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Insights on the antibacterial activities of nanoparticles

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ABSTRACT

Nanoparticles are referred to materials of 1-100 nm in size. These nanoparticles have many industrial, agricultural, and medicinal applications. Gold, zinc, silver, and copper nanoparticles may be exploited in microbiology because they can interfere with their growth and inhibit the process of infection; thus, they can be used as novel antimicrobial agents. The mechanism of action includes damage to the cell membrane, formation of reactive oxygen species, inhibition of intracellular enzymes, and may affect DNA replication. The synergistic effects of their activities have been illustrated in numerous research papers all over the world.

Introduction

The Greek word “nano” means short and refers to materials of one to billion (10^{-9}) or nanometers [1]. Nanoparticles (NP) are interesting due to their ability to be used in a variety of fields, such as medicine, agriculture, engineering, and industry, in addition to their unique properties, which have led to the development of simple techniques for synthesizing metal particles at the nanoscale [2, 3]. Nanoparticles offer solutions for environmental and biological challenges, and their distinctive characteristics depend on the total shape and size of the nanoparticles and their distribution [2]. Their unique properties include the following:

1. Small size from 1 to 100 nm.
2. The surface area is large compared with their size.
3. Unique chemical and biological properties.
4. The structure is solid despite its small atomic composition.
5. Severe tolerance to high temperatures, electrical conductivity, and improved stimulated surface activity [4].

The over and repeated use of antibiotics has resulted in a reduction in their ability to work against infectious diseases, and it is necessary now to find medicinal procedures to overcome this problem. The multi-resistance of bacterial species toward currently used antibiotics has increased, rendering them ineffective in controlling infections, which poses a serious challenge in health sectors [5].

Therefore, the development of new antimicrobial systems against resistant pathogens represents a significant challenge to the successful treatment of disease. Nanoparticle techniques were established with this regard to develop a new class of nanoantibiotics that may become effective therapy against bacterial infections. These nanoantibiotics have no adverse effects and increase their ability against resistant microbes by overcoming their development of resistance in addition to their low cost [6, 7]. Their effects may be due to (1) the synthesis of reactive species (2) disruption of the bacterial cell wall (3) Inhibition of nucleic acid synthesis and intracellular enzyme activity [8].

Zinc oxide nanoparticles

These nanoparticles are important in medicine because of their optical, electrical, and chemical characteristics [9] and strong activity against *Staphylococcus aureus* and *Salmonella typhimurium* [10]. The mechanism of action may be due to (i) direct contact of zinc nanoparticles with the bacterial cell wall and its damage (ii) release of zinc ions, and (iii) production of reactive oxygen particles [11, 12]. Liu et al. [13] studied the inhibitory effect of 70-nm-sized zinc oxide nanoparticles (ZnO NP) of 70 nm size against the food borne *Escherichia coli* at concentrations of 3-12 mmol/l and found that inhibition increased with increasing ZnO NP concentration, where the complete inhibition was at 12 mmol/l. Raman spectra and electron microscopy revealed changes in lipid and protein contents, indicating damage to the bacterial plasma membrane leading to leakage of contents and death. The study of Lee et al.[14] on the effect of ZnO NP in *Pseudomonas aeruginosa* exhibited that it can inhibit biofilm formation at a concentration of 1 mM. Furthermore, ZnO NP inhibited the production of pyocyanin, *Pseudomonas* quinolone signal, and the siderophore, pyochelin, thus affecting the virulence of the organism. A study on *S. aureus* by Ghazi and Alsammak [15] found a synergistic effect of ZnO NP and erythromycin against the bacterial growth of *S. aureus*. The minimum inhibitory concentration (MIC) of Erythromycin with the nanoparticles decreased to 19.5-156.25 mg/ml compared with the antibiotic alone 1250-5000 mg/ml. In another study of the bactericidal effects of ZnO NPs against *E. coli, S. aureus, P. aeruginosa,* and *B. subtilis*, these particles inhibited the growth of the Gram-negative organisms E. coli and P. aeruginosa at IC100 values of 0.6 millimolar while for the Gram-positive organisms *S. aureus* and *B. subtilis* were 1.0 and 0.8 milliolar, respectively [16].

Biosynthesis of ZnO NPs was performed by *Lactobacillus* and tested against pathogenic bacteria infecting birds, which showed substantial inhibition as tested by (MIC) and minimum bactericidal concentration (MBC) experiments. *S. aureus* was more sensitive than the other pathogens. Moreover, ZnO NP revealed significant eradication of biofilm formation [17]. Different explanations have been suggested for the action of these nanoparticles on bacteria, and one of these mechanisms is that ZnO NPs may interfere with Nor A protein, which is responsible for antibiotic resistance, via the efflux of quinolones from cells [18]. Furthermore, Bhande et al. [19] suggested that antibiotics showed a synergistic effect with Zinc nanoparticles against extended-spectrum ß-lactamase-producing bacteria since adding nanoparticles increased the permeability of the cell membrane leading to leakage of proteins from bacterial cells.

Silver nanoparticles

Hu et al. [20] reported that silver nanoparticles are effective against bacteria and viruses and are not toxic to the human body at low levels. The shape of nanoparticles affects their antimicrobial activities since truncated triangular nanoplates show more inhibition than spherical and rod-shaped nanoplates; thus, transmission electron microscopy revealed changes in the plasma membrane of *E. coli* causing death [21]. Jacob et al. [22] reported that nanoparticles are inserted into the bacterial wall and form "pits" in the plasma membrane, causing changes in its permeability leading to death. Chemical synthesis of NPs involves chemicals and generates toxic by-products in the environment; therefore, scientists have directed their research toward the biosynthesis of NPs from plants and microorganisms, especially fungi, since these organisms have many extracellular enzymes that can reduce metallic ions to form NPs [23, 24]. The biosynthesized silver nanoparticles may inhibit DNA replication and damage the cell membrane, leading to the loss of cytoplasmic components or inhibiting bacterial enzymes [25, 26]. Another explanation is that silver nanoparticles aggregate on the cell envelope and produce free radicals that affect membrane function [27].

In the study of Salih et al. [28], sliver NP particles were green synthesized from olive leaves, and the results were confirmed using UV-visible spectrophotometry and scanning electron microscopy. In an in vitro study, silver NPs were more effective than sulfadiazine (used as control) *in vitro* against pathogenic *P. aeruginosa* because there was a significant difference in all concentrations employed (12.5-200 µg/ml). Ibrahim et al. [29] presented the green synthesis of silver NP by cinnamon plants and studied the inhibition of *S. aureus* at different concentrations (10, 15, 25, 50, and 100) µg/ml and compared the results with those of cefotaxime. The inhibitory activity was higher at higher concentrations. However, using Achillea, an Arabian desert plant, to green-synthesize silver NPs, it was found that the nanoparticles produced had higher bactericidal activity against the gram-negative bacteria *P. aeruginosa* (MIC of 2.34 µg/ml) than The Gram-positive bacteria *S. aureus* (MIC 9.37 µg/ml).

Sliver NP was synthesized by the bacterium Streptococcus pyogenes and tested at concentrations of 20, 40, 60, 80, and 100 µg/ml against *S. aureus*, *P. aeruginosa*, *E. coli*, and *Candida albicans* isolated from wounds and burns in Baghdad. The synthesized nanoparticles strongly inhibited pathogens. Silver NPs can interfere with phosphate and sulfur, causing DNA breakdown and thereby affecting DNA replication, as Morones et al. [30] stated.

Gold nanoparticles

Researchers have studied the antimicrobial effects of zinc (Zn), silver (Ag), gold (Au), titanium (Ti), iron (Fe), and copper (Cu) due to increased bacterial resistance to commonly used antibiotics [31]. Gold has been used for the treatment of lupus erythematous, urticaria, psoriasis, and other skin inflammatory diseases in addition to its role in dentistry [32]. Green synthesis of Au NPs was achieved using pepper plants to study their effects in combination with colicins isolated from *E. coli* strains obtained from urinary tract infections. These synthesized spherical NPs had diameters of 30-70 and detected by UV-visible spectrometry and electron microscopy [33]. This study showed the synergistic effect of these NPs along with colicins because the results were higher than those of colicine or NPs alone against *P. aeruginosa* as pathogenic bacteria. In addition, Alkhafaji and Hashim [34] suggested that spherical Au NPs along with amoxicillin + clavulanic acid are synergistic because the MICs were lower than those of the antibiotic used or the nanos alone. Aloe vera extract was used in the biological synthesis of Au NPs, and the results were confirmed by atomic force microscopy [35]. The antibacterial activity of the synthesized NPs was also tested against *P. aeruginosa*. The NPs were added with the antibiotic ceftazidime to strengthen the antibiotic activity, and the results of the experiments suggested that NPs can prevail over the resistance mechanisms of pathogenic microbes.

Gold NPs are more active against Gram-negative bacteria, *E. coli* than *S. aureus*, which is a Gram-positive pathogen suggested by Salman et al. [36] , due to the composition of the cell wall since the study suggested that the zone diameter of inhibition in *E. coli* was 14 mm while 10 mm in *S. aureus* cases. Several mechanisms have been proposed for the antibacterial actions (a) formation of vesicles that cause cell membrane holes [37, 38,39], (b) increased Reactive oxygen species production and (3) inhibition of transcription processes in both microorganisms [23, 37, 38].

Copper nanoparticles

Copper may be used as an antibacterial agent, and Cu nanoparticles are commonly used today, such as in dentistry, to inhibit pathogens in the mouth [39]. Copper can affect bacteria in different ways (1) it generates reactive oxygen species (2) it binds to the cofactors of metalloproteins inside microbes (4) it enhances innate immunity by forming reactive oxygen species inside phagocytes [40, 41].

Flores-Rábago et al. [42] synthesized CuO nanoparticles using the green method via *Ganderma sessile*, which produced nanoparticles in the sizes of 4.5 and 5.2 nm from the supernatant and extracts of the fungus, respectively. These nanoparticles were analyzed using different analytical tools such as Dynamic scattering, electron microscopy, and X-ray diffraction. These CuO NPs showed antibacterial activity against *S. aureus*, *E. coli,* and *P. aeruginosa* with maximum IC50s of 10.2, 8.5 and 4.1µg/mL, respectively. Sharma et al., [43,44,45] also indicated that antimicrobial activity was dose dependent in their study of synthesized CuO NPs toward *E. coli*.

Conclusions

The increased microbial resistance to currently available and used antibiotics has urged scientists to investigate metal nanoparticles against human pathogens as promising novel antimicrobials to combat infections caused by resistant bacteria.

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Competing Interests

The authors declare that they have no conflicts of interest.

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