Chapter 06

Evaluation of Anti-Bacterial Efficacy of Nanoparticles against Major Mastitis Associated Pathogens

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ABSTRACT

The physicochemical features of nanoparticles offer a novel method to combat bacterial infections and antibiotic resistance using nanotechnology. These particles, which have a size range of 1 to 100 nanometers, have improved surface areas, changed optical, chemical, and magnetic characteristics, and quantum effects. These features enable precision targeting and minimal toxicity in customized medicine. Silver, gold, copper, zinc oxide, and other metal and metal oxide nanoparticles have demonstrated exceptional antibacterial activity against a variety of diseases. Particularly noteworthy for their extraordinary properties are zinc oxide nanoparticles, which are used in healthcare, cosmetics, medicine, and agriculture. Customized nanoparticle patterns may be achieved by a variety of synthesis techniques, such as chemical reduction and green synthesis. The processes behind the antibacterial effect include rupture of cell membranes, formation of reactive oxygen species, and modification of enzyme activity, which are all affected by the size, shape, charge, and environment of nanoparticles. Additionally, membrane proteins that are affected by nanoparticles can denature proteins and cause cell death. The study's overall findings highlighted the advantages of nanoparticles antibacterial activity having more alone against some bacteria but in combination with traditional antibiotics were somehow reduced against bacteria. Some studies suggest that improving nanoparticle formulations could be an effective way to combat bacterial infections and address the growing issue of antibiotic-resistant bacteria. To sum up, nanoparticles are a viable tool for improving illness management and battling antibiotic resistance.

KEYWORDS
Nanoparticles, Antibacterial activity, Antibiotic resistance, Nanotechnology, Biofilm inhibition

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INTRODUCTION

A prevalent illness that commonly affects entire herds of cattle is bovine mastitis. Resistant bacteria with the ability to form biofilms are frequently the reason. Because of the remarkable qualities of nanoparticles, the quickly developing scientific field known as nano-biotechnology may be able to treat this sickness. The purpose of the study was to look at how treatment with copper and silver nanoparticles, either separately or in combination, inhibited the biofilms produced by mastitis pathogens (Pedersen et al., 2021).

New alternative treatments for cow mastitis may employ nanoparticles. We identified the nanoparticles' physicochemical characteristics, minimal inhibitory concentration, and interactions with the cell membrane, besides measuring the degree of biofilm reduction. According to the findings, out of all the nanomaterials examined, the silver–copper complex was the most active (biofilm was decreased by almost 100% at a concentration of 200ppm for each tested microorganism species). But individual silver nanoparticles were equally effective (biofilm was reduced by about 100% at

200ppm, but the level of decrease was less at 50 and 100ppm than for the complex) (Joshi et al., 2020).

A wide range of bacterial pathogen-caused illnesses, along with the emergence of multidrug resistance in their genes, necessitate the development of novel therapeutic compounds or new vectors for efficient drug administration and improved disease management. Nanoparticles have become a distinctive class of drugs in the last decade and are being utilized in a wide array of industrial domains, comprising medicines, cosmetics, healthcare, and agriculture (Mascarenhas-Melo et al., 2023).

Nanotechnology is an emerging field with the potential to completely transform various scientific disciplines. Because of their size and form, nanomaterial has a wide diversity of uses and are an important topic in both basic and applied sciences (Nasrollahzadeh et al., 2019).

Particles with a size series of 1 to 100 nanometers in at least one aspect are called nanoparticles. Materials like as metals, metal oxides, polymers, and carbon-based materials such as graphene can be castoff to create them. Because of their small size, these particles have special characteristics not seen in bulk materials, such as improved surface area, quantum effects, and changed chemical, optical, and magnetic assets (Rizwan et al., 2021).

Current investigation using metal nanoparticles like as silver, gold, copper, and iron as well as metal oxide nanoparticles such as ZnO, CuO, Ti_2O, and FeO nanoparticles remains to use nanoparticles as an antibacterial agent (Naseem et al., 2021).

Nanoparticles have a vast external area to bulk relation, which allows ligands to drag to the surface of the nanoparticle in large numbers and consequently interact with receptors on the surface of bacteria. Nanoparticles have strong antimicrobial action. The current effort focuses on the distinct mechanisms that numerous nanoparticles used to regulate bacteria, as well as their differential bond to the surfaces of Gram positive and Gram negative bacteria (Elbourne et al., 2019).

Kinds of Nanoparticles

Metal nanoparticles, which are prepared for metals such as iron, gold, silver, or platinum, have a wide range of usages in fields like electronics, environmental remediation, medicine, and catalysis.

Alkaline oxide nanoparticles, such iron oxide (Fe_2O_3), zinc oxide (ZnO), and titanium dioxide (TiO_2), are utilized as pigments, sunscreens, sensors, and catalysts.

Carbon nanoparticles—which include graphene, fullerenes, and carbon nanotubes (CNTs)—are used in a number of industries, including composites, electronics, energy storage, and medicinal research.

Polymeric nanoparticles, which come from either natural or synthetic polymers, are used in cosmetics, imaging agents, and medicine delivery.

Semiconductor nanoparticles, known as quantum dots, which have size-dependent optical and electrical characteristics, are essential parts of solar cells, displays, and biomedical imaging.

Lipid-based nanoparticles, which are composed of lipids or compounds that resemble lipids, are essential components of gene therapy and medication delivery systems (Soltys et al., 2021).

Various techniques are utilized in the creation of nanoparticles, each designed to provide particles with specific possessions, including size, shape, and composition. Here are a few typical techniques:

To create nanoparticles, chemical reduction involves reducing metal ions in a solution; for example, to make gold nanoparticles, reduce gold ions with agents such as citrate or sodium borohydride. The Sol-Gel Process, which is regularly used for metal oxide nanoparticles such as titania or silica, uses the hydrolysis and condensation of metal alkaline oxides or chlorides in a solution to make a colloidal suspension of nanoparticles.

In a limited micro emulsion system, micro emulsion permits for the founding of nanoparticles inside micelles, providing control over the size and disparity of the particles. By consuming a triggering agent to remove metal salts from a solution, precipitation makes nanoparticles. The size and form of the final product may be controlled by varying reaction parameters, such as pH, temperature, and concentration (Sharma et al., 2018).

Synthesis of Nanoparticles by Biologically

Green synthesis is an environmentally benign method of making nanoparticles with special features by reducing metal ions and creating nanoparticles from natural sources, such as plant extracts or microorganisms. Without the usage of chemical reduction agents, laser ablation creates nanoparticles via ablation of a target material in a liquid environment using a high-energy laser. By electrochemically reducing metal ions onto an electrode surface, electrochemical deposition generates nanoparticles with attractive control over their size and structure. By regulatory the size and form of nanoparticles during synthesis, templates such as porous materials or biological molecules are castoff in template-assisted synthesis to give further control over the possessions of the final product. These methods show numerous ways to the synthesis of nanoparticles, each with distinctive benefits and chances for modified nanoparticle design as shown in Fig. 1 (Roostaei et al., 2023).

This is only one of the numerous methods by which nanoparticles can be created. Scientists continually develop new techniques to modify nanoparticles for specific applications in medicine, electronics, biomedical imaging, and catalysis. The choice of production process is dependent upon several aspects, including cost-effectiveness, scalability, and preferred nanoparticle assets. Each approach has merits and demerits (Zahin et al., 2020).

Categorization of Nanoparticles

Various categorization techniques, comprising dynamic light scattering (DLS), energy-dispersive X-ray analysis (EDAX), atomic force microscopy (AFM), Fourier transform infrared spectroscopy (FT-IR), scanning electron microscopy (SEM), transmission electron microscopy (TEM), UV–visible spectroscopy (UV–Vis), and X-ray diffraction spectroscopy (XRD), may be engaged to closely observe the figure, dimension, surface characteristics, and additional biological possessions. There are numerous imaging technologies existing for use in the medical industry nowadays. The most popular ones are ultrasonic (USI), optical, and magnetic resonance imaging (MRI). Magnetic and luminescent/fluorescent nanoparticles have made major contributions to the development of bio imaging techniques among these imaging instruments. Magnetic NPs are usually utilized for MRI, although fluorescent NPs, such AuNPs, are commonly employed for OI. Apart from inorganic nanoparticles like iron oxides and aurum, viral particles have also been shown to be useful for imaging. This section will cover the uses of these NPs for MRI and OI, as well as provide some examples of inorganic and organic NPs employed in these fields (Patil et al., 2022).

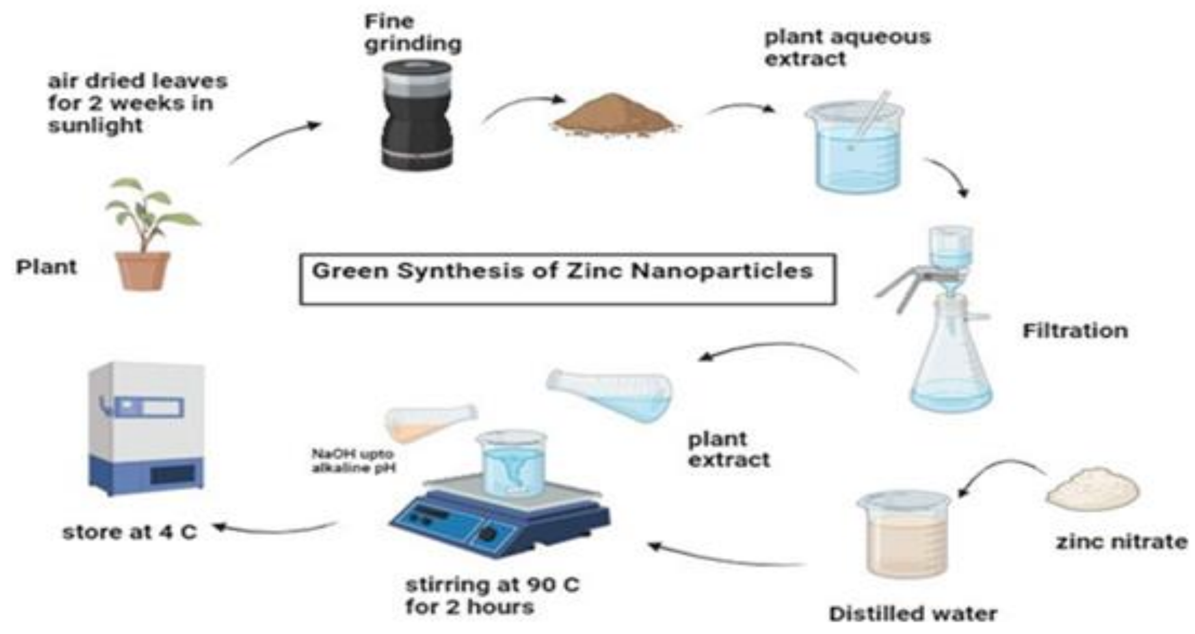

Fig.1: Biological synthesis of zinc oxide nanoparticles.

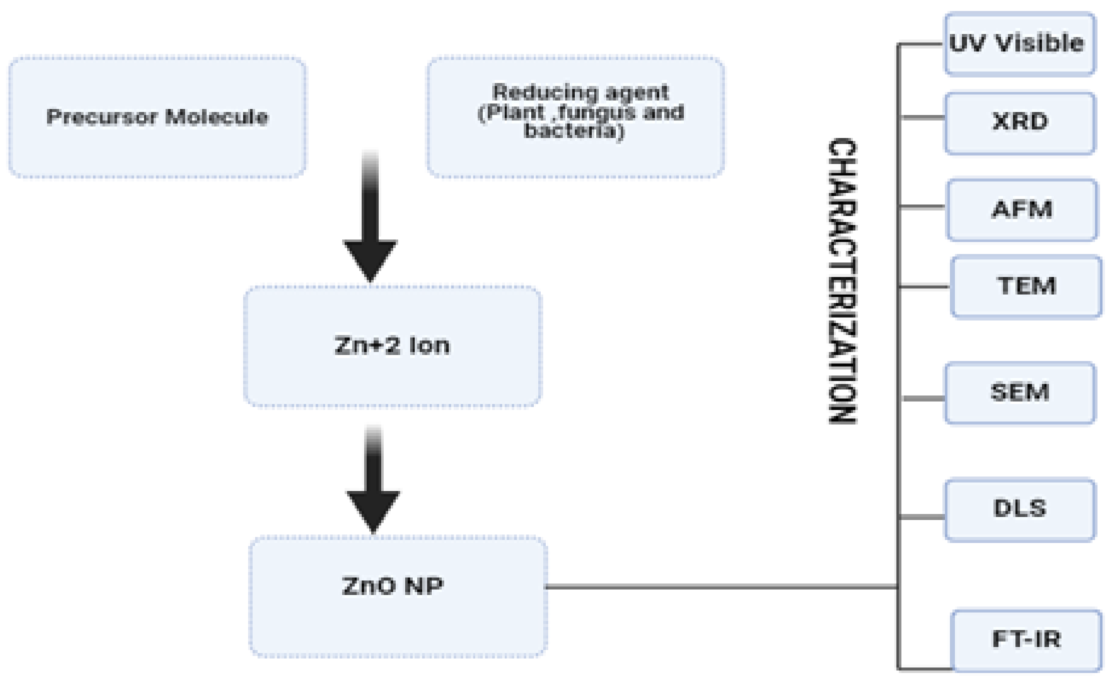

Fig. 2: Green synthesis of zinc nanoparticle and their characterization.

Kinetics of Nanoparticles

Some of the nanoparticle's physicochemical characteristics are changed by its form. The form of the nanoparticle determines how it interacts with the bacterial membrane. Its effective surface area and active facets are altered by the transition from a spherical to a rod-shaped to a triangular form. Compared to rod- or spherically shaped nanoparticles, triangle-shaped nanoparticles exhibit superior bacterial cell membrane contact and, thus, greater toxicity. The discharge of a Zn^{+2} ion from zincoxide nanopartical is also influenced by its shape. Shape has an impact on Zn^{+2} ion release and nanoparticle dissolubility in the water medium by influencing total surface area. When compared to rod-shaped ions, three dimension-shaped zinc-oxide nanoparticle releases Zn^{+2} ion additional efficiently (Agarwal et al., 2018).

Mechanism of Nanoparticles

The advancement of nanotechnology presents novel opportunities for managing microorganisms resistant to drugs as well as associated illnesses and infections. The wide range of organic phytochemicals surrounding green-synthesized nanoparticles helps them interact with various microbial surface receptors, such as proteins, lipids, phospholipids, and lipoteichoic acid. The bacterial complication of the nanoparticle stops the development and production of biofilms (Dua et al., 2023).

The current study also shows how many physiological characteristics of nanoparticles, such as their size, shape, surface charge, and concentration, affect their ability to prevent bacterial growth. It has also been shown how various working circumstances, such as temperature and pH, affect the antibacterial activity of nanoparticles (Pareek et al., 2018).

NPS have demonstrated effectiveness in substituting particular direct sick genes implicated in cancer, specific viral infections, and other genetic illnesses. They are also employed as gene delivery devices. Sadly, the immunological reactions that cationic nanoparticles can elicit restrict their application. Moreover, NPs have been applied to cellular imaging to identify alterations in cells both in vivo and in vitro. NPS can be more effectively targeted by conjugating them with moieties like antibodies and other ligands. Despite their potential proficiency as medicine or gene transporters, there are less NPs in medical usage than one would assume centered on the vast premedical investigations. This is mostly because of possible toxicity caused by poorly understood mechanisms, which is particularly true when NPS are taken on a long-term basis. Like any other substance or medication, the delivery technique and exposure to nanoparticles (NPS) dictate their toxicity. NPS can penetrate the body through the skin, be injected, swallowed, or breathed. The organ-specific toxicity of NPS upon exposure is determined by the injection method and systemic dispersion. Unintentional exposures include inhaling particulate particles from the environment or industry sites (Dionisi and Silva, 2016).

Nanoparticles have become highly effective antibacterial agents in the last ten years, providing tailored medication with low toxicity and precise targeting. They have demonstrated potential in the fight against bacteria resistant to antibiotics by obstructing their food supply or rupturing their cell membranes. Nanoparticles' high surface-area-to-volume ratio allows them to host a wide variety of ligands, which improves the targeting of harmful microorganisms. Silver, gold, copper, iron, zinc oxide, titanium oxide, and copper oxide are just a few of the alkali and alkaline oxide nanoparticle that have shown antibacterial qualities. Particularly zinc oxide nanoparticles have attracted a lot of interest because of their special optical, electrical, and therapeutic properties. Because of their quick electron transport kinetics and high degree of biocompatibility, ZnO nanoparticles are a good fit for biological membrane applications (Jiang et al., 2018).

Using plant components, bacteria, fungi, algae, and organic materials to create nanoparticles is known as "green synthesis" (Fig. 2). Plant metabolites function as both a reducing and stabilizing agent, hence no additional stabilizing agent is required. Phytochemicals are easily manipulated at the laboratory scale and may help to create specialized medicinal uses for nanoparticles. Because they have multiple pharmacologically energetic biological molecules coated on their exterior, which enables numerous ligand-based conjugation of the nanoparticles with receptors microbial membranes, nanoparticles synthesized through the green route, for example, typically display enhanced antimicrobial action than nanoparticles derived physically or chemically (Fadaka et al., 2021).

These biomolecules, which are mostly flavones, organic acids, amides, polysaccharides, ketone, aldehyde, and quinones, are recognized to have important therapeutic effects against a variety of human pathogens. A recent investigation against microbial pathogenic spp. *E. coli, S. aureus, B. subtillis*, and *K. pneumonia* showed that the biologically produced silver nanoparticle (AgNP) produced a greater zone of inhibition than the chemically generated one. Tri-sodium and lemon-synthesized silver nanoparticles showed comparable outcomes, with lemon manufactured silver nanoparticles exhibiting superior antimicrobial activity contrary to both G+ and G- microbes (Gurunathan, 2019).

Influence of zinc oxide nanoparticles size, numerous microorganisms may be controlled by zinc oxide nanoparticles. The antibacterial properties of zinc oxide nanoparticles diminish as their size increases. The presence of soluble Zn^{+2} ions or the pH shift brought on by ZnO NP dissolving in water are thought to be the causes of ZnO NP's antibacterial action. Because a nanoparticle's solubility and size are inversely correlated, there must be an effective Zn^{+2} ion present to limit bacterial growth as shown in Fig. 3 (Ali et al., 2018).

Pharmacodynamics of Nanoparticles

A number of mechanisms are employed by nanoparticles to function as antibacterial agents. Loss of cell membrane integrity brought on by phospholipid bilayer breakdown is regarded as one of the most significant mechanisms. The use of nanoparticles as Reactive oxygen species (ROS)-induced oxidative stress is yet another significant mechanism. By preventing or changing the cycles of DNA replication, protein synthesis, nutrients metabolism, and respiration, this reactive oxygen species molecule contributes to additional cell demised (Sies and Jones, 2020).

Bacterial membranes are easily penetrated by smaller nanoparticles, which result in membrane leakage and cell death. It is believed that the chief contrivance of microbial reticence is the penetration of nanoparticles into bacterial cells, which is significantly influenced by the size of the particles. Since aggregation causes the particles to become larger as a whole, it may potentially affect the antibacterial activity of the nanoparticles. Aggregation also limits the dispersion capacity of nanoparticles in aqueous media, impairing their overall anti-microbial activity as well as their potential to interact with bacterial cells (Ogunsona et al., 2020).

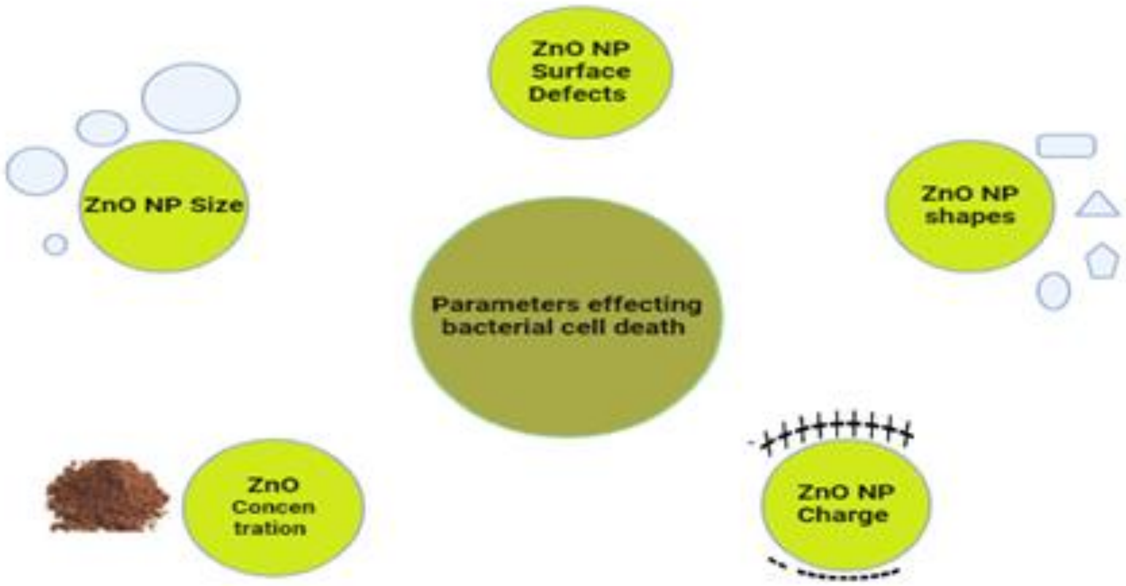

Fig. 3: Impact of shape and size of ZnO-NP.

The external charge Because of their stronger electrostatic attraction to negatively charged cell membrane surfaces, positively charged nanoparticles exhibit greater toxicity towards microorganisms. Influence of the operational environment (culture media pH and temperature) ZnO NP's antibacterial activity is supported by a high temperature and an acidic pH (4–5). The assertion is supported by the findings. An acidic pH promotes more nanoparticle dissolution in the medium. The nominal Zn^{+2} ion concentration in media and, consequently, the antimicrobial activity is increased by the increased solubility of nanoparticles. Similar outcomes were recorded in another experiment. In which the medium's Zn^{+2} ion content was raised by lowering the pH from 9 to 7 (Stanić and Tanasković, 2020).

Raising the temperature causes ZnO NP to become more soluble. Another way that temperature contributes to the growth of ZnO NP's antibacterial activity is through the increased production of reactive oxygen species (ROS) by bacterial cells when exposed to high temperatures. ZnO NP's have superior antibacterial feat than soluble zinc compounds like zinc chloride because of their vigorous directing perspective, capacity to produce ROS in the cell membrane and subsequently disrupt cell membrane integrity, and ability to further aid in protein, lipid, and DNA denaturation. As a result, Zinc chloride's antibacterial activity is mostly related to its capacity to oxidize thiol groups on glycolytic enzymes, hence suppressing the glycolytic process due to the Zn^{+2} ion's unique attraction for the S group (Godoy-Gallardo et al., 2021).

It is known that certain nanoparticles have efflux pump-inhibiting properties. Bacterial cell membranes include efflux pumps, which are involved in expelling waste products and hazardous substances from the cell. These pumps are also known to carry antibiotics out of the cell, extending the life of the cell. When excess Zn^{+2} ions inside the cell reach dangerous amounts, Zn^{+2} efflux trailer protein (cation diffusion facilitator and P-type ATPase) exports them out of the cell. Because the bacterial cell could not recover with nutritional replacement. And another report that ZnONP had a bactericidal rather than bacteriostatic impact on *C. jejuni* bacterial culture (Ogunsona et al., 2020).

ZnO-NPs Adjoining and its Movement Inside the Microbial Cell

The outer layer of the peptidoglycan, triple layer that makes up the cell walls of gram-positive bacteria contains porins. Ion channels called porins are found in the outer layer of peptidoglycan and help passive passage of nanoparticles throughout the cell. Porin has other functions that include recognition, cell-to-cell communication, and nutrition absorption by the cell. Shows the various strategies used by gram + and gram - bacteria for the attachment and internal transport of ZnO nanoparticles. Depending on their size and shape, ZnO NP can also be swallowed via membrane diffusion through membrane-based holes, nonspecific uptake, or endocytosis (David, 2021).

Zinc oxide nanoparticles have a tendency to liquefy in water solutions and release Zn^{+2} ions when a surface's free energy changes. The electrostatic desirability of Zn^{+2} ions to negatively charged membranes is also deliberated to be a typical mechanism of nanoparticles addition to the cell surface. The concentration of Zn^{+2} rises in the microbial cytoplasm due to the native breakdown of linked zinc oxide nanoparticles, which results in membrane outflow and the loss of the proton motive force (Du et al., 2021).

Gram-negative bacteria are more vulnerable to the harmful effects of nanoparticles than gram-positive bacteria because the former have a thinner peptidoglycan layer and are less resistant to the interaction of nanoparticles with their cell membranes. Therefore, the first contact between nanoparticles and bacteria is significantly influenced by the thickness, content, and structure of the cell wall (Tavares et al., 2020).

Membrane permeability is reduced and cell death results from interactions between nanoparticles and membrane proteins that inactivate them. The morphology, size, and shape of the nanoparticle all influence its propensity to surround itself with a protein corona. They connect with a thiol group on this protein corona, which unfolds proteins and has the ability to denature them, ultimately resulting in cell death. Protein surface thiol or sulfhydryl (-SH) groups are reacted with by nanoparticles to generate a persistent S-metagroup, which inactivates the protein. Protein hydrogen ion loss reduces membrane permeability and results in cell death. Zn^{+2} release from the ZnO compound into the media containing bacteria and inhibition of enzymes is necessary for the basic metabolic processes that sustain life (Siddiqi et al., 2018).

Conclusion

Nanotechnology presents a revolutionary avenue for addressing bacterial infections and antibiotic resistance, with nanoparticles emerging as potent antibacterial agents due to their unique physicochemical properties. These nanoparticles, usually extending from 1 to 100 nanometers in size, display distinct characteristics such as greater surface area, quantum effects, and improved optical, chemical, and magnetic properties, allowing accurate targeting and negligible toxicity in personalized medicine. Alkali and alkaline oxide nanoparticles, containing silver, gold, copper, iron, zinc oxide, titanium oxide, and copper oxide, have confirmed significant antibacterial efficacy against a broad spectrum of pathogens. Amid these, zinc oxide nanoparticles (ZnO NPs) have gathered particular consideration for their excellent optical, electrical, and medicinal points, making them suitable for numerous applications in medicine, cosmetics, healthcare, and agriculture. The creation of nanoparticles hires various methods, such as chemical reduction, sol-gel process, micro emulsion, and precipitation, as well as ecologically friendly methods like green synthesis and laser ablation, each donation unique advantages for custom-made nanoparticle design. The antimicrobial action of nanoparticles are accredited to several mechanisms, including disruption of cell membrane integrity, generation of reactive oxygen species (ROS)-induced oxidative stress, inhibition of efflux pumps, and modulation of enzymatic action. The size, shape, surface charge, and operational echo of nanoparticles comedy crucial roles in defining their antimicrobial efficacy, with smaller nanoparticles exhibiting higher toxicity and positively charged nanoparticles representing improved electrostatic attraction to bacterial cell membranes. Additionally, nanoparticles intermingle with membrane proteins and induce protein corona formation, prominent to protein denaturation and following cell death. Inclusively, nanoparticles hold huge prospective as effective antimicrobial agents, proposing new avenues for opposing antibiotic-resistant pathogens and enlightening disease management.

REFERENCES

Agarwal, H., Menon, S., Kumar, S. V., and Rajeshkumar, S. J. C.-b. i. (2018). Mechanistic study on antibacterial action of zinc oxide nanoparticles synthesized using green route. *286*, 60-70.

Ali, A., Phull, A.-R., and Zia, M. J. N. R. (2018). Elemental zinc to zinc nanoparticles: Is ZnO NPs crucial for life? Synthesis, toxicological, and environmental concerns. *7*(5), 413-441.

David, O. M. (2021). The impact of nanoparticles on the proteome of cultured human cells.

Du, M., Zhao, W., Ma, R., Xu, H., Shan, C., Liu, K., and Jiao, Z. J. J. o. H. M. (2021). Visible-light-driven photocatalytic inactivation of S. aureus in aqueous environment by hydrophilic zinc oxide (ZnO) nanoparticles based on the interfacial electron transfer in S. aureus/ZnO composites. *418*, 126013.

Dua, S., Ahmed, H., and Arfin, N. (2023). Soft nanomaterials and their applications. In *Nanomaterials: the Building Blocks of Modern Technology: Synthesis, Properties and Applications* (pp. 27-68). Springer.

Dionisi, D. and I.M. Silva. 2016. Production of ethanol, organic acids and hydrogen: an opportunity for mixed culture biotechnology? Reviews in Environmental Science and Bio/Technology. 15:213-242.

Elbourne, A., Chapman, J., Gelmi, A., Cozzolino, D., Crawford, R. J., Truong, V. K. J. J. o. C., and Science, I. (2019). Bacterial-nanostructure interactions: The role of cell elasticity and adhesion forces. *546*, 192-210.

Fadaka, A. O., Sibuyi, N. R. S., Madiehe, A. M., and Meyer, M. J. P. (2021). Nanotechnology-based delivery systems for antimicrobial peptides. *13*(11), 1795.

Godoy-Gallardo, M., Eckhard, U., Delgado, L. M., de Roo Puente, Y. J., Hoyos-Nogués, M., Gil, F. J., and Perez, R. A. J. B. M. (2021). Antibacterial approaches in tissue engineering using metal ions and nanoparticles: From mechanisms to applications. *6*(12), 4470-4490.

Gurunathan, S. J. A. J. o. C. (2019). Rapid biological synthesis of silver nanoparticles and their enhanced antibacterial effects against Escherichia fergusonii and Streptococcus mutans. *12*(2), 168-180.

Jiang, J., Pi, J., Cai, J. J. B. c., and Applications. (2018). The advancing of zinc oxide nanoparticles for biomedical applications. *2018*.

Joshi, A. S., Singh, P., and Mijakovic, I. (2020). Interactions of gold and silver nanoparticles with bacterial biofilms: Molecular interactions behind inhibition and resistance. *International Journal of Molecular Sciences*, *21*(20), 7658.

Mascarenhas-Melo, F., Mathur, A., Murugappan, S., Sharma, A., Tanwar, K., Dua, K., and Biopharmaceutics. (2023). Inorganic nanoparticles in dermopharmaceutical and cosmetic products: Properties, formulation development, toxicity, and regulatory issues. *192*, 25-40.

Naseem, T., Durrani, T. J. E. C., and Ecotoxicology. (2021). The role of some important metal oxide nanoparticles for wastewater and antibacterial applications: A review. *3*, 59-75.

Nasrollahzadeh, M., Sajadi, S. M., Sajjadi, M., and Issaabadi, Z. (2019). An introduction to nanotechnology. In *Interface Science and Technology* (Vol. 28, pp. 1-27). Elsevier.

Ogunsona, E. O., Muthuraj, R., Ojogbo, E., Valerio, O., and Mekonnen, T. H. J. A. M. T. (2020). Engineered nanomaterials for antimicrobial applications: A review. *18*, 100473.

Pareek, V., Gupta, R., Panwar, J. J. M. S., and C, E. (2018). Do physico-chemical properties of silver nanoparticles decide their interaction with biological media and bactericidal action? A review. *90*, 739-749.

Patil, R. M., Deshpande, P. P., Aalhate, M., Gananadhamu, S., Singh, P. K. J. S., and Interfaces. (2022). An update on sophisticated and advanced analytical tools for surface characterization of nanoparticles. 102165.

Pedersen, R. R., Krömker, V., Bjarnsholt, T., Dahl-Pedersen, K., Buhl, R., and Jørgensen, E. (2021). Biofilm research in bovine mastitis. *Frontiers in Veterinary Science*, *8*, 656810.

Rizwan, M., Shoukat, A., Ayub, A., Razzaq, B., and Tahir, M. B. (2021). Types and classification of nanomaterials. In *Nanomaterials: synthesis, Characterization, Hazards and Safety* (pp. 31-54). Elsevier.

Roostaei, T., Rahimpour, M. R., Zhao, H., Eisapour, M., Chen, Z., Hu, J. J. A. i. C., and Science, I. (2023). Recent advances and progress in biotemplate catalysts for electrochemical energy storage and conversion. 102958.

Sharma, M., Pathak, M., and Kapoor, P. N. J. A. J. C. (2018). The sol-gel method: pathway to ultrapure and homogeneous mixed metal oxide nanoparticles. *30*(7), 1405-1412.

Siddiqi, K. S., ur Rahman, A., Tajuddin, n., and Husen, A. J. N. R. l. (2018). Properties of zinc oxide nanoparticles and their activity against microbes. *13*, 1-13.

Sies, H., and Jones, D. P. J. N. R. M. C. b. (2020). Reactive oxygen species (ROS) as pleiotropic physiological signalling agents. *21*(7), 363-383.

Soltys, L., Olkhovyy, O., Tatarchuk, T., and Naushad, M. J. M. (2021). Green synthesis of metal and metal oxide nanoparticles: Principles of green chemistry and raw materials. *7*(11), 145.

Stanić, V., and Tanasković, S. B. (2020). Antibacterial activity of metal oxide nanoparticles. In *Nanotoxicity* (pp. 241-274). Elsevier.

Tavares, T. D., Antunes, J. C., Padrão, J., Ribeiro, A. I., Zille, A., Amorim, M. T. P., and Felgueiras, H. P. J. A. (2020). Activity of specialized biomolecules against gram-positive and gram-negative bacteria. *9*(6), 314.

Zahin, N., Anwar, R., Tewari, D., Kabir, M. T., Sajid, A., Mathew, B., and Research, P. (2020). Nanoparticles and its biomedical applications in health and diseases: special focus on drug delivery. *27*, 19151-19168.