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THE HIGH PENETRABILITY OF NANOPARTICLES INTO BACTERIAL MEMBRANES: A KEY OF A POTENTIAL APPLICATION

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Abstract: Currently, nanoparticles have gained considerable attention for the treatment of bacterial infectious diseases. The possibility for using this technology as an alternative therapeutic strategy for controlling microbial biofilms, colonizations and infections has been the subject of intense investigations. Even though, the potential toxicity and disadvantage of using nanoparticles, researchers focused on their high penetrability into bacterial membranes, capabilities to disrupt biofilm formation and the role of chemotaxis in this interaction. Face to this significant debate, we discuss the link between metal resistance, bacterial chemotaxis and the promising use of nanoparticles (NP). *P. aeruginosa* has emerged as a model organism for biofilm studies, the aim of this review is to provide a concise and comprehensive survey of certain relevant aspects related to the research on nanoparticles and these bacteria.

1. Introduction. 2. Chemotaxis in *Pseudomonas* species. 3. Heavy metal ions, nanoparticles *vis a vis Pseudomonas aeruginosa*. 4. Mode action of nanoparticles in bacterial cell. 4.1. Direct interaction with the bacterial cell wall. 4.2. Inhibition of biofilm formation. 4.3. Generation of reactive oxygen species (ROS). 4.4. Induction of intracellular effects. 5. Conclusion

K e y w o r d s: biofilm, chemotaxis, metal, nanoparticles

1. Introduction

Pseudomonas aeruginosa is a major nosocomial pathogen representing a critical threat for human health [74] because of its tolerance and rapid development of resistance towards almost all current antimicrobial therapies [47]. In humans, their infections tend to occur in association with epithelial cell damage to the skin, eye or medical devices such as catheters, ventilators or in immune compromised individuals. In addition to these illnesses, *P. aeruginosa* lung infections are common in individuals with chronic obstructive pulmonary disease (COPD), ventilator-associated pneumonia (VAP), and cystic fibrosis (CF) [83]. It has been recognized that this bacterium can also modulate the immune response, reminiscent of helminth parasites, and antibiotic resistance due to the production of extracellular enzymes (e.g. β-lactamase) [60].

Furthermore, its survival in the host in the early stages of infection is supported by the secretion of toxins and virulence factors, including pyocyanin and its proteases elastase and alkaline protease (AprA) [49]. *Pseudomonas aeruginosa* has been recognized as an opportunistic pathogen that is the most common bacterium associated with nosocomial infections and ventilator-associated pneumonia [62].

It may turn out that recent studies have reported several innovative therapeutic technologies. Research studies have demonstrated pronounced effectiveness in fighting these biofilms, which are responsible for microbial resistance [62] and persistent infections [14]. However, with an acquired resistance to antibiotics or biocides, *P. aeruginosa* persist and are difficult to treat or eradicate. Notably, its adaptability and high intrinsic antibiotic resistance enable it to survive in a wide range of other natural and artificial settings, including surfaces in medical facilities [49]. Peterson and Kaur [65] reported that all known mechanisms of antibiotics resistances can be displayed by this bacterium (intrinsic, acquired, and adaptive); sometimes all within the same isolate.

The widespread use of broad-spectrum antibiotics has led to the appearance of multidrug-resistant (MDR) *Pseudomonas* spp. Thus, the continuous emergence of bacterial resistance has challenged the research community to develop novel antibiotic agents; there is a pressing need to identify alternate drugs. Among the most promising of these novel antibiotic agents or drugs

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are metal NPs. These particles used as innovative tools for combating the high rates of antimicrobial resistance have shown promising uses. Furthermore, recent studies have been carried out on the use of nanoparticles (NPs) and offer new prospects to develop novel formulations, based on their distinct types of sizes, shapes and flexible antimicrobial properties [77]. These authors mentioned that nanoparticles (e.g., metallic, organic, carbon nanotubes, etc.) may circumvent drug resistance mechanisms in bacteria and, associated with their antimicrobial potential, inhibit biofilm formation or other important processes.

On the other hand, NPs are more toxic to human health in comparison to large-sized particles of the same chemical substance, and it is usually suggested that toxicities are inversely proportional to the size of the NPs [91]. Silver nanoparticles (NPs) are toxic to bacteria, and are currently used in everything from medical devices to sport socks and washing machines to deter microbial growth. Silver is a particularly toxic heavy metal as it interferes with the electron transport chain and binds to DNA [79].

However, the use of nanoparticles still presents a challenge to therapy and much more research is needed in order to overcome bacteria-nanoparticles interaction. Nanoparticles often have interesting characteristics, including toxicity, that may attract or deter motile bacteria from encountering them. Nanomaterials could potentially act as chemoattractants by creating favorable environments for hydrogenotrophic microorganisms, or could be chemorepellents because of the release of toxic ions [37]. Since a long time, mechanisms of chemotaxis remain unclear because of the complex chemotaxis systems in certain bacteria species.

In this review, we will summarize the current research on nanoparticles and how these one can be applied in the future to fight multidrug resistant *Pseudomonas* spp. A better understanding of this chemotaxis signaling pathways is necessary for the development of innovative nanoparticles therapeutic strategies to fight against this extremely problematic human or environmental pathogen.

2. Chemotaxis in *Pseudomonas* species

Bacterial chemotaxis is a biased movement towards higher concentrations of life-sustaining nutrients and lower concentrations of toxins. It involves sensing a gradient of chemicals as small as a few molecules [84]. Interestingly, the bacterial movement and under the influence of a chemical gradient, either toward (positive chemotaxis) or away (negative chemotaxis) from the gradient helps bacteria to find optimum conditions for their growth and survival [29]. This is achieved through a variety of signal transduction pathways that most commonly include one-component systems, two-component systems, and chemoreceptor-based signaling cascades [57], also referred to as chemotaxis or chemosensory systems [84].

Chemotaxis in *Pseudomonas* species is one of the most diversified and best-understood signal transduction networks. It is interesting to point out that most strains possess one or two sets of the chemotaxis genes. Interestingly, genome analysis reveals that a large number of environmental motile bacteria possess several genes involved in chemosensing and chemotatic signal transduction. Motile bacteria sense changes in the concentration of chemicals in their environment and respond in a behavioral manner [1]. They have the ability to sense changes in the concentration of chemicals in the environment and respond by altering their pattern of motility using the two chemotaxis pathways [54] reviewed clearly by Ortega et al. [57].

Furthermore, the chemoeffector repertoire of *Pseudomonads* is very diverse and includes organic and amino acids, aromatic hydrocarbons, sugars, fatty acids, peptides, bivalent metal ions, inorganic anions, herbicides, morphine, as well as purine and pyrimidine bases [72]. *Pseudomonas* strains have extraordinary metabolic versatility and a large number of chemoreceptors. Ortega et al. [58] concluded that three chemosensory pathways in *P. aeruginosa* utilize one chemoreceptor per pathway, whereas the fourth pathway, which is the main system controlling chemotaxis, utilizes the other 23 chemoreceptors. As mentioned by Ortega et al. [58] the three model strains analyzed contain 26 chemoreceptors (PAO1), 27 chemoreceptors (KT2440), and 37 chemoreceptors (Pfl0-1).

For instance, when a toxic compound is present in the environment, bacteria can detect it and swim away [52]. *Via* this response researcher could understand the tolerance or resistance to certain metals, used as nanoparticules. It has been well established that essential metals, such as, iron and zinc, control diverse cellular metabolisms and biofilm formation in *P. aeruginosa* [78]. Furthermore, biofilm cells of *P. aeruginosa* are much more resistant to heavy metal stress than their planktonic counterparts [78, 53].

Harrison et al. [28] has also shown that ions of several metals, such as, silver, copper, and gallium, exert bactericidal and antibiofilm activities against *P. aeruginosa*. Meliani and bensoltane [54] reported that when a toxic compound is present in the environment such as Cadmium nitrate ($Cd(NO_3)_2$ or lead acetate ($Pb(C_2H_3O_2)_2$), bacteria can detect it and swim or swarm away. The motility patterns seems to be dependent or correlated to the heavy metal either chemoattractant or chemorepellent. Assessing the application nanoparticles requires on understanding of

the mobility, the reactivity and specially the chemotactic response of the pathogen or engineered microorganism [54].

3. Heavy metal ions, nanoparticles *vis a vis Pseudomonas aeruginosa*

Metal contamination has been linked to birth defects, cancer, skin lesions, mental and physical retardation, learning disabilities, liver and kidney damage and a host of other diseases [75]. Thus, heavy metals pose a critical concern to human health and environmental issues due to their high occurrence as a contaminant, low solubility in biota and the classification of several heavy metals as carcinogenic and mutagenic [17].

Heavy metals are the primary inorganic contaminants, which include cadmium, chromium, copper, lead, mercury, nickel and zinc etc. It was observed that some bacteria could survive and grow even at high metal ion concentrations such as *Pseudomonas stutzeri*, *Pseudomonas aeruginosa* [25]. If one accepts that zinc oxide nanoparticles (NPs) are also considered for use as new antimicrobial agents generation , the ability of using other heavy metal can be possible, the question of Why and How? Still remains.

It quickly became apparent that the effects of heavy metal ions on *P. aeruginosa* have been well studied with regard to toxicity and metal resistance [78, 27]. In the case of Pseudomonas aeruginosa their resistance mechanisms include the mer operon that reduces toxic Hg^{2+} to volatile Hg^{0}, which then diffuses out of the cell [59]. Moreover, bacterial biofilm tolerance to antimicrobials, including metals, is currently regarded as a multifactorial phenomenon [27]. Several researchers have reported that biofilms are capable of removing heavy metal ions from bulk liquid [39] and the use of biofilms to remove heavy metals from wastewater has been investigated [88]. It was determined that biofilms were anywhere from 2 to 600 times more resistant to heavy metal stress than free-swimming cells [78].

It is also interesting to note that the structure dependent metabolic heterogeneity may also explain, in part, the tolerance of bacterial biofilms to metal ions. In *P. aeruginosa* biofilms that are less than 100 μm thick, the cells that are nearest to the substratum are in anoxic zones and are slow growing, which leads to an intrinsic tolerance to killing by antibiotics relative to the aerobic fast growers in the outer biofilm layers [53].

As reported by Wagner-Döbler et al. [85] electron microscopy revealed that a *P. aeruginosa* biofilm was capable of sequestering heavy metals and that there was surface-associated precipitation of lanthanum by biofilm cells, while mercury-reducing Pseudomonas putida biofilms were found to accumulate elemental mercury on the exterior of the biofilms.

Another line of research is devoted to nanotechnology, which produced materials of various types at nanoscale level. The continuous emergence of bacterial resistance has challenged the research community to develop novel antibiotic agents. Among the most promising of these novel antibiotic agents are metal NPs, which have shown strong antibacterial activity in an overwhelming number of studies [76]. Nanoparticles (NPs) are wide class of materials that include particulate substances, which have one dimension less than 100 nm at least [40]. These inorganic particles of either simple or complex nature, display unique, physical and chemical properties and represent an increasingly important material in the development of novel nanodevices which can be used in numerous physical, biological, biomedical and pharmaceutical applications [48]. It is also noteworthy that nanoparticles (NPs) show unique and considerably changed chemical, physical, and biological properties compared to bulk of the same chemical composition, due to their high surface-to volume ratio. NPs exhibit size and shape-dependent properties which are of interest for applications ranging from biosensing, catalysts to optics and antimicrobial activity [33]. With an antimicrobial one, nanoparticles are used for their high penetrability into bacterial membranes. They can disrupt biofilm formation, possess multiple antimicrobial mechanisms, and are good carriers of antibiotics [86]. The metallic and antimicrobial agent-loaded nanoparticles have been extensively studied, the nanocomposite films displayed a significant antibacterial activity against *Escherichia coli* and *Staphylococcus aureus* [95]. In chemotaxis experiments of Kirschling [37], it was demonstrated that while *V. gazogenes* did not see silver as a chemorepellant, the silver resistant *Pseudomonas* sp. was repelled by 50 nm silver nanoparticles.

Furthermore, AshaRani et al. [4] reported that AgNPs are being used increasingly in wound dressings, catheters and various households products due to their antimicrobial activity. Antimicrobial agents are extremely vital in textile, medicine, water disinfection and food packaging. Therefore, the antimicrobial characteristics of inorganic NPs add more potency to this important aspect, as compared to organic compounds, which are relatively toxic to the biological systems [26]. On the other hand, understanding these phenomena will allow researchers to explain the application of nanotherapy.

4. Mode action of nanoparticles in bacterial cell

Nowadays, it is known the disadvantage of using nanoparticles and their potential toxicity, but these tiny materials presented a great antimicrobial activity and

have been used in a variety of chemical, biological and biomedical applications [34]. NPs have a number of features, which make them favorable as vectors for drugs to combat disease-causing pathogens. These include their enhancement of drug solubility and stability [32]; their ease of synthesis [22] and their modulated release [77] or biocompatibility with target components cells. Slavin et al. [76] reported that the most effective NPs *vis a vis* bacteria, are those containing Ag, Au, Al, Cu, Ce, Cd, Mg, Ni, Se, Pd, Ti, Zn, and super-paramagnetic Fe. Other NPs such as CuONPs, TiONPs, AuNPs, and Fe_3O_2NPs, have also demonstrated bactericidal effects [30]. Among the metal-containing NPs, Au NPs have moderate antibacterial activity unless their surface is modified. Ag NPs are the most effective nano-weapon against bacterial infections [70].

It is worth noting that the mode of action of NPs is direct contact with the bacterial cell wall, without the need to penetrate the cell. Ma and Lin [50] mentioned that once NPs come into contact with cell surfaces, they may be adsorbed on the cell walls or membranes by multiple forces, and then it is likely that they will enter the cells through various routes. The biophysicochemical interactions at the interfaces between the NPs and cells, in conclusion, mainly include adsorption and internalization.

Thus, NPs need to be in contact with bacterial cells to achieve their antibacterial function *via* the known accepted forms of electrostatic attraction, van der Waals forces, receptor-ligand and hydrophobic interactions. Ma and Lin [50] summarize schematically the main adsorption mechanisms at the NP cell interfaces. They mentioned that the NPs with bio interfaces can be combined by van der Waals forces, a common attracting force. NPs with hydrophobic surfaces would be adsorbed on the hydrophobic surface zones of the cells through hydrophobic forces. In addition, Qiu et al. [66] reported that the electrostatic attraction, as another important and general adsorption mechanism can cause the charged NPs to become adsorbed on the cell surfaces with opposite charges. Gram positive bacteria have a highly negative charge on the surface of the cell wall. For example, LPS provides negatively charged regions on the cell wall of Gram-negative bacteria that attracts NPs; and, since teichoic acid is only expressed in Gram-positive bacteria, the NPs are distributed along the phosphate chain. As such, the antimicrobial effect is more foreshadowed in Gram positive than negative bacteria [86]. Other specific interactions are also included like the hydrogen bonding and receptor ligand interactions, depending on the surface properties of both NPs and cells [70].

NPs do not present the same mechanisms of action of standard antibiotics but they can exert a multitude of mechanisms (Fig. 1).

4.1. Direct interaction with the bacterial cell wall

Both Gram-positive and negative bacteria have a negatively charged cell wall, a characteristic that is hypothesized to influence the interactions between the cell walls of the bacteria and NPs or ions released from them. The components of the cell membrane produce different adsorption pathways for NPs and Gram-positive and Gram-negative bacteria [43]. Studies performed in Gram-negative bacteria such as *Salmonella typhimurium* showed that the cell wall is populated with a mosaic of anionic surfaces domains rather than a continuous layer [51].

Moreover, Gram-negative bacteria, such as *Escherichia coli*, bacterial cells are covered by a layer of lipopolysaccharides (1–3 μm thick) and peptidoglycans (~ 8 nm thick). In the case of Gram-positive bacteria like *Staphylococcus aureus* possess a peptidoglycan layer much thicker than Gram-negative bacteria, spanning over 80 nm with covalently attached teichoic and teichuronic acids [76]. Baek and An [5] reported that Gram-negative bacteria *Escherichia coli* are highly susceptible whereas Gram-positive *Staphylococcus aureus* and *Bacillus subtilis* are less susceptible to CuO NPs, a trend that corresponds with Khan et al. [36] findings on silver and cobalt nanoparticles. For example, Ag and ZnO NPs have been reported to exert antibacterial activity by release of Ag^{+} and Zn^{++} that disrupt the membrane [15, 18].

4.2. Inhibition of biofilm formation

NPs have emerged as alternative antimicrobial approach to combat biofilms and for treating severe bacterial infections [56]. The antibacterial activity of NPs against multidrug-resistant (MDR) bacteria and biofilms depends on a number of factors, namely, their large surface area in contact with bacteria through the mentioned interactions; on the nanoparticle size and stability; together with the drug concentration [46]. The molecular mechanisms, by which metal-based NPs annihilate MDR bacteria, resulting in disturbance in respiration and inhibition of cellular growth, have been extensively reviewed [15, 18]. Fabrega et al. [19] results suggested that *Pseudomonas putida* biofilms are impacted by the treatment with AgNPs. Furthermore, Kalishwaralal et al. [35] concluded that AgNPs are able to induce the detachment of *P. aeruginosa* and *S. epidermidis* with rapidity and efficiency, opening clinical possibilities of alternative therapies. Antibiofilm action of AgNPs of 8.3 nm in diameter stabilized by hydrolyzed casein peptides on Gram-negative bacteria (*E. coli*, *P. aeruginosa* and *Serratia proteamaculans*) was investigated by Radzig et al. [69]. Gurunathan et al.

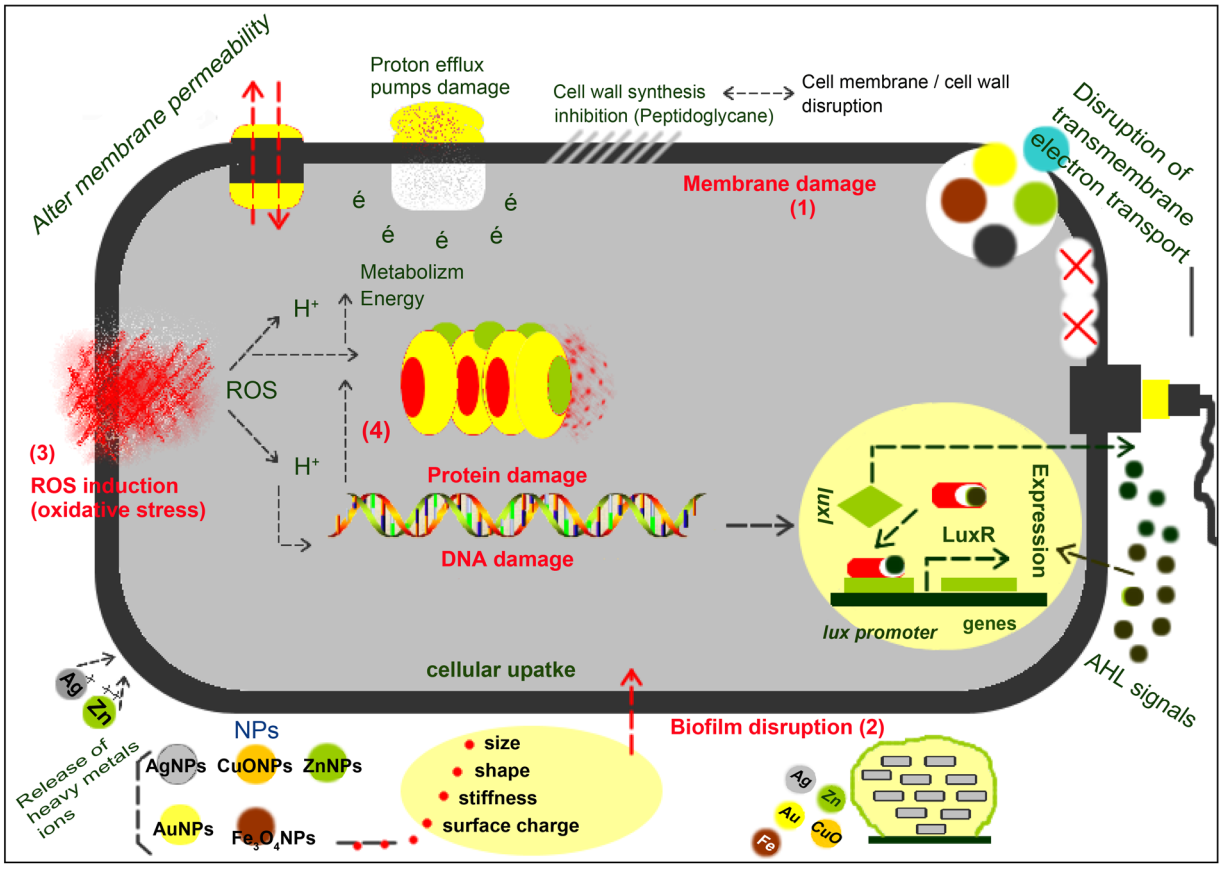


Fig.1. Different actions of NPs in bacterial cells [1, 2, 3, 4]

With different size, shape, stiffness and surface charge NPs cross the bacterial membrane and disrupt cell membrane and wall, influencing several pathways. NPs trigger a generation of oxidative stress (ROS) that damage cellular proteins and cell's basic components (DNA, ribosomes, enzymes), leading to changes in cell membrane permeability, metabolism pathways and biofilm disruption.

[24] analyzed the antibacterial and antibiofilm activity of antibiotics these nanoparticles, or combinations of both against *P. aeruginosa*, *Shigella flexneri*, *S. aureus*, and *Streptococcus pneumoniae*. The anti-biofilm activity of silver nanoparticles was also demonstrated in Ansari et al. [2] study. These authors reported that biofilms from clinical isolates of *P. aeruginosa* treated with gum arabic capped silver nanoparticles (GA-AgNPs) showed a concentration dependent inhibition of bacterial growth and treatment of catheters with GA-AgNPs at 50 μg/mL resulted in 95% inhibition of bacterial colonization of the plastic catheter surface. In another interesting study, it was proved a synergistic activity of chitosan and AgNPs to reduce the growth of *S. aureus*, *E. coli*, *S. epidermidis*, *P. aeruginosa* strains and to disrupt mature biofilms [71].

Furthermore, and in another report, thirty-six metal ions have been investigated to identify antivirulence and antibiofilm metal ions. Zinc ions and ZnO nanoparticles were found to markedly inhibit biofilm formation and the production of pyocyanin, *Pseudomonas* quinolone signals (PQS), pyochelin, and hemolytic activity of *P. aeruginosa* without affecting the growth of planktonic cells [41]. TiO_2, ZnO, $BiVO_4$, Cu- and Ni-based NPs have been utilized for this purpose due to their suitable antibacterial efficacies [63, 67]. Fabrega et al. [19] demonstrated the inhibition of marine biofilm by Ag NPs, and reported a concentration dependent reduction in biofilm formation.ZnO NPs [41] are also documented to inhibit the microbial biofilm formation. YF_2 [42] and Se NPs [23] restrain growth and biofilm formation of *E. coli* and *S. aureus.* TiO_2 [89] CdS [16] $KMgF_2$ [42] and Bi NPs [31] have also been reported to disrupt bacterial biofilms.

Another engineered nanoparticle was found to improve the survival rate and the bacterial clearance in a mouse model of *P. aeruginosa* lung infection [41]. In addition, attachment of antibiotics to nanoparticle surfaces has been found to significantly enhance the efficacy of both antibiotics and nanoparticles. In this regard, silver nanoparticles attached to ampicillin have a higher killing rate of ampicillin resistant *P. aeruginosa* isolates in vitro compared to the silver nanoparticles without ampicillin bound [10].

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hemolytic activity of *P. aeruginosa* without affecting the growth of planktonic cells. Transcriptome analyses showed that ZnO nanoparticles induce the zinc cation efflux pump *czc* operon and several important transcriptional regulators (porin gene *opdT* and type III repressor *ptrA*) [41].

4.3. Generation of reactive oxygen species (ROS)

The interaction of NPs with bacteria generally triggers oxidative stress mechanisms, enzymatic inhibition, protein deactivation and changes in gene expression. Still, the most common antibacterial mechanisms are related to oxidative stress, metal ion release, and non-oxidative mechanisms [86]. As reported by these authors, ROS is a generic term for molecules and reactive intermediates that have strong positive redox potential, and different types of NPs produce different types of ROS by reducing oxygen molecules. Reactive oxygen species (ROS) are natural by products of cellular oxidative metabolism and play important roles in the modulation of cell survival, cell death, differentiation, cell signaling, and inflammation-related factor production [55]. Different NPs may generate distinctive ROS, such as superoxide (O^{-2}) or hydroxyl radical ($\cdot OH$), hydrogen peroxide (H_2O_2), and $1[O_2]$) [86]. Umamaheswari et al. [81] demonstrated that the antibacterial activity of AuNPs against *E. coli*, *S. typhi*, *P. aeruginosa* and *K. pneumoniae* were due to oxidative stress caused by increased intracellular ROS. In another important study using different metal NPs, AgNPs were shown to generate superoxide radicals and hydroxyl radicals, whereas Au, Ni, and Si NPs generated only singlet oxygen, which upon entering the cell produced an antibacterial effect [94].

Under high levels of stress, the levels of ROS can increase significantly and it is hypothesized that their generation is one of the focal NP mechanisms of action that inhibit bacterial growth [61, 45]. Compared with microparticles or their bulk of origin, NPs possess unique physicochemical properties (size, surface area, shape, solubility, and aggregation status) that correlate with their potential to generate ROS [87]. Previous reports illustrated the impact of reactive surfaces of NPs in ROS production [82]. Excessive ROS caused lipid peroxidation, membrane permeability augmentation, and oxidation damage of DNA, RNA, and proteins in bacteria. Bao et al [6] also found that AgNPs could inhibit new DNA synthesis in the cells.

Furthermore, several research reports evidenced the role of oxidative stress in NP-induced antimicrobial activity. Biologically-synthesized AgNPs showed potent antimicrobial activity against Pseudomonas aeruginosa, Escherichia coli, and Staphylococcus aureus. The significant antimicrobial effect of AgNP is attributed to its potential up-regulation of ROS and reactive nitrogen intermediates that eventually leads to killing of the bacteria [68]. In the same way, nanosilver ions are used as the center of catalytic activity to activate the oxygen in air or water, leading to the production of hydroxyl radicals and reactive oxygen ions, which prevent the proliferation of bacteria or kill them [92]. Furthermore, ROS are beneficial to increasing the gene expression levels of oxidative proteins, which is a key mechanism in bacterial cell apoptosis [90].

These authors reported the significant antimicrobial effect of AgNP, which is attributed to its potential up-regulation of ROS and reactive nitrogen intermediates that eventually leads to killing of the bacteria. Iron oxide NP (IONPs) that coated with the positively charged chitosan possesses special interface that showed significant production of ROS, which is involved in its significant antimicrobial activity against Escherichia coli and Bacillus subtilis [3].

4.4. Induction of intracellular effects

As mentioned above AgNPs are potent inducers of reactive oxygen species. The augmented reactive species levels are known to affect and damage the major bio-molecules, such as nucleic acids and proteins [93]. This nanoparticle-generated oxidative stress, in turn, may also affect the cellular metabolic systems, thereby resulting in increased productivity of certain metabolites [8]. The entry of AgNPs induces ROS that will inhibit ATP production and DNA replication [15]. Feng et al. [21] reported the presence of silver ions and sulfur in the electron-dense granules observed after silver ions treatment in the cytoplasm of bacterial cells suggests an interaction with nucleic acids that probably results in impairment of DNA replication.

Others researchers reported that the plausible mechanism of action of TiO_2 NPs against the bacteria could be ROS generation, DNA damage after internalization, peroxidation of membrane phospholipids and inhibition of respiration [38, 80]. Additionally, it has been described that iron oxide NPs can damage macromolecules, including DNA and proteins, through the formation of ROS [44]. Sarwar et al. [73] data demonstrated that nanosized ZnO caused significant oxidative stress to *Vibrio cholerae*, the damage inflicted was DNA degradation, protein leakage, membrane depolarization and fluidity.

Another study observed that copper oxide NPs generate ROS that often leads to chromosomal DNA degradation, which seems to highlight a "particle-specific" action rather than resulting from the release of metallic ions [12].

Inhibition of DNA replication and DNA degradation has also been reported with Cu NPs in Chatterjee

et al. [13] study. Thus, the potentials of NPs for use as tags of DNA, proteins, microbes, and other cellular molecules make them promising materials for various diagnostic applications [11].

5. Conclusion

Beside certain toxicities associated with nanoparticles, there has been growing interest in the development of their use in medical applications; they are suitable candidates for the treatment of various bacterial infections. This review provided a proposed hypothesis of the application of metals in another positive way of nanotechnology. However, future studies that utilize nanoparticles need to focus on understanding the bacterial chemotaxis to optimize their functioning in medical applications.

Conflict of interest

The authors declare no conflict of interest.

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