxidation, and DNA damage, which eventually leads to cell death, as illustrated in Figure 4 (Touati 2000).



**Figure 4** | Potential antimicrobial mechanism of metal nanoparticles in bacterial cells – the ROS effect.

### 3. ANTIMICROBIAL PROPERTIES OF METAL NANOPARTICLES

The unique antimicrobial property of metal materials promotes the rapid growth of metal nanoparticles and the growth of nanotechnology has drawn attention to its applications in different fields such as surface disinfection, water treatment, and medical hygiene (Besinis *et al.* 2015; Sundberg *et al.* 2015; Rikta 2019). Metal-based nanoparticles have occupied 37% of the nanotechnology market (Sharma *et al.* 2017). Over 30 types of metal and metal composite nanomaterials have the potential to interact with microorganisms (Weber & Rutala 2013). In this section, the antimicrobial properties of metal nanoparticles were discussed following the order of metal type: silver, copper, titanium, iron, and zinc. In connection to water disinfection, we highlighted the applications of the most commonly studied metal-based nanoparticles in the microbial control and water treatment fields. The various factors are also introduced which may impact the antimicrobial performance of nanoparticles in this section, including nanoparticle characteristics, nanoparticle concentration, the coating on the nanoparticles, microorganism strain, and initial concentration of microorganisms. The metal-based nanoparticles' synthesis methods (biosynthesis, liquid chemical reduction, microwave-assisted polyol method, co-precipitation, gel-combustion, etc.), applications, and microbial interaction mechanisms effect are also discussed in this section. This section is to review the state of the art of metal nanoparticles in antimicrobial applications and interprets the potential impact factors of the antimicrobial metal nanoparticles. Furthermore, the links between the impact factors and potential antimicrobial mechanisms are considered and discussed.

#### 3.1. Silver-based nanoparticles (nAg)

Researchers have studied the antimicrobial properties of silver, and the disinfection performance of nAg has been tested in various applications such as hospital hygiene, wound healing, and food packaging (Mohanta *et al.* 2017; Gong *et al.* 2018; Deshmukh *et al.* 2019). Table 1 shows the antimicrobial performance of nAg, and microorganism type and concentration, synthesis method, and nanoparticle characteristics are listed for comparison.

From Table 1, it can be observed that under the same synthesis method, physical and chemical factors such as temperature, pressure, stabilizer, and capping agent concentration affect the shape and size of metal nanoparticles. For instance, in Gao *et al.*'s study, nAg was synthesized using the liquid chemical reduction method and PVP as a surface modification agent (Gao *et al.* 2013). Under the same reduction process, the addition amount of surface modification agent and aging time directly controlled the size and shape variation of nAg. That change in characteristics largely impacted its antimicrobial efficiency as demonstrated in the table. The MIC of triangular nanoplates was almost two times higher than the same-size spherical nAg, which means spherical nAg had superior antimicrobial performance (Gao *et al.* 2013). Similarly, Hong *et al.* also studied the shape effect on the antibacterial activity of silver nanoparticles. They reported that silver nanocubes had the highest antibacterial performance compared to silver nanowires and silver nanospheres under the same concentration (Hong *et al.* 2016). The effective contact area and facet activities vary between different shapes of nanoparticles, and that contributes to the stronger or weaker antimicrobial activities of nanoparticles. It can be observed that a smaller size of nanoparticles can enhance their antimicrobial activities. That is mainly due to the increased specific surface area-to-mass ratio and surface-area-to-volume ratio; thus, it affects the number of active sites (Asghar *et al.* 2018). As discussed in Section 2, mechanism A contact-killing effect may play an important role in the antimicrobial activities of nAg as the size and shape of nanoparticles are decisive factors in its antimicrobial performance. The smaller size of nanoparticles may facilitate their intrusion into the bacteria cell and enhance its contact with cells as shown in Figure 2. Also, the spherical shape of nanoparticles may enhance the mobility of nanoparticles and that may also contribute to a stronger contact-killing effect. Thus, the antibacterial efficiency was higher when the nanoparticle size is smaller or its shape was spherical. Previous studies proved the attachment of nAg to the proteins' disulfide groups (Elechiguerra *et al.* 2005) and Feng *et al.* visualized the attachment between nAg and *E. coli* cells which further prove the effect of mechanism A (Feng *et al.* 2000). Mechanism B and mechanism C may also contribute to the superior performance of nAg; however, the size-dependent and shape-dependent performance reflects that mechanisms B and C should not be the dominant mechanisms.

The concentration of the nAg is another critical factor in achieving the desired inhibition of microorganisms growth in Hong *et al.*'s study that increasing the concentration of nAg enhanced its antibacterial activities no matter the shape of nAg (Hong *et al.* 2016). That may correspond to mechanism B and mechanism C, increased concentration of nAg enhanced the toxicity of silver ion as demonstrated in mechanism B and also accelerated the generation of ROS (Frei *et al.* 2023). Therefore, the concentration of nAg is positively correlated to its antimicrobial efficiency.

**Table 1** | Parameters and results of the studies on the antimicrobial properties of silver nanomaterials

Microorganism type	Microorganism concentration	Synthesis method	Characteristic of NM	Disinfection efficiency	Reference
<i>E. coli</i>	OD <sub>600</sub> = 0.05	Biosynthesis method using green tea leaves extract.	Nanospheres; Size: 20–90 nm.	No growth inhibition was observed under 50 mg/ml nAg.	Sun <i>et al.</i> (2014)
<i>S. aureus</i> (Methicillin-resistant strain)	OD <sub>600</sub> = 0.2; approximately 10 <sup>6</sup> CFU/ml.	Biosynthesis method using green tea leaves extract.	Nanospheres; Size: 10–15 nm.	MIC: 8 ± 0.8 µg/ml after 24 h of shaking.	Asghar <i>et al.</i> (2018)
<i>S. aureus</i> (Methicillin-resistant strain)	OD <sub>600</sub> = 0.2; approximately 10 <sup>6</sup> CFU/ml.	Biosynthesis method using black tea leaves extract.	Nanospheres; Size: 14–20 nm.	MIC: 8 ± 1.1 µg/ml after 24 h of shaking.	Asghar <i>et al.</i> (2018)
<i>Aspergillus flavus</i>	10 <sup>6</sup> spores/ml	Biosynthesis method using green tea leaves extract.	Nanospheres; Size: 10–15 nm.	81.0 ± 3.0% reduction after 15 days of treatment by 100 µg/ml nAg.	Asghar <i>et al.</i> (2018)
<i>Aspergillus flavus</i>	10 <sup>6</sup> spores/ml	Biosynthesis method using black tea leaves extract.	Nanospheres; Size: 14–20 nm.	77.7 ± 3.0% reduction after 15 days of treatment by 100 µg/ml nAg.	Asghar <i>et al.</i> (2018)
<i>E. coli</i>	10 <sup>8</sup> CFU/ml	Liquid chemical reduction method using L-ascorbic acid as a reductant, polyvinyl pyrrolidone (PVP) as a surface modification agent.	Triangle nanoplates; Size: 40–60 nm.	MIC: 15.6 µg/ml after 24 h of shaking.	Gao <i>et al.</i> (2013)
<i>E. coli</i>	10 <sup>8</sup> CFU/ml	Liquid chemical reduction method using L-ascorbic acid as a reductant, PVP as a surface modification agent with prolonging aging time to 5 days.	Nanospheres; Size: 40–60 nm.	MIC: 7.8 µg/ml after 24 h of shaking.	Gao <i>et al.</i> (2013)
<i>E. coli</i>	10 <sup>6</sup> CFU/ml	Microwave-assisted method based on the polyol method with no addition of NaCl.	Nanospheres; Size: 60 ± 15 nm.	MIC: 100 ± 6.0 µg/ml after 24 h of incubation at 200 rpm.	Hong <i>et al.</i> (2016)
<i>E. coli</i>	10 <sup>6</sup> CFU/ml	Microwave-assisted method based on the polyol method with 1 mg addition of NaCl.	Nanocubes; Size: 55 ± 10 nm.	MIC: 75 ± 4.6 µg/ml after 24 h of incubation at 200 rpm.	Hong <i>et al.</i> (2016)
<i>E. coli</i>	10 <sup>6</sup> CFU/ml	Microwave-assisted method based on the polyol method with 5 mg addition of NaCl.	Nanowires; Size: 60 nm diameter and 2–4 µm length.	MIC: > 100 µg/ml after 24 h of incubation at 200 rpm.	Hong <i>et al.</i> (2016)
<i>E. coli</i> (Drug-resistant species isolated from a hospital)	0.5 McFarland Standard	Microwave irradiation method using lemongrass leaves extract.	Nanospherical; Mean size: 32 nm.	ZI: 16 mm after 18 h of treatment by 15 µL of 50% nAg.	Masurkar <i>et al.</i> (2011)
<i>A. niger</i>	1 to 5 × 10 <sup>6</sup> spores/ml	Microwave irradiation method using			Masurkar <i>et al.</i> (2011)

(Continued.)

**Table 1** | Continued

Microorganism type	Microorganism concentration	Synthesis method	Characteristic of NM	Disinfection efficiency	Reference
		lemongrass leaves extract.	Nanospherical; Mean size: 32 nm.	ZI: 17 mm after 18 h of treatment by 15 µL of 50% nAg.	
<i>E. coli</i> (isolated from garden soil samples)	N/A	Biosynthesis method using neem leaves extract.	Nanospherical.	ZI: 6 mm after treatment by 12 µg/ml nAg.	Verma & Mehata (2016)
Murine norovirus (MNV)	6 log TCID <sub>50</sub> /ml	Liquid chemical reduction method.	Size: 7 ± 3 nm.	5 Log <sub>10</sub> reduction after 30 days by 21 mg/L nAg.	Castro-Mayorga <i>et al.</i> (2017)

MIC, minimum inhibitory concentrations; NM: nanomaterial; ZI, zone of inhibition.

Besides the wet chemical preparation methods as listed in Table 1, the biosynthesis method is also discussed. Many researchers proposed and examined the antimicrobial performance of biosynthesized nAg using plant tissues. That is expected to be a green and sustainable preparation method for nanoparticles. Five studies are briefly reviewed in Table 1, which used the extract of tea leaves, lemongrass leaves, or neem leaves to synthesize nAg (Masurkar *et al.* 2011; Sun *et al.* 2014; Verma & Mehata 2016; Asghar *et al.* 2018). Lemongrass leaves synthesized nAg was proven effective in inactivating drug-resistant bacteria strains, and nAg prepared using neem leaves extract also demonstrated active antimicrobial activities (Masurkar *et al.* 2011; Verma & Mehata 2016). Comparatively, nAg synthesized by green tea leaves showed limited antibacterial activities on *E. coli*, according to Sun *et al.*'s study (Sun *et al.* 2014). However, Asghar *et al.* also prepared nAg using green tea leaf extract using a different synthesis method and reported a significant reduction in drug-resistant *S. aureus* (Asghar *et al.* 2018). That is mainly due to the characteristic difference of the synthesized nanoparticles. The results demonstrated that the synthesis method, synthesis material, and synthesis parameters (e.g., plant extract dosage, pH, etc.) can affect the property of the final product (size or shape). The various characteristics of the final product can further affect the antimicrobial performance. As discussed previously, the size and shape traits are closely related to the movement of the material and interaction with the cell, which lead to mechanism A contact-killing playing an important role in antimicrobial activities. Comparatively, concentration may enhance the contribution of mechanism B and mechanism C by releasing more metal ions or generating ROS and eventually increasing the inactivation rate. Therefore, the three mechanisms contributed more or less with different character traits and may vary with external or internal environment change.

Silver nanoparticles have a higher cost compared to other metal materials, and that limited their further application though they have superior antimicrobial performance. Therefore, in addition to the intrinsic nAg, more and more researchers investigated the antimicrobial performance of different coatings onto the nAg to reduce the cost and develop the synergistic effect by incorporating two antimicrobial materials. Amato *et al.* coated nAg with glutathione (GSH-nAg), and the MIC of *E. coli* and *S. aureus* were determined as 180 and 15 µg/ml, respectively (Amato *et al.* 2011). nAg modified with silica and lignin hybrid materials was also effective in inhibiting five strains of microorganisms growth under 1,500 µg/100 µL dosage (Klapiszewski *et al.* 2015). In Liang *et al.*'s study, the synergistic effect of materials was proven by comparing the bacterial viability after the chitosan and chitosan/nAg composite treatment. The chitosan materials showed limited inhibition toward all strains, but the chitosan/nAg composite (0.5 mmol/L nAg) significantly inhibited four drug-resistant strains (Liang *et al.* 2016). However, the comparison of the antimicrobial efficiency of nAg and chitosan/nAg composite was not conducted in the study. Moreover, Deng *et al.* combined various antibiotics with nAg, and the bacterial growth inhibition was enhanced by combined materials compared to the nAg or antibiotics solely. However, the mechanism of the synergistic effect was undetermined (Deng *et al.* 2016). The coated nAg could be an alternative antimicrobial agent in future applications due to its enhanced antimicrobial activities.

### 3.2. Copper-based nanoparticles (nCu)

Copper is an essential element that functions as a cofactor during aerobic metabolism, and its antimicrobial properties have attracted the attention of scientists (Ibrahim *et al.* 2011). The US EPA listed copper as an effective antimicrobial agent (Ibrahim *et al.* 2011). Compared to silver, copper's economic feasibility and availability



further expand its applicability. In this section, several published articles that investigated the antimicrobial activities of nCu are reviewed. Table 2 summarizes the application of nCu in the inhibition of microorganism growth along with the respective synthesis method, physicochemical properties, dosage, pathogen species, and disinfection efficiency.

Three studies are summarized in Table 2, which involved three types of synthesis methods for copper-based nanoparticles: co-precipitation method, gel-combustion method, and biosynthesis method (Azam *et al.* 2012; Laha *et al.* 2014; Lv *et al.* 2018). Different synthesis methods lead to diversification of shape, size, area-to-volume ratio, surface reactivity, and size of prepared nanomaterials, which eventually contribute to different antimicrobial efficiency. Laha *et al.* synthesized two different shapes of nCuO: nanosphere and nanosheet (Laha *et al.* 2014). The results showed that spherical nCuO has better disinfection performance on Gram-negative bacteria; comparatively, the nanosheet CuO NPs are more effective in inactivating Gram-positive bacteria. Gram-positive bacteria have thicker layers of peptidoglycan but lack an outer membrane compared to Gram-negative bacteria. Based on mechanism A, the antimicrobial activities of metal nanoparticles are caused by the contact-killing effect. The spherical characteristic may ease the transportation of nCuO across the bacterial outer

**Table 2** | Parameters and results of the studies conducting antimicrobial experiments using copper nanomaterials

Microorganism type	Microorganism concentration (CFU/ml)	Synthesis method	Characteristic of NM	Disinfection efficiency	Reference
<i>E. coli</i>	10 <sup>6</sup>	Co-precipitation method uses copper acetate, NaOH as the stabilizer	Nanospherical; Size (nm): 33.20 ± 6.18.	MIC: 0.20 ± 0.05 mg/ml after 24 h of shaking.	Laha <i>et al.</i> (2014)
<i>E. coli</i>	10 <sup>6</sup>	Co-precipitation method uses copper nitrate, NaOH as the stabilizer	Nanosheet; Size: 257.12 ± 13.6 × 42 ± 5.10 nm.	MIC: 0.28 ± 0.02 mg/ml after 24 h of contact.	Laha <i>et al.</i> (2014)
<i>B. subtilis</i>	10 <sup>6</sup>	Co-precipitation method uses copper acetate, NaOH as the stabilizer	Nanospherical; Size: 33.20 ± 6.18 nm.	MIC: 0.36 ± 0 mg/ml after 24 h of shaking.	Laha <i>et al.</i> (2014)
<i>B. subtilis</i>	10 <sup>6</sup>	Co-precipitation method uses copper nitrate, NaOH as the stabilizer	Nanosheet; Size: 257.12 ± 13.6 × 42 ± 5.10 nm.	MIC: 0.22 ± 0.03 mg/ml after 24 h of shaking.	Laha <i>et al.</i> (2014)
<i>E. coli</i>	10 <sup>6</sup>	Gel-combustion method uses cupric nitrate trihydrate and citric acid	Nanocrystal; Size: 20 nm.	MIC: 0.02 ± 0.003 mg/ml after 24 h of incubation.	Azam <i>et al.</i> (2012)
<i>E. coli</i>	10 <sup>6</sup>	Gel-combustion method uses cupric nitrate trihydrate and citric acid	Nanocrystal; Size: 27 nm.	MIC: 0.065 ± 0.01 mg/ml after 24 h of incubation.	Azam <i>et al.</i> (2012)
<i>B. subtilis</i>	10 <sup>6</sup>	Gel-combustion method uses cupric nitrate trihydrate and citric acid	Nanocrystal; Size: 20 nm.	MIC: 0.03 ± 0.01 mg/ml after 24 h of incubation.	Azam <i>et al.</i> (2012)
<i>B. subtilis</i>	10 <sup>6</sup>	Gel-combustion method uses cupric nitrate trihydrate and citric acid	Nanocrystal; Size: 27 nm.	MIC: 0.07 ± 0.01 mg/ml after 24 h of incubation.	Azam <i>et al.</i> (2012)
<i>E. coli</i>	10 <sup>5</sup>	Biosynthesis method using <i>Shewanella loihica</i> PV-4	Nanospherical; Size: 12.71 ± 3.48 nm.	Antimicrobial efficiency: 94.3 ± 0.1% after 12 h of shaking.	Lv <i>et al.</i> (2018)

MIC, minimum inhibitory concentration; NM: nanomaterial.

membrane and the layers of peptidoglycan and that might be the reason that spherical nCuO has a better disinfection performance on Gram-negative bacteria (Vincent *et al.* 2018). Comparatively, Gram-positive bacteria have a weaker cell structure for resisting antimicrobial agents. Nanosheets have a higher contact area compared to nanosphere; thus, a higher disinfection efficiency was performed on Gram-negative bacteria with the treatment of nanosheets without the need to penetrate the outer membrane (Taglietti *et al.* 2012). Similarly, Sadani *et al.* proved the effective disinfection of non-developed virus and Gram-negative bacteria achieved by surface contracting with nCu and the structural damage of cells was visualized (Sadani *et al.* 2011). That supported the mechanism A contact-killing effect considering the structural characteristics of the non-enveloped virus and Gram-negative bacteria. The experiment was carried out on dry surfaces with no medium-facilitated movement and that further demonstrated the metal materials are capable of physically damaging the cell structure. Strain types, contamination levels, nanoparticle concentrations, and contact time are also imperative factors that impact the antimicrobial activities of nCu, according to Table 2. Therefore, the characteristics and dosage of metal nanoparticles can be optimized to achieve effective antimicrobial activities for specific pathogens under different environmental conditions.

Lv *et al.* developed an innovative synthesis method of nCu utilizing the bacterial colony of *Shewanella loihica* PV-4 to reduce Cu(II) to nCu. Similar to the nAg, physical and chemical factors also directly affect the shape and size of nCu (Lv *et al.* 2018). For example, as reported in Azam *et al.*'s study, annealing temperatures determined the size of nCu, and lower annealing temperatures resulted in a smaller nanocrystal size (Azam *et al.* 2012). That small size of nCu led to a robust bactericidal effect as reported in the study, which is consistent with the previously reviewed studies on nAg and linked to the mechanism A (Azam *et al.* 2012).

It is challenging to synthesize pure copper nanomaterials because copper is easily oxidized and agglomerated in the ambient air environment (Usman *et al.* 2013). In Akhavan and Ghaderi's study, the toxicity of nCu and nCuO to bacteria were compared, and nCu was found to be more toxic (Akhavan & Ghaderi 2010). On the contrary, the nCuO-embedded polypropylene (PP) matrix showed more effective inhibition of *E. coli* growth than the nCu embedded PP matrix. In addition, the study reported that the oxidation state of copper helped the release of copper ions so that the antimicrobial activities were enhanced (Delgado *et al.* 2011). However, whether the oxide layer of nCu will facilitate or hinder antimicrobial activities is debatable, and that requires a further understanding of the mechanism of metal materials' antimicrobial properties.

### 3.3. Titania-based nanoparticles (nTiO<sub>2</sub>)

In recent years, governments and scientists have advocated solar water disinfection due to its sustainability. It may also benefit the areas without access to centralized water treatment facilities (Wang *et al.* 2017; Kumaravel *et al.* 2021). nTiO<sub>2</sub> is one of the most studied photocatalysts for microbe inactivation, an effective disinfection strategy (Zhang *et al.* 2019). The first study using TiO<sub>2</sub> on microbial inactivation was published in 1985, and the publications exponentially increased during the past three decades (Matsunaga *et al.* 1985). TiO<sub>2</sub> is the most explored metal oxide in photocatalysis due to its excellent characteristics, including low toxicity, photostability, commercial availability, thermal and chemical stability, strong oxidizing ability, electronic configuration, and reasonable price (Lee *et al.* 2019; Patil *et al.* 2019). Researchers give keen attention to size, area, structure, and porosity as they play a significant role in improving the photocatalytic performance of TiO<sub>2</sub>. Various methods have been used for TiO<sub>2</sub> preparation, such as sol-gel, chemical, and physical vapour deposition, hydrothermal, solvothermal, microwave-assisted, and electrodeposition (Naseem & Durrani 2021).

Titanium is an n-type semiconductor due to oxygen deficiencies with a wide bandgap that can be excited by UV radiation (Foster *et al.* 2011). That light-induced excitation could generate reactive species like O<sub>2</sub><sup>-</sup> and ·OH. The generated ROS will further react to generate H<sub>2</sub>O<sub>2</sub>, ·OOH, and more ·OH in the solution, which can damage the cells (Wang *et al.* 2017). Three crystalline phases of TiO<sub>2</sub> nanoparticles have been commonly applied in nanoscale antimicrobial applications: rutile TiO<sub>2</sub> nanoparticles (nR-TiO<sub>2</sub>) and anatase (nA-TiO<sub>2</sub>), and brookite (nB-TiO<sub>2</sub>), which are differentiated by their physiochemical properties like hardness, conductivity, stability, etc. (Foster *et al.* 2011). Pantaroto *et al.* evaluated the antibacterial performance of nR-TiO<sub>2</sub>, nA-TiO<sub>2</sub>, and the mixture of nR-TiO<sub>2</sub> and nA-TiO<sub>2</sub> (nM-TiO<sub>2</sub>) by treating oral multispecies biofilms (Pantaroto *et al.* 2018). The prepared materials were exposed to 1-h UV-A light to form light-induced ROS. The study showed that nA-TiO<sub>2</sub> could reduce 99% of *Streptococcus sanguinis*, *Actinomyces naeslundii*, and *Fusobacterium nucleatum*; comparatively, nR-TiO<sub>2</sub> showed a limited biocidal effect. The result agrees with most studies that anatase is more effective in antimicrobial activities than rutile (Foster *et al.* 2011). However, the mixture, nM-TiO<sub>2</sub>, showed the highest

antibacterial efficiency among the tested three materials. That may be due to the decreased recombination of electrons and holes, and more ROS formed (Nair *et al.* 2011). The broad-spectrum property of nTiO<sub>2</sub> has been demonstrated in several studies on inactivating bacteria (Shah *et al.* 2008), fungi (Sawada *et al.* 2005), algae (Rodríguez *et al.* 2010), protozoa (Ryu *et al.* 2008), viruses (Ditta *et al.* 2008), and bacterial toxins (Khan *et al.* 2010). However, the limitation of the TiO<sub>2</sub> application is that TiO<sub>2</sub> can only be activated under UV-A irradiation.

The dominant antimicrobial mechanism of nTiO<sub>2</sub> was indicated to be the mechanism C: ROS effect. It is reported that ·OH, O<sub>2</sub>, H<sub>2</sub>O<sub>2</sub>, and O<sub>2</sub><sup>-</sup> are formed at the photocatalysis surface. Rutile and anatase phases of TiO<sub>2</sub> are reactive to the formation of ROS and ROS in rutile phase have a shorter lifetime compared to ROS in anatase phase (Nair *et al.* 2011). That illustrated the rationale underlying the higher antimicrobial performance of anatase phase nTiO<sub>2</sub>. Furthermore, the mixture of anatase and rutile phases showed the highest antimicrobial efficiency. This may cause the heterojunction formation through the close contact of valance and conduction band edge (Cao *et al.* 2016).

For utilizing the photocatalytic property of TiO<sub>2</sub> in a natural environment, many researchers worked on using modified TiO<sub>2</sub> under sunlight to enhance its antimicrobial efficiency. Noble metals, due to their surface plasmon resonance, can absorb visible light and are considered excellent dopant materials to reduce the bandgap of TiO<sub>2</sub> photocatalyst and increase its overall photocatalytic activity (Ismail & Bahnemann 2011). Devipriya *et al.* (2012) synthesized Pt-doped nTiO<sub>2</sub> by a simple photoreduction method. The synthesis was performed by dissolving P25-TiO<sub>2</sub> and H<sub>2</sub>PtCl<sub>6</sub>·6H<sub>2</sub>O in methanol solution; the milky white solution turned grayish, which confirmed the deposition of Pt on nTiO<sub>2</sub>. The Pt deposition successfully shifted the optical absorption of nTiO<sub>2</sub> from UV to the visible light region. Experimental data revealed the optimal loading of Pt into nTiO<sub>2</sub> was 0.5%, and the nanocomposite material was applied for the inactivation of *E. coli*. The Pt/nTiO<sub>2</sub> and P25-TiO<sub>2</sub> achieved complete inactivation in 50 and 90 min, respectively, under visible light irradiation (Devipriya *et al.* 2012). In one study, the antibacterial performance of lead-doped TiO<sub>2</sub> was tested under artificial light illumination. The results indicated that the antibacterial efficiency of lead-doped TiO<sub>2</sub> was enhanced by 13% compared to TiO<sub>2</sub> treatment (Erkan *et al.* 2006).

Coupling TiO<sub>2</sub> with carbon-based material or polymers is also common to enhance the photocatalytic activities of TiO<sub>2</sub>. Graphene oxide-supported TiO<sub>2</sub> was doped with Cu element in Dhanasekar *et al.*'s study. The results suggested that the modified TiO<sub>2</sub> improved the antimicrobial activities of four pathogen species under visible light irradiation (Dhanasekar *et al.* 2018).

Ion doping of TiO<sub>2</sub> is also a widely applied technique to modify TiO<sub>2</sub>, as it can effectively improve the visible light response of TiO<sub>2</sub> by reducing the bandgap of TiO<sub>2</sub>. Hou *et al.* synthesized N-doped TiO<sub>2</sub> using TiO<sub>2</sub> nanotube arrays by immersing them in hot ammonium solution (Hou *et al.* 2014). They reported that N-doped nanotubes had a higher surface area, superior electrical conductivity, and higher visible light absorption than original nanotubes. The bandgap of the N-doped material was 2.84 eV and facilitated the photogenerated carrier's separation. Sulfur doping on TiO<sub>2</sub> can significantly increase the surface area of TiO<sub>2</sub> and display excellent visible light response as reported by Yu *et al.* (2005). They synthesized sulfur-doped TiO<sub>2</sub> by the sol-gel method and applied it for the inactivation of *Micrococcus lylae*. The sulfur-doped TiO<sub>2</sub> showed superior bactericidal performance under visible light while base TiO<sub>2</sub> showed weak photoactivity. In another study, carbon-doped TiO<sub>2</sub> nanoparticles were prepared by a calcination-assisted solvothermal method using TiCl<sub>3</sub> and ethanol as precursors. The characterization results of the samples confirmed the doping of carbon atoms into TiO<sub>2</sub> lattice by substitution of the oxygen vacancies, resulting in higher visible light adsorption by the nanocomposite. The bandgap of 3.2 eV was significantly reduced to 2.39 eV, and the synthesized material exhibited higher photoactivity compared to commercially available TiO<sub>2</sub> and N-doped TiO<sub>2</sub> materials (Wu *et al.* 2013).

### 3.4. Iron-based nanoparticles (nFe)

Extensive studies investigated the applications of iron-based nanoparticles in multi-fields such as degradation of environmental pollutants (Li *et al.* 2003; Zhang & Elliott 2006; Machado *et al.* 2013), CO<sub>2</sub> sequestration (Vinoba *et al.* 2012), and inactivating microorganisms (Lee *et al.* 2008; Mahdy *et al.* 2012). Its magnetic property also contributes to high reusability, demonstrating a promising perspective for *in situ* remediations (Mosaib *et al.* 2013; Alqadami *et al.* 2017). Many researchers carried out their antimicrobial studies using nanoscale zero-valent iron particles (nZVI) and iron oxide nanoparticles (IONP) to inactivate bacteria, viruses, and fungi. The studies involved various synthesis methods, including sol-gel processing (Ba-Abbad *et al.* 2017), wet chemical processing (Chaki *et al.* 2015), thermal decomposition (Amara *et al.* 2009), green material synthesis (Asghar *et al.* 2018), etc.

That leads to different morphologies, sizes, and properties of iron-based nanoparticles. This section reviews the antimicrobial studies using iron-based nanoparticles according to the targeted microbes types.

Bacteria inactivation is the most studied topic in investigating the antimicrobial performance of iron-based nanoparticles. Plachtová *et al.* investigated the cytotoxic effect of green tea-synthesized iron-based nanoparticles on Gram-positive bacteria, Gram-negative bacteria, cyanobacteria, and microalgae (Plachtová *et al.* 2018). The results demonstrate the antimicrobial potential of iron-based nanoparticles with effective and broad-range inactivation of microorganisms. Bensaida *et al.* added different concentration levels of nZVI synthesized by the chemical reduction method into wastewater samples that have a mixed bacterial community, and the colony numbers of bacteria were determined (Bensaida *et al.* 2021). The study found that when a low concentration of nZVI was added, the aggregation and adsorption properties of nZVI could protect the cells from contact damage, and also because iron is a trace element needed by the bacterial cells, the low dose of nZVI can enhance the bacteria growth. However, when the dosage was increased to 1 g/L, the inhibition of bacteria growth was observed. This study demonstrates that the dosage of antimicrobial agents plays a vital role in their antimicrobial applications. Lee *et al.* used nZVI synthesized by wet chemical method to test the inactivation of *E. coli* in liquid under two conditions: air-saturated condition or deaerated condition (Lee *et al.* 2008). The study found a higher inactivation rate of *E. coli* by nZVI in the absence of oxygen and that was related to the lower oxide layer formed on the surface of nZVI compared to the air-saturated setup. That oxide layer deposit on the nZVI surface was proved to reduce its antibacterial activities and could also change the morphology of nZVI to fibers. Moreover, some other studies indicated that ROS triggered by oxidized nZVI via Fenton reaction (Equations (1) and (2)) could facilitate the antibacterial process and enhance the cytotoxicity of nZVI (Babuponnusami & Muthukumar 2014; Lefevre *et al.* 2016; Ševců *et al.* 2011). That aligns with the antimicrobial mechanism C:



The accumulated ROS could inhibit the activities of certain bacterial enzymes and damage DNA from inactivating bacteria (Dixon & Stockwell 2014). Furthermore, the concentration of ROS generated is correlated to bacterial strain species and the dosage of nZVI (Chen *et al.* 2013; Daraei *et al.* 2019).

Besides bacteria, the susceptibility of viruses to nZVI was also studied. In Kim *et al.*'s study, 5.3 log inactivation was achieved by adding 0.9 mM nZVI into the bacteriophage MS2 suspensions after 30 min of contact (Kim *et al.* 2011). Since the morphology of MS2 is different from bacteria with a rigid protein capsid, the mechanism was explained as a coeffect of Fenton reaction and physical damage to its capsid by nZVI. Similarly, Cheng *et al.* investigated the inhibition of  $\phi$ 2 coliphage with exposure to nZVI. They also concluded that the generated ROS played a dominant role in the virus inactivation under aerobic conditions. Under anaerobic conditions, the interaction between nZVI and the viruses made the predominant contribution (Cheng *et al.* 2016).

The antifungal activities of IONP were also determined in Parveen *et al.*'s study. The inhibition of spore germination was tested against five species. The IONP was synthesized using tannic acid as the reducing and capping agent, and the inhibition rate was over 70% for all species with the addition of 0.5 mg/ml IONP (Parveen *et al.* 2018). In Diao and Yao's study, *A. versicolor* was treated by nZVI at three levels: 0.1, 1, and 10 mg/ml (Diao & Yao 2009). There was no inhibition effect observed under the three tested levels, and nZVI was observed to oxidize simultaneously. The limited impact on fungus was concluded as the structural difference between fungus and bacteria since fungus has an extremely rigid cell wall, leading to a higher resistance to nZVI. To expand the applicability of nZVI, many studies synthesized magnetic nZVI and IONP by combining their magnetic and antimicrobial properties. For example, Prodan *et al.* synthesized magnetic IONP by co-precipitation method and validated its effective performance against bacteria and fungus species in suspension and biofilms (Prodan *et al.* 2013). Its magnetic property also provides its potential in different applications.

### 3.5. Zinc-based nanoparticles (nZn)

Zinc is an essential trace element in organisms and involves more than 300 enzymes (Haase *et al.* 2008). Zinc oxide nanoparticles (nZnO) are believed to be nontoxic and biocompatible with humans and animals (Raghupathi *et al.* 2011). nZnO has been described as a multifunctional metal nanoparticle due to its electrical and optical properties as a semiconductor (Janotti & Van de Walle 2009). Zinc oxide has three crystal structures:



cubic rocksalt, hexagonal wurtzite, and cubic zinc blend (Espitia *et al.* 2012). Rocksalt structure generally requires high pressure and is therefore relatively rare, while hexagonal wurtzite structure is thermodynamically stable and can be yielded at room temperature and pressure; therefore, it is the most extensively investigated structure (Özgür *et al.* 2005; Lee *et al.* 2016). For example, Chen *et al.* synthesized ZnO nanoparticles via a bio-synthesis route using leaf extracts and zinc acetate solution. The XRD peaks of the prepared nanoparticles were ascribed to a hexagonal wurtzite structure. The prepared nanoparticles had a bandgap of 3.35 eV and were applied for the antibacterial activity of Gram-positive *S. aureus* and Gram-negative *P. vulgaris* (Chen *et al.* 2019). Similarly, another group synthesized thin ZnO films by depositing ZnO on a glass surface using the atomic layer deposition method. SEM and XRD characterization confirmed the films had hexagonal wurtzite structures. ZnO films showed excellent efficiency against the inactivation of *S. aureus* (Park *et al.* 2017). nZnO has a bandgap of 3.37 eV and bond energy of 60 meV; however, the bandgap depends entirely on the synthesis method as it significantly impacts the electronic structure and properties of ZnO (Asthana *et al.* 2011).

nZnO has been considered an effective antimicrobial agent, and it has been applied in the biomedical field (Jiang *et al.* 2018). Jones *et al.* conducted viability tests against *S. aureus* using nZnO under fluorescent lighting conditions and dark conditions (Jones *et al.* 2008). Their findings showed that nZnO exhibited antibacterial activities under both conditions, and the inhibition rate was significantly higher under the fluorescent lighting condition. That demonstrates the photoactivation of nZnO performed under the low intensity of UV illumination can still promote its antibacterial activities. Similarly, Zhou *et al.* prepared hydroxyapatite/ZnO composite nanoparticles (nHA/ZnO), and their antibacterial activities on Gram-positive and Gram-negative bacteria were determined under ambient light and dark conditions (Zhou *et al.* 2008). The antibacterial property of nHA/ZnO was proved. The antibacterial rate was around 8% higher under the ambient light condition than in the no-light condition. The authors indicated that the enhanced antibacterial activities of the composite under ambient light were due to the improved photocatalysis efficiency (Sirelkhatim *et al.* 2015). The photocatalysis process induced a higher level of  $O_2^-$  and  $\cdot OH$  generated, leading to higher antibacterial efficiency by damaging the bacterial cells (Seven *et al.* 2004; Sirelkhatim *et al.* 2015). Although the photocatalysis process of nZnO could contribute to a higher antibacterial rate, it has been reported that the antibacterial activities of nZnO are mainly due to the released  $Zn^{2+}$  ions (Siddiqi & Husen 2018). The released ions could bind with biomolecules of bacterial cells to interrupt cell growth and effectively inactivate bacteria.

nZnO can be developed into different shapes, such as nanosheets, nanowires, and nanorods. The toxicity of nZnO can be adapted according to the targeted microorganisms, contamination level, application field, etc., by controlling its synthesis reaction parameters to alter its morphology. Many researchers have determined the effect of physicochemical parameters on microorganism inhibition. Pasquet *et al.* reported the influence of several physicochemical parameters, including crystal size, specific area, mean pore size, total porous volume, and median diameter (Pasquet *et al.* 2014). The minimum inhibition concentration (MIC) is negatively correlated to the specific area, mean pore size, total porous volume, and median diameter, no matter the tested bacteria strains.

In another study, nZnO was prepared by the wet chemical approach, and different sizes of nZnO were tested for antibacterial performance (Raghupathi *et al.* 2011). The study demonstrates that the antibacterial efficiency of nZnO is size-dependent. The smaller particle size leads to a lower percentage of viable cells recovered. However, no size effect on nZnO cytotoxicity was observed in Franklin *et al.*'s study (Franklin *et al.* 2007). The morphology of nZnO was also reported to play an essential role in inhibiting microorganism growth. Three different morphology types of nZnO were synthesized by the solvothermal method using different solvents: rod-like, flower-like, and spherical shape (Talebian *et al.* 2013). The flower-like nZnO showed the highest biocide efficiency under both light and dark conditions, which has the highest specific surface area. Furthermore, the photoluminescence was measured in the study and the flower-like nZnO showed the highest intensity, which is considered to result in higher interstitial surface defects, and that corresponds to the hydroxyl radical formation. Therefore, the flower-like morphology showed more effective bacteria inactivation.

The fate of nZnO in wastewater was investigated, and the study found that no nZnO was observed in the effluent, and the majority of nZnO was transformed into three Zn-containing species ( $ZnS$ ,  $Zn_3(PO_4)_2$ , and Zn associated Fe oxy/hydroxides) (Ma *et al.* 2014). The transformed species needs further investigation on its human and environmental effect to have a better understanding of the risk of nZnO application.

Many studies have reported superior photocatalytic activity by nZnO compared to nTiO<sub>2</sub> (Farbod & Jafarpour 2012). However, the vulnerability of nZnO to photocorrosion and dissolution at extreme pH values has hampered the progress in water disinfection applications (Di Paola *et al.* 2012). Extensive research has been



dedicated to solving these issues. For example, surface modification of ZnO via other materials is considered the most promising one. The formation of a passive layer on ZnO is a proven method that impedes the photocorrosion and dissolution of nZnO (Lee *et al.* 2016). Zhang *et al.* synthesized nZnO hybridized with carbon layers. They noticed that hybridization significantly improved the structure and adsorption capability of the nanoparticles (Zhang *et al.* 2013). Moreover, the prepared nanoparticles displayed excellent response for more than 700 h, while pristine nZnO, due to the impact of photocorrosion got completely deactivated after 100 h. Compared to pristine nZnO, hybridized nZnO exhibited a much better photo-response at acidic pH conditions. Similarly, nanocomposite material based on reduced graphene oxide (rGO) and ZnO was prepared via the solvothermal synthesis in an ethanol-water solvent. They reported that the hybridization of ZnO with rGO successfully inhibited the photocorrosion and improved the photocatalytic response of nZnO (Zhang *et al.* 2013).

### 3.6. Comparison of antimicrobial metal-based nanoparticles

Table 3 summarizes the reviewed studies in Section 3 and evaluates the antimicrobial performance of different reviewed synthesis methods of each metal type. This evaluation was carried out with the consideration of antimicrobial efficiency, sustainability, and economic feasibility.

The breakdown of the evaluation on antimicrobial metal nanoparticles is demonstrated in Table 3. nAg synthesized by biosynthesis method received a relatively high score due to its high antimicrobial efficiency and sustainability. The biosynthesis method has been considered to be a green synthesis method compared to other synthesis methods since it uses more natural materials. Furthermore, it has been indicated that nAg has the highest antimicrobial efficiency compared to other metal-based nanoparticles. In Asghar *et al.*'s study, the antimicrobial efficiency was also compared between iron, copper, and silver nanoparticles. nAg showed the highest antimicrobial efficiency among the three nanoparticles (Asghar *et al.* 2018). The antifungal and antiviral activities of nAg were also demonstrated in reviewed studies, which implicates its potential in inhibiting a broad spectrum of microorganisms (Castro-Mayorga *et al.* 2017; Asghar *et al.* 2018). However, the high cost of nAg is the biggest barrier to its large-scale application.

The highest score was given to nFe synthesized by biosynthesis method considering its economic feasibility, sustainability, and reusability. Even though the antimicrobial efficiency of nFe is lower than nAg or nCu under the same condition, the overall scoring was still the highest due to its other superior traits. nCu was also considered to have high potential for antimicrobial application with its property of affordable price and effective antimicrobial performance. Comparatively, nZnO and nTiO<sub>2</sub> were given lower scores due to their photocatalysis

**Table 3** | Comparison of metal nanoparticles and synthesis methods

Metal type	Applicable synthesis method	Characteristic of synthesized nanoparticles	Merit-based evaluation		
			Antimicrobial efficiency	Sustainability	Economic feasibility
nAg	Liquid chemical reduction method	Triangle nanoplates and nanospheres	+++	+	+
	Microwave-assisted method	Nanosphere, nanowire, and nanocubes	+++	+	+
	Biosynthesis method	Nanosphere	+++	++	+
nCu	Co-precipitation method	Nanosphere and nanosheet	++	+	++
	Gel-combustion method	Nanocrystal	++	+	++
	Biosynthesis method	Nanosphere	++	++	++
nTiO <sub>2</sub>	Magnetron sputter deposition	Nanosphere	+	+	+++
nFe	Biosynthesis method	Nanosphere	+	+++	+++
	Chemical reduction method	Nanosphere	+	++	+++
nZnO	Biosynthesis method	Nanosphere	+	++	++
	Liquid chemical reduction method	Nanosphere	+	+	++
	Solvothermal method	Flower-like shape	+	+	++

+: Poor, ++: Average, +++: Good.

property requiring energy to achieve the desired antimicrobial efficiency. Moreover, the price of the materials is another consideration.

The reviewed studies only covered a few of the studies on antimicrobial nanoparticles and the evaluation is performed based on those studies. The evaluation might be subjective; however, it can give readers a general idea of the pros and cons of each metal-based nanoparticle.

#### 4. METAL MATERIAL APPLICATION IN WATER DISINFECTION

Since the antimicrobial activities of metal nanoparticles have been revealed in intensive studies, more and more researchers have started exploring the further application of metal materials in various fields, including water disinfection. This section manifests the application of metal materials in water disinfection with the consideration of research magnitude (types of metal materials, species of microorganisms, and experimental scales), efficiency (disinfection rate under different conditions), and applicability (synthesis method and water types). The feasibility of water disinfection with metal materials is further discussed via reviewing the water disinfection performance and analyzing the potential mechanisms. Table 4 is a summary of research that applied metal-based nanoparticles in water disinfection. The water type, metal type, application method, testing condition, and disinfection performance are reviewed and compared.

Table 4 classified the reviewed studies according to the water type and metal type and it is clear that more studies were carried out at laboratory scale with synthetic water to eliminate the impact of other factors on the results. Research conducted with synthetic contaminated water has recognized the antimicrobial properties of silver. nAg showed a superior disinfection performance under similar conditions targeting the same microorganisms and that has enabled its application in future water purification. Instead of applying nAg in water, the most common application of nAg in water disinfection is incorporating nAg and supportive materials for simultaneous filtration and disinfection. Coating metal nanoparticles on a three-dimensional porous medium is a popular option that could stabilize the nanoparticles on the material surface. The medium can function as a filter to screen out suspended solids in environment samples. For example, Lin *et al.* developed three methods to prepare alginate beads with nAg. They filled them into a column to achieve filtration and disinfection by contaminated water passing through it (Lin *et al.* 2013). The alginate and composite beads were both found effective in inhibiting *E. coli* growth by column testing, and the composite beads showed a superior disinfection performance. The disinfection activity of alginate beads was considered to contribute to physical filtration that could trap the microorganism while the water passes through the materials. Furthermore, the silver ions were released that highly impact bacterial growth inhibition. The composite beads achieved physical filtration and adopted the antimicrobial properties of nAg that synergistic effect led to an effective microorganism inactivation.

Similarly, some researchers anchored nAg on polymer materials for water disinfection (Lalley *et al.* 2014). That could exploit the microporous, stable, and insoluble characteristics of the adopted polymer materials to improve the antimicrobial performance of nAg. In Jain and Pradeep's study, nAg was coated on polyurethane foam, and its water disinfection efficiency was tested. The study indicated the binding mechanism of nAg and polyurethane foam is due to the interaction between the nitrogen atom of the foam and nAg (Jain & Pradeep 2005). The coated material was tested with *E. coli* contaminated water at a constant flow rate of 0.5 L/min, and no bacteria growth was found on the material after 4 h of treatment. The results demonstrated the potential application of nAg-coated filters on household water disinfection. Another study anchored nAg on methacrylic acid copolymer beads and proved its reliability in contaminated water of the synthesized beads with the effective killing efficiency on both Gram-positive and Gram-negative strains, which further validates its broad spectrum of microorganism inhibition in water (Gangadharan *et al.* 2010). The composite beads were reported to be durable in water since nAg interacts with the carboxylic functional group on the polymer beads. Therefore, composite materials can utilize the antibacterial properties of nAg and improve its stability with supportive materials while achieving physical filtration to further enhance the disinfection performance.

Compared to binding nAg with polymers, the cellulose substrate was proposed to be an economically-feasible and renewable alternative as the support material for nAg (Praveena & Aris 2015). The filtration-disinfection concept was also adopted in studies using cellulose fibres as supporting materials. Praveena *et al.* coated nAg on cellulose paper and demonstrated the high and stable bactericidal efficiency and low silver leaching risk (Praveena *et al.* 2016). Moreover, the material preparation process was indicated to be fast and easy to operate, evincing the practicability of nAg-coated cellulose filter paper for point-of-use water disinfection. Dankovich and

**Table 4** | Metal nanoparticles application in water disinfection

Water type	Metal type	Application method	Testing condition	Disinfection performance	Reference
Synthetic pathogen-contaminated water	nAg	Incorporating nAg with alginate beads and composite beads	Microorganism: <i>E. coli</i> . Initial concentration > 10 <sup>5</sup> CFU/ml.	Over 5 log reduction with one minute retention time.	Lin <i>et al.</i> (2013)
		Anchoring nAg onto polymer materials	Microorganism: <i>E. coli</i> . Initial concentration: 10 <sup>5</sup> CFU/ml. Constant flow rate of 0.5 L/min	100% killing rate after 4 h of treatment.	Jain & Pradeep (2005)
	nAg stabilized with PVP	Microorganism: <i>E. coli</i> . Initial concentration: 10 <sup>10</sup> CFU/ml	Over 85% disinfection rate after 20 h of incubation.	Zhang <i>et al.</i> (2012)	
	Anchoring nAg on methacrylic acid copolymer beads	Microorganisms: <i>E. coli</i> , <i>P. aeruginosa</i> , <i>B. subtilis</i> , and <i>S. aureus</i> . Initial concentration: 10–300 × 10 <sup>6</sup> CFU/ml	Over 99.9% killing rates for all tested strains after 6 h of treatment.	Gangadharan <i>et al.</i> (2010)	
	Impregnating paper sheets with nAg	Microorganisms: <i>E. faecalis</i> and <i>E. coli</i> . Initial concentration: 10 <sup>9</sup> CFU/ml	Log 7.6 (±1.3) and Log 3.4 (±0.9) reductions of <i>E. coli</i> and <i>E. faecalis</i> after 4 h of treatment.	Dankovich & Gray (2011)	
	Synthesizing nanocomposite of chitosan and silver	Microorganisms: <i>S. aureus</i> , <i>E. coli</i> , and <i>A. flavus</i> were tested. Initial concentration: 1.5 × 10 <sup>8</sup> to 5.0 × 10 <sup>8</sup> CFU/ml	Log 4.2, Log 3.2, and Log 4.3 reduction of <i>S. aureus</i> , <i>E. coli</i> , and <i>A. flavus</i> after 30 min of contact time.	Morsi <i>et al.</i> (2017)	
	nCu	Stabilizing nCu on graphene-based sponges	Microorganism: <i>E. coli</i> contaminated water. Initial concentration: 10 <sup>7</sup> CFU/ml	2–3 log reduction with 5 min of contact time.	Deng <i>et al.</i> (2017)
		Impregnating ceramic membranes with nCu	Microorganism: <i>E. coli</i>	88.7–99.9% killing rate.	Biron <i>et al.</i> (2018)
		Synthesize nanocomposite of chitosan and copper	Microorganisms: <i>S. aureus</i> , <i>E. coli</i> , and <i>A. flavus</i> . Initial concentration: 1.5 × 10 <sup>8</sup> to 5.0 × 10 <sup>8</sup> CFU/ml	Log 3.7, Log 2.2, and Log 3.5 reduction of <i>S. aureus</i> , <i>E. coli</i> , and <i>A. flavus</i> after 30 min of contact time	Morsi <i>et al.</i> (2017)
	nFe	Applying nFe only	Microorganism: <i>E. coli</i> contaminated water. Initial concentration: 10 <sup>6</sup> CFU/ml	Log 3.93 after 10 min of treatment.	Santos <i>et al.</i> (2021)
nTiO <sub>2</sub>	Applying nTiO <sub>2</sub> with a UV lamp	Microorganism: <i>E. coli</i> . Initial concentration: 2.42 × 10 <sup>6</sup> CFU/ml. Continuously fed water at 1 m <sup>3</sup> /h.	Log 3.05 reduction of <i>E. coli</i> .	Yu <i>et al.</i> (2016)	
Surface water	nAg	nAg stabilized with PVP	Initial concentration: 10 <sup>10</sup> CFU/ml	Around 75% disinfection rate of <i>E. coli</i> after 20 h of incubation.	Zhang <i>et al.</i> (2012)
	nCu	Applying clay filters and copper mesh	River water samples	100% killing rate of <i>E. coli</i> by immersing the material in 300 ml of water for 5 h.	Varkey & Dlamini (2012)

(Continued.)

Table 4 | Continued

Water type	Metal type	Application method	Testing condition	Disinfection performance	Reference
	nZnO	nZnO under natural environment	Water samples from two lakes. Initial concentration: 18,500 and 70,000 CFU/ml for two lakes.	After 90 min of treatment, the concentration of cells was reduced to 1 and 50 CFU/ml, respectively.	Rajeswari & Agwaral (2020)
Groundwater	nAg	Coating nAg on glass beads and wools	Continuously flow at a 2 ml/min flow rate. Initial concentration: 85–150 CFU/ml	100% killing rates in the first 8,500 min of treatment.	Mthombeni <i>et al.</i> (2012)
		nAg stabilized with PVP	Initial concentration: 10 <sup>10</sup> CFU/ml	Around 80% disinfection rate of <i>E. coli</i> after 20 h of incubation.	Zhang <i>et al.</i> (2012)
Sea water	nAg	nAg stabilized with PVP	Initial concentration: 10 <sup>10</sup> CFU/ml	Over 65% disinfection rate of <i>E. coli</i> after 20 h of incubation.	Zhang <i>et al.</i> (2012)
Wastewater	nTiO <sub>2</sub>	Applying nTiO <sub>2</sub> under natural sunlight	Microorganisms: <i>Fusarium solani</i> spores and <i>E. coli</i> . Urban wastewater effluent. Initial concentration: 10 <sup>6</sup> CFU/ml for <i>E. coli</i> and 10 <sup>3</sup> CFU/ml for <i>F. solani</i> spores	Log 4.5 reduction of <i>E. coli</i> and Log 2 reduction of spores under the same condition.	García-Fernández <i>et al.</i> (2015)
	nZnO	nZnO under UV-A lighting conditions	Wastewater-isolated bacteria strains	A 5-log reduction after 2 h of treatment.	Zammit <i>et al.</i> (2018)

Gray performed similar research and showed a promising result, impregnated paper sheets with nAg and tested their antibacterial efficiency and silver concentration in the effluent (Dankovich & Gray 2011). Liu *et al.* (2021) carried out a study on determining the anti-biofouling effect of nAg-coated cellulose filter paper by permeation test. The study elaborated that the flow rate decline was slowed down in the nAg-coated cellulose material group due to the synergy between anti-adhesion and antibacterial activities of nAg. The anti-biofouling property can be beneficial for large-scale wastewater treatment in the future, and the concept may also be applied to membrane technologies.

Similar to nAg-based materials, nCu has been anchored on alginate beads, microporous polymer, cellulose paper, etc., and applied in water disinfection (Yu *et al.* 2013; Dankovich & Smith 2014; Harikumar & Aravind 2016). The studies illustrated the effective inhibition of microorganisms by nCu composite and revealed an alternative water disinfection technology. In Deng *et al.*'s study, the graphene-based sponge was prepared, and nCu was stabilized on the surface of the sponge, the composite material was inserted in a column for simultaneous filtration and disinfection. The antibacterial property of that novel composite filter was proved (Deng *et al.* 2017).

Another study impregnated ceramic membranes with nCu and that composite material achieved high water disinfection performance (Biron *et al.* 2018). The study also demonstrated that higher copper content led to more effective bacterial inhibition. Morsi *et al.* (2017) fabricated several multifunctional nanocomposites to inactivate bacteria and fungi in wastewater samples, including the composite of chitosan and nAg (CNT/nAg) and chitosan and nCu (CNT/nCu), and others. It was found that CNT/nAg had a better antibacterial and antifungal performance than the CNT/nCu after 30 min of treatment. That corresponds to the reviewed studies in Section 3.6 that nAg is more effective in antimicrobial applications than other commonly studied metal nanoparticles (Morsi *et al.* 2017; Asghar *et al.* 2018). However, the synergetic mechanisms have not been fully understood.

nFe was also studied in synthetic water to investigate its potential in water disinfection. As discussed in Section 3.4, the magnetic property of iron is one of its advantages and has been exploited and applied for different

purposes by researchers. Compared to nCu or nAg, fewer studies applied the filtration-disinfection theory since the magnetic property of iron helped to extend its application durability through magnetic separation and recycling (Xu *et al.* 2012). Santos *et al.* (2021) prepared several magnetic nanoparticles based on IONP and tested their water disinfection efficiency in single and multiple pathogens water environments. The result indicated IONP alone had an effective inhibition on *E. coli* growth, but while targeting multiple pathogens, impregnated IONP with nAg or nCu or carbon nanotube would lead to a better result. In Pina *et al.*'s study, IONP was coated with polyethyleneglycol (PEG) and functionalized with arginine tryptophan. The synthesized material displayed broad antibacterial activities, which effectively inactivated both Gram-positive and Gram-negative bacteria strains in water environments (Pina *et al.* 2014). The promising experimental results and the magnetic property mean the material can be an alternative technology for water disinfection. Furthermore, one study indicated that the magnetic and antimicrobial properties of IONP could also contribute to biofilm control by driving IONP to disrupt the matrix of biofilm (Li *et al.* 2019).

Photodisinfection also attracted interest in water disinfection; thus, nTiO<sub>2</sub> has been employed and developed as a point-of-use water device (Sordo *et al.* 2010; Dimapilis *et al.* 2018). Yu *et al.* (2016) developed a pilot-scale photocatalytic disinfection device using nTiO<sub>2</sub> and a UV lamp to treat continuously fed water. The study compared the UV disinfection performance and the photocatalysis disinfection performance. The results showed photocatalysis consistently removed three times or more *E. coli* no matter the flow rate changes. The study also indicated the deposition method of nTiO<sub>2</sub> could highly impact the disinfection stability after several runs. Therefore, altering nanoparticle synthesis or coating methods may extend the nano-enabled device's durability and reliability.

Synthetic water allows researchers to have better control over the experimental conditions. It can eliminate the natural variations and impurities present in real water. That helps the researchers to ensure that the disinfection performance was caused by the metal materials rather than external factors. However, the further develop the water disinfection application of metal nanomaterials, the more real water conditions are necessary to evaluate the applicability and stability of metal nanomaterials. Therefore, researchers have adopted surface water, groundwater, seawater, and wastewater to study and compare the water disinfection efficiency of different metal nanomaterials.

For example, Varkey and Dlamini developed a point-of-use surface water treatment system that employed clay filters and copper mesh as antibacterial agents (Varkey & Dlamini 2012). The developed system proved stable, cheap, and can treat raw water onsite. Furthermore, nZnO was also used in surface water disinfection with and without utilizing its photocatalysis property. For example, researchers synthesized nZnO using lemon extract in one study and tested the nZnO disinfection efficiency in natural water environments (Rajeswari & Agrawal 2020). The lake water samples had a high initial bacteria concentration at 18,500 and 70,000 CFU/ml. After 90 min of treatment, the concentration was reduced to 50 and 1 CFU/ml. Another study utilized the photocatalysis property of nZnO to treat wastewater-isolated bacteria strains under UV-A lighting conditions (Zammit *et al.* 2018). It showed that nZnO can achieve a 5-log reduction of bacteria after 2 h of treatment, and also doping nZnO with cerium can accelerate the disinfection process. The utilization of photocatalytic metal nanoparticles in water disinfection can benefit people who live in areas with high solar radiation and without access to reliable water sources. However, photocatalytic water disinfection can be a relatively slow process. It requires sufficient contact time between the nanomaterial and microorganisms, as well as exposure to UV light. The disinfection rate may not be as fast as other disinfection methods, which could be a limitation in scenarios where rapid disinfection is required (He *et al.* 2021).

Instead of surface water, one study conducted a column experiment using nAg-coated glass beads and wools to inactivate *E. coli* in groundwater (Mthombeni *et al.* 2012). That column treated continuously flowed groundwater for over 8,500 min at a 2 ml/min flow rate. The study utilizes the antimicrobial mechanism A and B to achieve satisfactory disinfection efficiency and reveals the long-term application potential of nAg-coated material. However, the flow rate is lower than a full-scale water treatment plant, which cannot meet household water consumption requirements, and the effluent safety was not evaluated. Another research group also investigated the bactericidal behaviour of nAg in different natural water environments: surface water, groundwater, seawater, and synthetic waters (Zhang *et al.* 2012). Compared to the surface water condition, the disinfection efficiency of nAg was higher in synthetic water which may be due to the presence of inorganic matter (NOM) being advantageous to the microorganisms. The toxicity of nAg can be hindered as the organic matter can be adsorbed onto the surface of the nanoparticles. This adsorption creates physical barriers between the nAg and *E. coli*,



potentially reducing their toxicity. Similarly, the fact that nAg was more effective in inactivating *E. coli* in groundwater compared to surface water is also due to the lower NOM content in groundwater. Furthermore, the disinfection efficiency of nAg in seawater conditions was even lower which may be caused by chloride ions ( $\text{Cl}^-$ ) contributing to reducing the toxicity of AgNPs. They react with the surfaces of the nanoparticles, leading to the formation of AgCl and further diminishing their toxic effects. Thus, water quality is one of the imperative factors which needs to be considered when nAg is applied in real water disinfection.

Unlike other water types, wastewater is considered to be the most challenging due to its containing a wide range of complex contaminants, including organic matter, nutrients, heavy metals, pathogens, and various industrial pollutants. That may impact the performance of metal nanomaterials in disinfection as previously discussed. One research group conducted a pilot-scale study to investigate  $\text{TiO}_2$  photocatalysis disinfection application in urban effluent treatment on a pilot scale under natural sunlight (García-Fernández *et al.* 2015). The study used *Fusarium solani* spores and *E. coli* as targeted mechanisms and determined the effect of temperature and dissolved oxygen (DO) on disinfection efficiency. The developed reactor exhibited a high inactivation rate on both microorganisms and higher temperature showed a positive correlation with the inactivation rate. The air injection also leads to higher killing efficiency of *Fusarium solani*. In Zhao *et al.*'s study, the microporous copper foam was adopted for wastewater disinfection and tested on a pilot scale with continuous wastewater feed (Zhao *et al.* 2020). The result reported a consistent killing efficiency of bacteria in a 12 h run and the leaching concentration of copper was indicated to be below relevant regulations. Another study also demonstrated the capability of copper-coated ceramic tablets to inactivate protozoa and viruses in water environments (Ehdaie *et al.* 2020). Some studies reported nCu could be applied for controlling superbugs which further shows the potential of nCu in water disinfection, especially for treating effluent from high-infection areas like hospitals (Gross *et al.* 2019). There is an interesting finding in reviewing copper-based materials applied in real water conditions; unlike the other metal materials, which are usually nanoscale size when applied in water disinfection, copper-based materials sizes tends to be larger and are visible under naked eyes. That may be due to the historical usage of copper and its inexpensive advantage that allows large amounts of copper to be applied for water treatment purposes. However, the further application of copper material in water disinfection may affect the taste and appearance of water. It may impart a metallic taste or cause discoloration, which can be unappealing to consumers. This can lead to a reduction in water quality perception and consumer acceptance (Sarkar *et al.* 2022).

Therefore, the effectiveness and potential of utilizing metal nanomaterials for water disinfection have been demonstrated across different water types, employing a variety of metal nanomaterials. The quality of water has been recognized as a critical factor that greatly influences disinfection performance. Additionally, the application method is also imperative for the disinfection performance from operational, economic, and effectiveness perspectives. It is worthwhile to investigate the application of metal nanomaterials further, as this could open up new avenues for their utilization.

## 5. FUTURE CHALLENGES AND PROSPECTS

Nanoscale metal materials have been proven to have excellent disinfection performance in water and wastewater due to their large surface-to-volume ratio, resulting in high surface exposure to microorganisms, leading to effective antimicrobial performance. The nanoscale metal materials are reported to have multi-tasking ability as they are able to overcome multiple limitations of conventional water treatment technologies such as chemical-resistant bacteria, toxic byproducts, and high energy consumption. Furthermore, there is an increasing trend in applying metal-based materials in pilot scales applications to disinfect environmental water. That can be promising not only for nanoparticle research but also for point-of-use water treatment technology. However, there are several limitations to applying the metal nanomaterial further in the water disinfection area and improper use may also pose a side effect to human and environmental health. In this section, the author articulated their own opinion on the future challenges and prospects of applying nanoscale metal materials in water disinfection. Three main challenges are identified and provide food for thought about the impact of applying nanoscale metal materials in future water disinfection applications. The limitations that hinder the application of metal-based nanoparticles to be a practical water treatment technology in point-of-use applications or full-scale wastewater treatment plants include health risks, economic feasibility, operational feasibility, and antimicrobial resistance. The risk of micropollutants and leaching metal ions into the environment will pose health risks and limit the application of metal nanoparticles. Some studies have reported the accumulation of silver

nanoparticles on the gills and kidneys of rainbow trout sampled from surface water; therefore, the health risks of metal nanoparticles have been validated years ago (Touati 2000). The application of metal nanomaterials in water application leaves nanoparticle residuals in the water environment, and that may hyper-accumulate in plant and animal bodies; eventually, that will have negative impacts on the human and the environment. Furthermore, metal nanoparticles may release metal ions into the water environment, which elevates the applied metal concentration. Even though some metals are essential elements in the environment, like copper and zinc, the high concentrations of each metal element pose increased health risks to humans and animals which have been widely studied (Karen *et al.* 1999; Ebrahimpour *et al.* 2010; Bui *et al.* 2016). Currently, the public expects higher water quality, which necessitates stricter water guidelines. The US EPA's Toxic Substance Act has considered investigating and regulating all nanoscale chemical substances to ensure human and environmental health (US EPA 2010). Therefore, a downstream separation process of applied nanoparticle residues will be necessarily required to avoid potential environmental pollution in a realistic scenario. The metal leaching risk should also be investigated when a metal material is developed and applied.

Also, the stability and long-term performance are concerns when applying the material in water. Metal nanomaterials can suffer from limited stability and durability in water treatment applications. Factors such as changes in pH, temperature, and the presence of other chemicals can influence their performance and effectiveness. Over time, these nanomaterials may undergo degradation, reducing their disinfection capabilities and requiring frequent replacement or replenishment. Future studies on incorporating metal materials with safe and robust materials may be a possible resolution which has attracted researchers' attention in recent years and research development on nanomaterial recycling technologies may also help to overcome the challenges.

Furthermore, it is difficult to upscale production from literature to industrial methods considering economic feasibility and operational feasibility. Simplifying the nanoparticle synthesis process and lowering the materials cost are critical challenges to applying the material in a water disinfection field. Especially for rural areas with low income, the cost of the technology is the main factor for market expansion. Adopting green synthesis methods and natural materials may also help to lower the cost, and improve productivity and sustainability. More economic feasibility and easy-to-operate synthesis methods are urgently needed to further scale up the application of metal nanomaterials in water disinfection. Lastly, whether the microorganism can develop resistance to the innovative nanoscale materials is undetermined. Some studies found copper-resistant bacteria strains in soil (Altimira *et al.* 2012). Long-term exposure to metal elements may lead to bacteria strains being adapted by acquiring metal genetic determinants. The multidrug resistance efflux pumps can develop co-resistance to antibiotics and metals, leading to the resistant strains being dominant in the environment (Yu *et al.* 2017). Therefore, this resistance could arise from the adaptive mechanisms of microorganisms, potentially reducing the long-term effectiveness of metal nanomaterials as disinfectants.

Therefore, it is important to note that ongoing research and development efforts are aimed at addressing these disadvantages, improving the performance, cost-effectiveness, and environmental impact of metal nanomaterials used in water disinfection. The limitations have to be tackled by intensive research before applying this technology in a realistic scenario to maintain a sustainable environment and ensure human and environmental health. Careful consideration of these drawbacks and continuous evaluation of their impact is crucial for their safe and efficient implementation in real-world applications.

## 6. CONCLUSION

The reviewed metal nanoparticles show promising antimicrobial performance in water disinfection applications, which overcomes the concerns of conventional water disinfection technologies. The metal nanoparticles may be developed for point-of-use water treatment systems to ease the lack of safe water in some rural and developing urban areas. Their antimicrobial efficiency may be impacted by altering size, shape, concentration, contact time, pathogen load, pathogen species, water quality, presence of UV irradiation, etc. Those factors may affect the contributions of antimicrobial mechanisms. Most researchers improve antimicrobial efficiency by applying various synthesis methods, which is the most straightforward and effective way. Currently, some studies upscaled the application of metal nanoparticles in water disinfection to examine its applicability. That also implies a bright future for nanotechnology and water treatment.

Although current economic considerations, undetermined human health, and environmental impacts preclude the application of nanotechnology-based water treatment processes in the immediate future, the increasing

interest in decentralized water treatment and reuse systems driven by concerns about stressed water distribution systems will likely stimulate research activities in this area in the coming decades. Future research addressing the scalability, economics, and safety of these systems will likely overcome many of the current limitations and create opportunities to revolutionize drinking water treatment.

#### DATA AVAILABILITY STATEMENT

All relevant data are included in the paper.

#### CONFLICT OF INTEREST

The authors declare there is no conflict.

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