

Nanotechnology as a Potential Method for Combating Multidrug-Resistant Bacteria: A Comprehensive Analysis & Future Prospects

Dr Chandra Sekhar Mohapatra

Associate Professor, Department of Pathology, Utkal University, SCB Medical College & Hospital, Cuttack

Dr. Shilpa Pande

Professor, Department of Applied Physics, Laxminarayan Institute of Technology RTM Nagpur University, Nagpur, Maharashtra

Shreesh Jain

Research Scholar, Rajdhani College, Delhi University, Raja Garden, Delhi

Panamareddy Bhavitha

Dentist, Department of Microbiology, Vydehi Institute of Dental Sciences, Bangalore

Sharad Vyankatrao Mali

Assistant Professor, Pharmacy, K.T.Patil college of pharmacy, Osmanabad, Maharashtra

Dr. Chahat Shikarwar

Junior Resident, Agra, Uttar Pradesh, India

Abstract:- Nanotechnology is emerging as new implementations that can be used directly or indirectly to combat lethal bacterial infections & surmount antibiotic resistance. Antibiotic overuse is on the rise due to factors including an ageing population, a rise in infectious illnesses, & the frequency of chronic conditions that need their treatment. The broad distribution of resistance genes at an environmental scale may be traced back to the extra & inadvisable utilisation of antibiotics by humans, which has led to the rise of bacteria resistance to existing antibiotics & the selective growth of other microbes. The widespread dissemination of resistance & the transfer of resistance genes across bacterial species resulted in the appearance of multidrug-resistant (MDR) pathogens. This concern is exacerbated by the formation of biofilms by microorganisms, which can increase bacterial resistance by up to a factor of 1,000 & promote a rise of MDR infections. Therefore, the purpose of the study is to review nanotechnology as a potential method for combating MDR bacteria: a comprehensive analysis & future prospects. The methodologies are discussed based on secondary sources (websites, Google Scholar & various internet sources). This research demonstrated that AgNPs are extremely potent nanoparticles (NPs) for the treatment of MDR bacteria. Antibacterial activity of Ag NPs was shown, & their efficacy against MDR bacteria was confirmed. In conclusion, the biosynthesis of pure Ag NPs with significant antibacterial MDR action seems to be a step in the right direction, thanks to this innovative approach.

Keywords:- Multi Drug Resistant Bacteria, Antibacterial Activity, Nanotechnology.

I. INTRODUCTION

The use of nanotechnology in the synthesis of novel antibiotics is an essential strategy because it can lead to improved compound-bacteria contact, increased bioavailability, higher absorption, faster transition of the drug inside the cell membrane, & improved mucoadhesion. To further improve drug delivery, controlled release strategies may be developed for encapsulated or surface-adsorbed drugs (Zaidi et al., 2017; Jamil & Imran, 2018). An innovative strategy is to utilise NPs of a metallic material including silver, which may impact the bacterial respiration system & stimulate the creation of reactive oxygen species (ROS). Synergistically, this approach with antimicrobials might be utilised to prevent and/or change cell wall formation, leading to its eventual breakdown (Poornasareena et al., 2023; Eswaran et al., 2023; Kumar et al., 2018).

A problem with employing NPs is that they may cause bacteria to become resistant to antibiotics or may even facilitate the propagation of MDR genes. In the study of Ansari et al. (2014), for instance, it was shown that NPs made of aluminium oxide promoted the horizontal conjugative transmission of MDR genes, boosting antibiotic resistance.

NPs may have microbicidal or microbiostatic properties when used to kill microorganisms. In the latter scenario, the host's immune cells trigger microbial death by preventing bacterial growth & stopping their metabolic processes. Therefore, encapsulation may enhance permeation via the membrane, circulation times, & efficiency; nanotechnology additionally addresses issues with drug solubility; & the drug may be directed to the body's action site (Rodzinski et al., 2016).

Since NPs can enter areas wherever pathogens are prevalent, the utilisation of NPs for the management of infectious disorders looks to hold promise. Many issues are yet to be tackled; lack of preclinical research & the necessity for management (Zaidi et al., 2017).

A possible strategy for battling is one that uses nanoscale agents. The majority of pathogenic bacteria's antibiotic-resistance mechanisms are irrelevant without penetration, which is how nanosized particles' antibacterial effects are primarily mediated (Beyth et al. 2018). Resultantly, NPs have a lower probability than conventional antibiotics to cause bacterial resistance. The potential of this has spurred intense study, with hundreds of articles already published, & spurred considerable anticipation that nanotechnology would give novel diagnostics & therapies for antimicrobial illnesses.

Antibiotic abuse & misuse by humans has caused widespread transmission of resistance genes at the environmental scale, allowing for the selective emergence of bacteria resistance in opposition to antibiotics now available & resistant nonpathogenic microbiota (Nitsch-Osuch et al., 2016). So, the capacity of these pathogens to resist the effects of antimicrobial drugs is of particular concern when it happens alongside *Enterococcus* species., including *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, as well as *Enterobacter* spp.

In recent years, nanotechnology & NPs were developed to fight & reduce bacterial resistance, also known as MDR. According to Horikoshi & Serpone (2013), NPs are artificial structures having diameters that range- 1 - 100 nm (nm). According to Horikoshi & Serpone (2013), nanomaterials are employed in a wide range of medical applications, including pharmaceuticals, systems for delivering drugs, & diagnosing imaging systems. The present study makes efforts to address solely the advancements in the development of antibacterial NPs with an emphasis on treating MDR bacteria since this subject is quickly advancing.

II. MATERIAL & METHOD

The secondary source of data was collected from various internet resources, Google Scholar, Websites, PubMed & many published article, journals etc.

III. RESULT & DISCUSSION

The usage of novel technologies for dealing with MDR bacteria is becoming increasingly important because, despite the fact that there are still antibiotics that are effectual, the ability of bacteria to resist them is continuously rising. Potentially novel strategies for combating the pandemic of drug-resistant microorganisms are discussed in this study. This may include making linkages between multiple strategies & using them in tandem with antibiotics to tackle this critical new problem.

A. Nanotechnology using nanoparticles for antibacterial activity

Microbicidal or microbiostatic effects may be present when NPs are utilised to get rid off bacteria. In the latter scenario, host immune cells cause microbial death by stopping the development of bacteria & stopping their metabolic processes. Since encapsulation can enhance efficiency, increase circulation times, & improve permeation through the membrane, problems with drug solubility can also be resolved by nanotechnology (Rodzinski et al., 2016). Additionally, it may be possible to direct the drug to the required action site in the body.

NPs show promise for mitigation of infectious illnesses, in particular because they may be able to go to sites where pathogens are concentrated. Toxicology data gaps, a paucity of preclinical investigation, & the necessity for regulation are just a few of the issues that have yet to be addressed (Zaidi et al., 2017).

Biocidal activity & wide antibacterial responses against Gram-positive & -negative bacteria have been greatly improved by using NPs as vectors for delivering antimicrobial moieties (Wang et al., 2016).

B. Different metallic nanoparticles against multidrug resistant bacteria

Utilizing metallic NPs can be an effective method for combating resistant microorganisms. Studies document the creation & utilisation of various metal NPs, metal-oxides, metal-halides, & bi-metallic compounds with antibacterial activities. Metal NPs, as well as Ag, Au, Zn, Cu, Ti, & Mg, were created (Zakharova et al., 2015). But their possible toxicity should be taken into account.

Eymard-Vernain et al. (2018) demonstrated magnesium oxide NPs exhibited antibacterial activity by primarily influencing gene expression associated with oxidative stress, as well as altering the bacterial membrane. Verma et al. (2018) illustrated that ZnO NPs had outstanding antibacterial activity along with a size based impact, as the usage of tinier NPs enhanced ROS & cell membrane disruption.

Regarding bacterial resistance or the potential for promoting the increase of MDR genes, one of the issues by means of the NP usage is raised. Ansari et al. (2014), described for instance, it was shown that Aluminium oxide NPs facilitated horizontal conjugative transfer of MDR genes, boosting antibiotic resistance.

The FDA (Food & Drug Administration) of the US has been aware of silver NPs' antibacterial action since 1920, resulting in them being the most researched metallic NPs. On bacteria, the action mechanisms AgNP have been studied in-depth. Consensus exists that adhesion of NPs to the cell membrane are capable of result in electrostatic changes, porosity modification, crack, cytoplasmic content seepage, interfering with bacterial respiratory system, inhibition of enzyme activity, & DNA destruction. The

construction of ROS is observed, by means of subsequent consequences on DNA (Yuan et al., 2017).

C. Silver nanoparticles for combating multidrug resistant bacteria

A new trend is to mix AgNPs with antibiotics to increase their efficacy against bacteria. In a recent study, Katya & colleagues shown with the purpose of the antibacterial efficacy of chloramphenicol & gentamicin in combination with AgNPs is superior to that of the two antibiotics used alone against MDR *E. faecalis* (Katva et al., 2018).

AgNPs immobilized on the surface of AgNP/NSPs were shown by Su & colleagues to exhibit potent antibacterial properties against MRSA & silver-resistant *E. coli* via the formation of ROS (Su et al., 2011).

AgNPs from *P. amarus* extract had remarkable antibacterial efficacy against *P. aeruginosa* MDR strains, according to research by Singh & colleagues (Singh K. et al., 2014). Currently, Gram-positive & -negative bacteria were treated with two distinct shaped AgNPs (spheres & rods), both of which shown potential antibacterial activity against various strains (Acharya et al., 2018).

According to McShan et al. (2015), combining AgNPs with tetracycline or neomycin, two separate classes of antibiotics, may have a synergistic impact that results in increased antibacterial activity at doses lower than the MIC of each NP's or antibiotic.

Tetracycline was used in the production of water-soluble AgNPs as a co-reducing & stabilizing agent, & Djafari & colleagues showed that these AgNPs were successful in combating tetracycline-resistant bacteria (Djafari et al., 2016).

Nanotechnology techniques have enormous promise for combating & curing microbial infections, but more testing of these substances' safety & cytotoxicity will be necessary before we can use them in clinical settings. The creation of production techniques that enable reasonably priced large-scale manufacturing is another challenge for the nanotechnology sector.

Numerous investigations show a willingness to get beyond obstacles & exploit the potential of nanomaterials for medicinal applications.

Importantly, previous studies are discussed were found towards have strong antibacterial action in opposition to different MDR disease causing bacteria, & are capable of treating infections. Together, NPs provide a potentially effective replacement for current methods of preventing & managing bacterial infections. To do this, antimicrobial NPs will be commercialized, & research will develop.

IV. CONCLUSION

MDR bacteria demonstrated to be a severe healthiness concern which has to be addressed on a worldwide level as they have emerged & grown. Nanomaterials provide a fresh, "outside the box" approach for treating recurrent MDR bacterial disease. To enhance the therapeutic potential & minimize host risk, it is crucial to optimize their physical characteristics, especially size & surface charge. Current concerns about the long-standing consequences of NPs on humans & complete protection are limiting clinical application. Future research should include a thorough understanding of the NP influence on gene expression due to concerns with metabolism, toxicity, stability, & gene-level mechanisms. Future studies should also explain the precise & in-depth mechanism by which NPs interact by means of biological system in order to create NPs having advantageous physico-chemical properties that would make NPs quicker to respond to various natural settings for beneficial remuneration exclusive of having a negative effect. In near future, AgNPs will serve as the next generation of antibiotics to treat MDR bacteria.

REFERENCES

- [1]. Acharya, D., Singha, K. M., Pandey, P., Mohanta, B., Rajkumari, J., & Singha, L. P. (2018). Shape dependent physical mutilation & lethal effects of silver nanoparticles on bacteria. *Scientific reports*, 8(1), 1-11.
- [2]. Ansari, M. A., Khan, H. M., Khan, A. A., Cameotra, S. S., Saquib, Q., & Musarrat, J. (2014). Interaction of Al₂O₃ nanoparticles with *Escherichia coli* & their cell envelope biomolecules. *Journal of applied microbiology*, 116(4), 772-783.
- [3]. Eswaran B., Abraham P., Monisha K., Varshini S, & Preethy R. (2023). Methods of Synthesis of Nanoparticles Used in Dentistry A Review Article. *International Journal of Innovative Science & Research Technology*, 8(1), 150–156.
- [4]. Eymard-Vernain, E., Luche, S., Rabilloud, T., & Lelong, C. (2018). Impact of nanoparticles on the *Bacillus subtilis* (3610) competence. *Sci. Rep.* 8: 2978, Correction in: *Sci. Rep.* 2018 8, 6486. doi: 10.1038/s41598-018-21402-0
- [5]. Horikoshi, S., & Serpone, N. (Eds.). (2013). *Microwaves in nanoparticle synthesis: fundamentals & applications*. John Wiley & Sons.
- [6]. Jafari, E., Khajouei, M. R., Hassanzadeh, F., Hakimelahi, G. H., & Khodarahmi, G. A. (2016). Quinazolinone & quinazoline derivatives: recent structures with potent antimicrobial & cytotoxic activities. *Research in pharmaceutical sciences*, 11(1), 1.
- [7]. Jamil, B., & Imran, M. (2018). Factors pivotal for designing of nanoantimicrobials: an exposition. *Critical reviews in microbiology*, 44(1), 79-94.

- [8]. Katva, S., Das, S., Moti, H. S., Jyoti, A., & Kaushik, S. (2018). Antibacterial synergy of silver nanoparticles with gentamicin & chloramphenicol against *Enterococcus faecalis*. *Pharmacogn. Mag*, 13(52), S828-S833.
- [9]. Kumar, T. S., & Madhumathi, K. (2016). Antibiotic delivery by nanobioceramics. *Therapeutic Delivery*, 7(8), 573-588.
- [10]. McShan, D., Zhang, Y., Deng, H., Ray, P. C., & Yu, H. (2015). Synergistic antibacterial effect of silver nanoparticles combined with ineffective antibiotics on drug resistant *Salmonella typhimurium* DT104. *Journal of Environmental Science & Health, Part C*, 33(3), 369-384.
- [11]. Nitsch-Osuch, A., Gyrzduk, E., Wardyn, A., Życinska, K., & Brydak, L. (2016). Antibiotic prescription practices among children with influenza. *Respiratory Contagion*, 25-31.
- [12]. Poornasareena T; Sathya M; Keerthiga K; Dr. Anishkumar M. 2023. "Silver Nanoparticles & its Applications." *International Journal of Innovative Science & Research Technology* 8(2): 1014-1018.
- [13]. Rodzinski, A., Guduru, R., Liang, P., Hadjikhani, A., Stewart, T., Stimpfil, E., ... & Khizroev, S. (2016). Targeted & controlled anticancer drug delivery & release with magnetoelectric nanoparticles. *Scientific reports*, 6(1), 20867.
- [14]. Singh, K., Panghal, M., Kadyan, S., Chaudhary, U., & Yadav, J. P. (2014). Green silver nanoparticles of *Phyllanthus amarus*: as an antibacterial agent against multi drug resistant clinical isolates of *Pseudomonas aeruginosa*. *Journal of nanobiotechnology*, 12(1), 1-9.
- [15]. Su, Z., Xie, E., & Li, Y. (2011). Entrepreneurial orientation & firm performance in new ventures & established firms. *Journal of small business management*, 49(4), 558-577.
- [16]. Verma, S. K., Jha, E., Panda, P. K., Das, J. K., Thirumurugan, A., Suar, M., et al. (2018). Molecular aspects of core-shell intrinsic defect induced enhanced antibacterial activity of ZnO nanocrystals. *Nanomedicine (Lond)* 13 (1), 43-68. doi: 10.2217/nmm-2017-0237
- [17]. Wang, Y., Wan, J., Miron, R. J., Zhao, Y., & Zhang, Y. (2016). Antibacterial properties & mechanisms of gold-silver nanocages. *Nanoscale*, 8(21), 11143-11152.
- [18]. Yuan, Y.-G., Peng, Q.-L., & Gurunathan, S. (2017). Effects of silver nanoparticles on multiple drug-resistant strains of *Staphylococcus aureus* & *Pseudomonas aeruginosa* from mastitis-infected goats: an alternative approach for antimicrobial therapy. *Int. J. Mol. Sci.* 18, 569. doi: 10.3390/ijms18030569
- [19]. Zakharova, O. V., Godymchuk, A. Y., Gusev, A. A., Gulchenko, S. I., Vasyukova, I. A., Kuznetsov, D. V. (2015). Considerable variation of antibacterial activity of Cu nanoparticles suspensions depending on the storage time, dispersive medium, & particle sizes. *BioMed Research International* 2015, Article ID 412530, 11. doi: 10.1155/2015/412530
- [20]. Zaidi, S., Misba, L., & Khan, A. U. (2017). Nanotherapeutics: a revolution in infection control in post antibiotic era. *Nanomedicine: Nanotechnology, Biology & Medicine*, 13(7), 2281-2301.