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Review Article

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An Overview of Nanoparticles as an Emerging Solution to Antibiotics Resistance

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Abstract The use of nanoparticles as an alternative to antibiotics resistance has been a major means to overcome the challenge of antibiotics resistance. The advent of nanotechnology is an eye opener in treating bacterial infections. According to some recent reports, metal oxide nanoparticles (MOxNps) like silver, iron oxide, zinc oxide, copper oxide and silver oxide have been studied extensively and found to have excellent antimicrobial properties. The present review aimed at summarizing the antimicrobial activity of some selected nanoparticles (silver, iron oxide and zinc oxide nanoparticles (ZnO-Nps). Antibacterial activity of nanoparticles is particle size dependant, and the influence of concentration also plays a key role in the antimicrobial activity. The direct interaction of the organisms with the nanoparticles brings about destruction of the cellular membrane; affect their metabolic process and morphology. Extensive research has demonstrated the application of nanoparticles as antimicrobial agent. Therefore, more attentions should be centred on nanoparticles as alternatives means of treating bacterial and fungal infections.

Keywords antimicrobial activity, nanoparticles, bacteria, fungi

Introduction

Indiscriminate antibiotics usage has contributed to ineffectiveness and affected the potency of some existing drugs. The search for new, effective bactericidal agent has been a subject of interest to researchers**.** Nanoparticles have been established as a good promising way to overcome this challenge [1–3]. High rate of chronic infection and mortality as a result of bacterial infections calls for an urgent attention. Antibiotics have been the major way of treating infections due to their affordability and the powerful effect. Although, direct evidences are obtained from various researches that the widespread use of antibiotics has resulted in the evolution of multidrug-resistant bacterial strains.

It is a thing of interest to know that most of the mechanisms of action of these antibiotics' resistance are insignificant because the mode of action of nanoparticles has to do with the direct interaction with the bacterial cell wall and not necessary to penetrate the cell. Therefore, a lot of interest has been on the use of nanoparticles or nanostructured material with antibacterial activity.

Nanomaterials has found its applications in different areas such as optical devices, fuel cells, catalysts, superconductors, biosensors, drug and gene delivery and so on [4–7]. Also, in drug delivery system nanomaterials have been applied for effective physicochemical and therapeutic enhancement [8,9]. More so, the applications of nanotechnology in pharmaceuticals and microbiology are capable of overcoming the challenges of resistance to antibiotics drugs [4,10–12]. In recent times, some metal and metal oxide nanoparticles have recently been tested for antibacterial properties.

Research has shown that the antimicrobial activity has been discovered in a variety of metal and (MOxNps), including silver (Ag), silver oxide (Ag_2O), gold (Au), calcium oxide (CaO), silica (Si), titanium dioxide (TiO_2), zinc oxide (ZnO), copper oxide (CuO), and magnesium oxide (MgO) [13–19]. Magnetic nanoparticles have also been shown to have excellent antibacterial activity [20]**.** The antibacterial activities of some selected nanoparticles (silver, iron oxide nanoparticles, and zinc oxide) were reviewed in this article.

Silver nanoparticles (AgNPs)

Silver nanoparticles shows a wide range of antibacterial and antifungal properties [21–24]. The use of silver nanoparticles has been applicable for both clinical and therapeutic sector due to the fact that silver nanoparticles are less reactive than silver ion. Hence their usefulness in both [25]. Antimicrobial properties of silver nanoparticles have been investigated against multi-drug resistant (MDR) and non-MDR bacteria strains [21,26–28].

The biosynthesis of silver nanoparticles from *Staphylococcus aureus* and their antibacterial activity against methicillin resistant *S. aureus* (MRSA) and methicillin resistant *Staphylococcus epidermidis* (MRSE) were investigated by Nanda and Saravanan (2009). They studied the application of AgNPs as antimicrobial agent against methicillin resistant MRSA, MRSE, *S. pyogenes, S. typhi* and *K. pneumoniae.* It was observed from their result that MRSA had the highest antibacterial activity, while MRSE and *S. pyogenes* had intermediate antibacterial activity, and *S. typhi* and *K. pneumoniae* had moderate antibacterial activity [29]. Nagy *et al*. (2011) also investigated antibacterial activity of silver nanoparticles embedded in zeolite membrane (AgNP-ZM). The authors reported that the membrane was found to be bacteriostatic against (MRSA) and could successfully kill *Escherichia coli* [30].

Green synthesis of silver nanoparticles using pu-erh tea leaves extract was reported by Loo *et al.* (2018) the antibacterial activity of the silver nanoparticles was evaluated against some selected gram-negative food borne pathogens. The MIC and MBC of AgNPs against *E. coli*, *K. pneumoniae*, *S. typhimurium*, and *S. enteritidis* were investigated. Report from this study revealed the excellent antimicrobial property of silver nanoparticles [31].

A cost-effective, rapid biosynthesis of silver nanoparticles, precisely from a medicinal plant (*Carduus crispus)*, was reported by Enerelt Urnukhsaikhan *et al.* (2021). Both Gram-negative and Gram-positive bacteria were used to assess the antibacterial properties of the synthesized nanoparticles. Both organisms were found to be effectively inhibited [32]. Similarly, evaluation of the antibacterial effect of silver nanoparticles was evaluated by Zarei *et al.* (2014) against four foodborne pathogens namely *Listeria monocytogenes*, *E. coli*, *S. typhimurium* and *Vibrio parahaemolyticus*. The result obtained confirmed that Ag nanoparticles exhibited an excellent antibacterial property on the tested pathogens [18].

Moreover, Bera *et al.* (2014) investigated the antimicrobial activity of fluorescent Ag nanoparticles (1–5 nm) against Gram-positive (*S. epidermidis* and *Bacillus megaterium*) and Gram-negative microorganisms (*Pseudomonas aeruginosa*). The activity of the nanoparticles was based on the shape and size of the nanoparticles. The authors reported excellent antimicrobial activity with the smaller sized nanoparticles which was due to the fact that the smaller particles could easily penetrate bacterial cell wall. It was also made known that Ag nanoparticles could be useful in wound dressing, bio-adhesives, biofilms and coating of biomedical materials [33].

Iron oxide nanoparticles (IONPs)

The toxic action of IONPs to several organisms both Gram-negative and Gram-positive organisms have been reported in Literature. Also, the susceptibility of IONPs to fungal species has also been reported. Using the well diffusion method, Saqib *et al.* (2018) evaluated the antibacterial efficacy of iron oxide nanoparticles (IONPs) against several strains of Gram positive and Gram negative bacteria, including *S. aureus*, *E. coli*, and *S. dysentery* (Wikler, 2009). Result obtained confirmed the excellent use of IONPs as an antibacterial agent [34]. Chatterjee *et al.* (2011) demonstrated the use of Fe_3O_4 nanoparticles as antibacterial agent against *E. coli*. The obtained result confirmed the inhibition of the *E. coli* by the Fe_3O_4 nanoparticles [35].

In another work by Behera *et al.* (2012) the bactericidal activity of IONPs was tested against ten human pathogenic bacteria which include *S. aureus, Shigella flexneri, B. licheniformis, B. brevis, Vibrio cholerae, P. aeruginosa, S. epidermidis, B. subtilis* and *E. coli*. It was reported that Gram-positive bacteria were more susceptible to the bactericidal activity of the synthesized IONPs than Gram-negative bacteria [36]. Prabhu *et al.* (2015) investigated the usage of Fe_3O_4 as an antibacterial agent. The nanoparticles were synthesized via chemical combustion method. The nanoparticles were further evaluated against *S. aureus* (Gram-positive and Gram-negative), *Xanthomonas*, *E. coli* and *Proteus vulgaris.* The results obtained confirmed that Fe_3O_4 nanoparticles have an excellent antibacterial action against the investigated microorganisms [37].

Furthermore, Nehra *et al.* (2018) reported that bare Fe_3O_4 nanoparticles and chitosan-coated Fe_3O_4 nanoparticles had antibacterial and antifungal activity against five organisms: *E. coli*, *B. subtilis*, *Candida albicans*, *Aspergillus niger* and *Fusarium solani*. The authors reported a better activity for the chitosan coated Nps compare to that of bare Fe_3O_4. The improved antimicrobial activity of the chitosan coated Fe_3O_4 was attributed to the surface coating with chitosan which eventually prevent aggregation of the nanoparticle. Also, the chitosan coated nanoparticles tends to be more stable than the bare magnetic nanoparticles [38].

Zinc oxide nanoparticles

Organic and inorganic antibacterial reagents are the two types of antibacterial agents now employed in the food industry. Inorganic antibacterial reagents are more stable at high temperatures and pressures than organic compounds (Sawai, 2003) [39]. (MOxNps), such as zinc oxide (ZnO), have attracted increased attention in recent years among inorganic antibacterial materials, not only because they are stable under rigorous processing conditions, but also because they are widely recognized as safe materials for humans and animals [40,41]. Several studies have demonstrated the ability of zinc oxide nanoparticles (ZnO-Nps) to inhibit both Gram-positive and negative bacteria. Several works have been done on ZnO-Nps which is an example of metal oxide nanoparticles revealing their selective toxicity to pathogenic organisms but also show little or no effect on human cells [42–44].

In a work reported by Huang *et al* (2008), ZnO-Nps was successfully synthesized and the antibacterial activity was evaluated against two pathogenic bacteria namely *Streptococcus agalactiae* and *S. aureus*. Result of their investigation revealed that the synthesized ZnO-Nps exhibited a strong antibacterial property at high concentration [45]. The toxic effect of ZnO-Nps was also investigated against *E. coli O157:H7* by Liu *et al.* (2009). Report indicated that the antimicrobial activity of ZnO-Nps is concentration dependent, according to this report, which implies that the antimicrobial activity increases as the concentration of ZnO-Nps increases. The authors also reported that the antimicrobial activity is shape and size dependent. It was further concluded that ZnO-Nps exhibited an excellent antibacterial property [46].

The antibacterial impact of ZnO-Nps on *Escherichia coli K88* was studied by Wang and co-workers in 2012. The author reported an excellent antibacterial action on *E. coli* K88. According to the findings, it was reported that the antibacterial activity increased as the concentration of the ZnO-Nps increases. The proposed mechanisms could be that the ZnO-Nps were able to destroy the membrane, thereby leading to cytosolic component leakage which eventually kills the bacteria cell. It was further concluded that these nanoparticles could serve as alternative to antibiotics both in humans and animals [47].

The evaluation of the antimicrobial property of ZnO-Nps was investigated by Mirhosseini *et al.* (2019). The effects of the different sizes and concentrations of the nanoparticles was investigated against different types of bacteria which are *S. mutans*, *Enterococcus faecalis*, *Lactobacillus fermentum*, and *C. albicans*. The result obtained revealed that the activity of the nanoparticles was proportional to the particle size. It was found that antimicrobial activity of the nanoparticles increased as the particles size decreases [48]. The use of ZnO-Nps as a strong bactericidal agent was also investigated by Narayanan *et al.* (2012). Synthesized nanoparticles were investigated using the well diffusion method against human pathogens such as *S. aureus, E. coli, K. pneumoniae*, *E. faecalis,* and *P. aeruginosa*. The antibacterial activity of standard antibiotics was also examined using the disc diffusion method against a human pathogen in order to compare the efficacy of the nanoparticles. The antibacterial activity of ZnO-Nps at various concentrations (20–100 μg/ml) was evaluated using the inhibitory zone. The results showed that the Zn oxide nanoparticles had outstanding antibacterial efficacy against all the tested pathogens. It was also found that the antibacterial property tends to increase with increasing concentration of the of ZnO-Nps [49].

The antibacterial effect of ZnO-Nps was also reported by Xie et al. against *Campylobacter jejuni*. From their result, it was proposed that the mechanism of ZnO-Nps could be as a result of oxidative stress and disruption of the cell membrane. Authors reported that the interaction with ZnO-Nps resulted membrane leakage, morphological changes and significant increase in oxidative stress gene expression in *C. jejuni* [50]. Emami-Karvani *et al* (2012) carried out an investigation on the antimicrobial activity of ZnO-Nps against Gram-positive (*S. aureus*) and Gram-negative (*E. coli*) bacteria. The antibacterial activity of ZnO-Nps was investigated as a function of concentration and particle size reduction. The antibacterial activity of ZnO-Nps was found to be particle size dependent, implying that the antibacterial activity increased as particle size decreased. Nevertheless, ZnO bulk did not show any remarkable antibacterial activity [51]. In another study carried out by Padmavathy and co-workers in 2008, the antibacterial activity of ZnO-Nps having different particle sizes was investigated. It was reported that the antibacterial activity of the nanoparticles was found to be enhanced when the particle size was reduced [52].

Conclusion

Antibiotic resistance has been a serious threat facing the world at large and employing nanoparticles as an alternative has been one of the most effective strategies for combating it. Several studies have reported the excellent antimicrobial properties of silver, iron oxide and zinc oxide nanoparticles. However, it is important to take into consideration some important factors like particle size, concentration of the nanoparticles as well as the shape of the nanoparticles as they tend to affect the antimicrobial activity of the nanoparticles. The above discussed nanoparticles has been studied and investigated and could be used as antimicrobials. Further investigations are required to find out the mechanism that would enhance the antimicrobial properties of these nanoparticles (silver, iron oxide and zinc oxide nanoparticles).

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