Cell. Mol. Biomed. Rep. (ISSN: 2823-2550)
https://doi.org/10.55705/cmbr.2022.361677.1065
2023, 3(1): 35-40

Mini Review Article

Antibacterial silver nanoparticles: effects on bacterial nucleic acids

Mehran Alavi[1, 2], Michael R. Hamblin[3, 4*]

Article info
Received: 11 Mar 2022
Revised: 29 Jun 2022
Accepted: 15 Oct 2022

Use your device to scan and read the article online

Keywords:
Genetic Mutations, Drug Efflux Pumps, Antibiotic Inactivation, Nanomaterials, Silver Nanoparticles, Bacterial Nucleic Acids

ABSTRACT

Various microorganisms are located on the human skin, mucous membrane and inside the human body. Many of these microorganisms are beneficial and few are even essential, however, some pathogens are known to cause infection and have the ability to attack and damage the host tissue. Treatment of infectious bacterial disease by antibiotics is one of the major conventional strategies. Gram-positive and Gram-negative bacteria have developed resistance to conventional antibiotics by various mechanisms, including overexpression of efflux pumps, preventing drug penetration into the cells, genetic mutations, increased production of competitive inhibitors of antibiotics, or overexpression of enzymes that inactivate or hydrolyze antibiotics. Consequently, finding a new approach to overcome these hindrances is vital for the treatment of severe bacterial infections. Nanomaterials can be effective therapeutic compounds, with unique properties compared to bulk materials. Metal and metal oxide nanoparticles, particularly silver nanoparticles, have demonstrated strong antibacterial activity against most (if not all) multidrug-resistant bacteria. Several antibacterial mechanisms have been proposed for these nanoparticles, however, their interaction with bacterial nucleic acids is not completely understood, so this review discusses recent advances in this area.

1. Introduction

Bacteria are located on the human skin, mucous membrane and inside the human body. Many are beneficial and few are even essential, however, some pathogens are known to cause infection. In some conditions, these microorganisms have the ability to attack and damage the host tissue [1]. Treatment of an infectious bacterial disease with antibiotics is one of the main conventional approaches. After the discovery of penicillin in 1928, the golden age of antibiotics was from the 1930s to the 1960s, when many antibiotics were created, unfortunately, this period ended because researchers could not keep up with the pace of antibiotic discovery against emerging resistant pathogens [2]. The main global causes of antibiotic resistance are, misuse of antibiotics in clinics, poor sanitation leading to antibiotic pollution, increased use of antibiotics in livestock, and selection pressure in patients who do not complete their course of drugs [3, 4].

Understanding the factors that influence the spread of drug resistance is important in the search for effective strategies to mitigate the resulting damage [5, 6]. In general, bacteria display two types of antibiotic resistance: 1) intrinsic resistance and 2)

[1]*Department of biological science, Faculty of Science, Kurdistan University, Sanandaj, Kurdistan, Iran*
[2]*Nanobiotechnology Department, Faculty of Innovative Science and Technology, Razi University, Kermanshah, Iran*
[3]*Wellman Centre for Photomedicine, Massachusetts General Hospital, Boston, MA 02114, USA*
[4]*Department of Dermatology, Harvard Medical School, Boston, MA 02115, USA*
***Corresponding Author**: Michael R. Hamblin (hamblin.lab@gmail.com)*

acquired resistance [7, 8]. The ability of a bacterial species to resist the action of a specific antibiotic due to inherent structural or functional characteristics is known as intrinsic resistance [9-11]. For example, *Pseudomonas aeruginosa* a Gram-negative bacterial species represents a very good example of intrinsic resistance, due to the lack of a sensitive target site for some specific antibiotics [12-14].

Various other mechanisms may also help bacteria to become resistant (the acquired resistance) to a variety of antibiotics, such as antibiotic efflux due to the presence of multidrug efflux pumps that remove all types of antibiotics from the bacterial cells, or poor drug penetration into the cells thus reducing the intracellular concentration of the antibiotic. Moreover, genetic mutations can alter the expression of the antibiotic target protein as an adaptive response, or lead to increased production of competitive inhibitors of antibiotics, along with antibiotic inactivation mediated by enzymes that modify (phosphotransferases and acetyltransferases modifying aminoglycoside) or hydrolyze (β-Lactamases hydrolyzing cephalosporins and penicillins) the antibiotics [15-18].

Many bacteria are commonly found in biofilms, where they grow embedded in an extracellular matrix composed of aggregated polymeric materials that surround the bacterial cells, and act as a diffusion barrier by trapping antibiotic molecules and breaking them down [19-21]. These extracellular polymeric materials are composed of polysaccharides, nucleic acids and proteins, and form highly structured networks that are resistant to the penetration of small molecules [22, 23].

One of the advantages of using nanotechnology in antimicrobial treatment is its potential to overcome existing microbial resistance, and also to prevent its further development [24]. Various organic and inorganic nanomaterials have been investigated in therapeutic applications to kill pathogens and treat infections [24]. The advantages of antibacterial nanomaterials compared to traditional antibiotics can be summarized as: I) overcoming existing antibiotic resistance mechanisms by disruption of the bacterial membrane and prevention of biofilm formation; II) attacking microbes using several different mechanisms at the same time; III) they can function as appropriate and efficient carriers of antibiotics [25-28]. Metal or metal oxide nanoparticles, particularly silver nanoparticles, have been investigated to kill bacteria while overcoming common antibiotic resistance mechanisms, such as permeability regulation, multidrug efflux pumps, antibiotic degradation, and gene mutations [29-31].

Nanoparticles have sizes of 10-100 nm and a high surface-to-volume ratio, providing them with greater antibacterial activity compared to bulk materials and allowing them to interact with biological macromolecules, including nucleic acids (DNA and RNA), proteins, and carbohydrates [32-34]. It is worth noting that there is limited knowledge about how DNA and RNA respond to silver nanoparticles, and what the mechanism is. Therefore in this review, we discuss the interaction of silver nanoparticles with bacterial nucleic acids.

2. Antibacterial activity of Ag NPs.

The strong antibacterial activity of AgNPs can inhibit or eradicate multidrug-resistant bacteria (both Gram-negative and Gram-positive species) by various mechanisms as illustrated in Figure 1 [35]. These mechanisms include membrane damage, cytoplasmic leakage, protein denaturation, enzyme inactivation, ribosomal disassembly, production of reactive oxygen species (ROS), free radical chain reactions, and finally damage to nucleic acids. In addition, Ag NPs can be modified with other materials which may have biological activity, by using various methods, including 3D printing, electrospinning, electrophoretic deposition, dip coating, drop casting, sol-gel, sol-gel + electrodeposition, biomimetic deposition, plasma spraying, layer-by-layer deposition, ion beam deposition, ion beam-assisted deposition, magnetron sputtering, chemical vapour deposition, the addition of titania nanotubes (TNTs) produced by anodization [36].

3. Genotoxicity of Ag NPs against bacteria

The rpsL gene encodes the ribosomal S12 polypeptide (an essential protein with the ability to interface with the decoding site resulting in resistance to the error-promoting antibiotic streptomycin), and some mutations in this gene have been shown to lead to changing the resistance capacity to streptomycin antibiotics [37].

One study investigated the effects of different types of silver nanoparticles on rpsL replication fidelity, and the frequency of mutations. The mutation frequencies were 1.63%, 1.54%, and 2.15% for silver nanopowder, Ag–Cu nanopowder, and colloidal Ag, respectively. They proposed that the genotoxicity mechanism of AgNPs involved increased mutation frequency resulting from the binding of AgNPs to double-stranded DNA [38]. In another comparative study, AgNPs with a mean diameter of 16 nm, a zeta potential of −41.2 mV, and a face-centered cubic crystal structure showed a higher affinity for binding to double-stranded DNA compared to single-stranded DNA. The thermal melting temperature (T_m: 50°C - 100°C) depends on several main factors involving salt amount, the composition of nucleotide sequence, and the length of DNA. In this regard, destabilization of DNA for both mammalian (Calf thymus) and bacterial (*E. coli* and *Micrococcus lysodeikticus*) sources after interaction with AgNPs was indicated by a reduction in T_m [39].

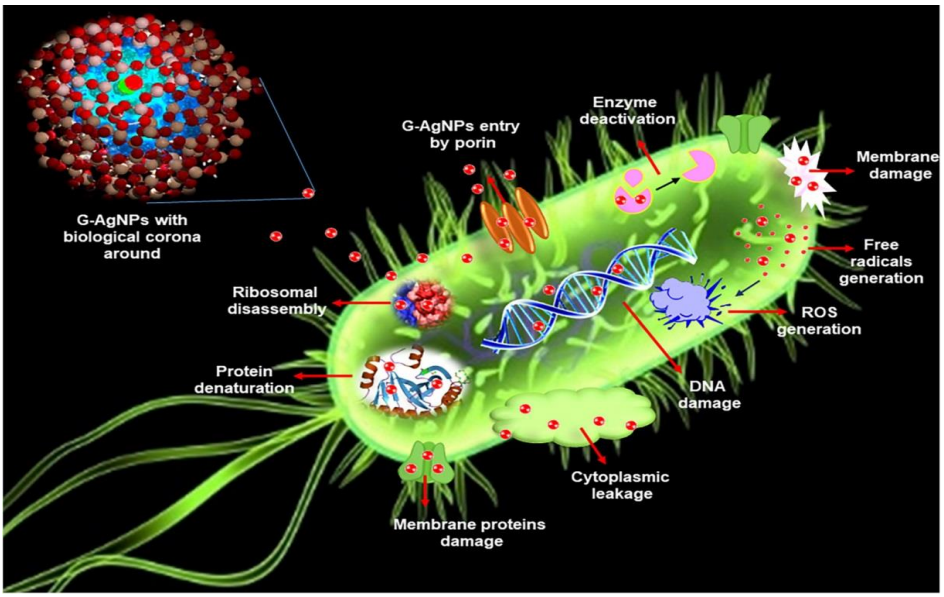

Fig. 1. The major antibacterial mechanisms resulting from the entry of green synthesized AgNPs (G-AgNPs) by porins or direct interaction followed by ROS production include damaging of the cellular wall, membrane, denaturation of biological macromolecules (proteins, enzymes, and DNA/RNA), cytoplasmic leakage, and ribosomal disassembly [35].

4. Conclusions

Notwithstanding the enormous success of conventional antibiotics in treating bacterial infections, the emergence of multidrug resistance has led to vital challenges to overcoming these bacteria. The improved antibacterial activity of nanomaterials in comparison with antibiotics may be based on several mechanisms, including overcoming antibiotic resistance mechanisms, damage to the bacterial envelope, and prevention of biofilm formation, fighting microbes using several mechanisms at the same time, and acting as suitable and efficient nanocarriers of other antibacterial agents. Silver nanoparticles can bind to double-stranded DNA and lead to increased mutation frequencies *in vitro* and *in vivo*. A higher affinity for binding to double-stranded DNA relative to single-stranded DNA and destabilization of DNA as a reduction of T_m have been found as the antibacterial functions of spherical AgNPs in the genome level. Care should be taken to avoid the possibility that

AgNPs could increase antibiotic resistance by causing mutations in resistance genes.

Conflict of Interest

The authors hereby declare that they have no conflict of interest.

Author's contributions

All authors read and approved the final manuscript.

Consent for publications

All authors have read and approved the final manuscript for publication.

Ethics approval and consent to participate

The authors did not use human or animals in the research

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

1. Patel BK, Patel KH, Huang RY, Lee CN, Moochhala SM (2022) The Gut-Skin Microbiota Axis and Its Role in Diabetic Wound Healing—A Review Based on Current Literature. Int J Mol Sci 23 (4): 2375. doi:https://doi.org/10.3390/ijms23042375
2. Hutchings MI, Truman AW, Wilkinson B (2019) Antibiotics: past, present and future. Curr Opin Microbiol 51): 72-80. doi:https://doi.org/10.1016/j.mib.2019.10.008
3. Collignon P, Beggs JJ, Walsh TR, Gandra S, Laxminarayan R (2018) Anthropological and socioeconomic factors contributing to global antimicrobial resistance: a univariate and multivariable analysis. The Lancet Planetary Health 2 (9): e398-e405. doi:https://doi.org/10.1016/S2542-5196(18)30186-4
4. Chokshi A, Sifri Z, Cennimo D, Horng H (2019) Global Contributors to Antibiotic Resistance. J Glob Infect Dis 11 (1): 36-42. doi:https://doi.org/10.4103/jgid.jgid_110_18
5. Ahmadi S, Ahmadi G, Ahmadi H (2022) A review on antifungal and antibacterial activities of some medicinal plants. Micro Nano Bio Aspects 1 (1): 10-17
6. Li Y, Kang X, Ed-Dra A, Zhou X, Jia C, Müller A, Liu Y, Kehrenberg C, Yue M (2022) Genome-Based Assessment of Antimicrobial Resistance and Virulence Potential of Isolates of Non-Pullorum/Gallinarum Salmonella Serovars Recovered from Dead Poultry in China. Microbiology Spectrum 10 (4): e00965-00922. doi:https://doi.org/10.1128/spectrum.00965-22
7. Reygaert WC (2018) An overview of the antimicrobial resistance mechanisms of bacteria. AIMS Microbiol 4 (3): 482-501. doi:https://doi.org/10.3934/microbiol.2018.3.482
8. Gil-Gil T, Martínez JL, Blanco P (2020) Mechanisms of antimicrobial resistance in Stenotrophomonas maltophilia: a review of current knowledge. Expert Rev Anti Infect Ther 18 (4): 335-347. doi:https://doi.org/10.1080/14787210.2020.1730178
9. Ndagi U, Falaki AA, Abdullahi M, Lawal MM, Soliman ME (2020) Antibiotic resistance: bioinformatics-based understanding as a functional strategy for drug design. RSC Advances 10 (31): 18451-18468. doi:https://doi.org/10.1039/D0RA01484B
10. Varghese M, Balachandran M (2021) Antibacterial efficiency of carbon dots against Gram-positive and Gram-negative bacteria: A review. Journal of Environmental Chemical Engineering 9 (6): 106821. doi:https://doi.org/10.1016/j.jece.2021.106821
11. Amraei S, Eslami G, Taherpour A, Hashemi A (2022) The role of ACT and FOX genes in Klebsiella pneumoniae strains isolated from hospitalized patients. Micro Nano Bio Aspects 1 (2): 18-25
12. Impey RE, Hawkins DA, Sutton JM, Soares da Costa TP (2020) Overcoming Intrinsic and Acquired Resistance Mechanisms Associated with the Cell Wall of Gram-Negative Bacteria. Antibiotics 9 (9): 623. doi:https://doi.org/10.3390/antibiotics9090623
13. Holger D, Kebriaei R, Morrisette T, Lev K, Alexander J, Rybak M (2021) Clinical Pharmacology of Bacteriophage Therapy: A Focus on Multidrug-Resistant Pseudomonas aeruginosa Infections. Antibiotics 10 (5): 556.

doi:https://doi.org/10.3390/antibiotics10050556
14. Capatina D, Feier B, Hosu O, Tertis M, Cristea C (2022) Analytical methods for the characterization and diagnosis of infection with Pseudomonas aeruginosa: A critical review. Anal Chim Acta 1204): 339696. doi:https://doi.org/10.1016/j.aca.2022.339696
15. Prajapati JD, Kleinekathöfer U, Winterhalter M (2021) How to Enter a Bacterium: Bacterial Porins and the Permeation of Antibiotics. Chem Rev 121 (9): 5158-5192. doi:https://doi.org/10.1021/acs.chemrev.0c01213
16. Wang Z, Liu X, Duan Y, Huang Y (2022) Infection microenvironment-related antibacterial nanotherapeutic strategies. Biomaterials 280): 121249. doi:https://doi.org/10.1016/j.biomaterials.2021.121249
17. Amraei S, Eslami G, Taherpour A, Hashemi A (2022) Relationship between MOX genes and antibiotic resistance in Klebsiella pneumoniae strains in nosocomial infections. Micro Nano Bio Aspects 1 (2): 12-17
18. Wang Q, Zhu L, Yu Y, Guan H, Xu Z (2021) Microbial Screening of Marine Natural Product Inhibitors for the 6′-Aminoglycoside Acetyltransferase 2″-Aminoglycoside Phosphotransferase [AAC(6′)-APH(2″)] Bifunctional Enzyme by Ultra-High Performance Liquid Chromatography–Mass Spectrometry (UHPLC-MS). Anal Lett 54 (18): 2895-2907. doi:https://doi.org/10.1080/00032719.2021.1903025
19. Alabresm A, Chandler SL, Benicewicz BC, Decho AW (2021) Nanotargeting of Resistant Infections with a Special Emphasis on the Biofilm Landscape. Bioconj Chem 32 (8): 1411-1430. doi:https://doi.org/10.1021/acs.bioconjchem.1c00116
20. Silva V, Capelo JL, Igrejas G, Poeta P (2022) Molecular Mechanisms of Antimicrobial Resistance in Staphylococcus aureus Biofilms. In: Akhtar N, Singh KS, Prerna, Goyal D (eds) Emerging Modalities in Mitigation of Antimicrobial Resistance. Springer International Publishing, Cham, pp 291-314. doi:https://doi.org/10.1007/978-3-030-84126-3_12
21. Chakraborty N, Jha D, Roy I, Kumar P, Gaurav SS, Marimuthu K, Ng O-T, Lakshminarayanan R, Verma NK, Gautam HK (2022) Nanobiotics against antimicrobial resistance: harnessing the power of nanoscale materials and technologies. Journal of Nanobiotechnology 20 (1): 375. doi:https://doi.org/10.1186/s12951-022-01573-9
22. Cascioferro S, Carbone D, Parrino B, Pecoraro C, Giovannetti E, Cirrincione G, Diana P (2021) Therapeutic Strategies To Counteract Antibiotic Resistance in MRSA Biofilm-Associated Infections. ChemMedChem 16 (1): 65-80. doi:https://doi.org/10.1002/cmdc.202000677
23. Uruén C, Chopo-Escuin G, Tommassen J, Mainar-Jaime RC, Arenas J (2021) Biofilms as Promoters of Bacterial Antibiotic Resistance and Tolerance. Antibiotics 10 (1): 3. doi:https://doi.org/10.3390/antibiotics10010003
24. Ma J, Jiang L, Liu G (2022) Cell membrane-coated nanoparticles for the treatment of bacterial infection. WIREs Nanomedicine and Nanobiotechnology n/a (n/a): e1825. doi:https://doi.org/10.1002/wnan.1825
25. Gupta A, Mumtaz S, Li C-H, Hussain I, Rotello VM (2019) Combatting antibiotic-resistant bacteria using nanomaterials. Chem Soc Rev 48 (2): 415-427. doi:https://doi.org/10.1039/C7CS00748E
26. Makabenta JMV, Nabawy A, Li C-H, Schmidt-Malan S, Patel R, Rotello VM (2021) Nanomaterial-based therapeutics for antibiotic-resistant bacterial infections. Nature Reviews Microbiology 19 (1): 23-36. doi:https://doi.org/10.1038/s41579-020-0420-1
27. Mamun MM, Sorinolu AJ, Munir M, Vejerano EP (2021) Nanoantibiotics: functions and properties at the nanoscale to combat antibiotic resistance. Frontiers in chemistry 9): 687660. doi:https://doi.org/10.3389/fchem.2021.687660
28. Alavi M, Kowalski R, Capasso R, Douglas Melo Coutinho H, Rose Alencar de Menezes I (2022) Various novel strategies for functionalization of gold and silver nanoparticles to hinder drug-resistant bacteria and cancer cells. Micro Nano Bio Aspects 1 (1): 38-48
29. Kotrange H, Najda A, Bains A, Gruszecki R, Chawla P, Tosif MM (2021) Metal and Metal Oxide Nanoparticle as a Novel Antibiotic Carrier for the Direct Delivery of Antibiotics.

Int J Mol Sci 22 (17): 9596. doi:https://doi.org/10.3390/ijms22179596
30. Dey N, Kamatchi C, Vickram AS, Anbarasu K, Thanigaivel S, Palanivelu J, Pugazhendhi A, Ponnusamy VK (2022) Role of nanomaterials in deactivating multiple drug resistance efflux pumps – A review. Environ Res 204): 111968. doi:https://doi.org/10.1016/j.envres.2021.111968
31. Alavi M, Thomas S, Sreedharan M (2022) Modification of silica nanoparticles for antibacterial activities: mechanism of action. Micro Nano Bio Aspects 1 (1): 49-58
32. Abdellatif AAH, Mohammed HA, Khan RA, Singh V, Bouazzaoui A, Yusuf M, Akhtar N, Khan M, Al-Subaiyel A, Mohammed SAA, Al-Omar MS (2021) Nano-scale delivery: A comprehensive review of nano-structured devices, preparative techniques, site-specificity designs, biomedical applications, commercial products, and references to safety, cellular uptake, and organ toxicity. Nanotechnology Reviews 10 (1): 1493-1559. doi:https://doi.org/10.1515/ntrev-2021-0096
33. Alavi M, Webster TJ, Li L (2022) Theranostic safe quantum dots for anticancer and bioimaging applications. Micro Nano Bio Aspects 1 (2): 1-11
34. Alavi M, Hamblin MR, Martinez F, Kennedy JF, Khan H (2022) Synergistic combinations of metal, metal oxide, or metalloid nanoparticles plus antibiotics against resistant and non-resistant bacteria. Micro Nano Bio Aspects 1 (1): 1-9
35. Singh P, Mijakovic I (2022) Strong antimicrobial activity of silver nanoparticles obtained by the green synthesis in Viridibacillus sp. extracts. Front Microbiol 13). doi:https://doi.org/10.3389/fmicb.2022.820048
36. Kravanja KA, Finšgar M (2022) A review of techniques for the application of bioactive coatings on metal-based implants to achieve controlled release of active ingredients. Materials & Design 217): 110653. doi:https://doi.org/10.1016/j.matdes.2022.110653
37. Demirci H, Wang L, Murphy FVt, Murphy EL, Carr JF, Blanchard SC, Jogl G, Dahlberg AE, Gregory ST (2013) The central role of protein S12 in organizing the structure of the decoding site of the ribosome. RNA 19 (12): 1791-1801. doi:https://doi.org/10.1261/rna.040030.113
38. Yang W, Shen C, Ji Q, An H, Wang J, Liu Q, Zhang Z (2009) Food storage material silver nanoparticles interfere with DNA replication fidelity and bind with DNA. Nanotechnology 20 (8): 085102. doi:https://doi.org/10.1088/0957-4484/20/8/085102
39. Pramanik S, Chatterjee S, Saha A, Devi PS, Suresh Kumar G (2016) Unraveling the Interaction of Silver Nanoparticles with Mammalian and Bacterial DNA. The Journal of Physical Chemistry B 120 (24): 5313-5324. doi:https://doi.org/10.1021/acs.jpcb.6b01586

How to Cite This Article:

Alavi M, Hamblin MR (2023) Antibacterial silver nanoparticles: effects on bacterial nucleic acids. Cellular, Molecular and Biomedical Reports 3 (1): 35-40. doi:10.55705/cmbr.2022.361677.1065

Download citation:

RIS; EndNote; Mendeley; BibTeX; APA; MLA; HARVARD; VANCOUVER