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Nanoparticle-mediated approaches to combat antibiotic resistance: a comprehensive review on current progress, mechanisms, and future perspectives

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Antibiotic resistance has become a serious global health issue that is responsible for millions of deaths each year globally. Multidrug resistant bacteria (MDR) are difficult to treat and pose a formidable health challenge to clinicians. The misuse of antibiotics has augmented the rise of resistant bacteria like ESKAPE (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* species), thus highlighting the urgent need for innovative strategies. The use of nanoparticles for disturbing bacterial growth, inhibiting biofilm formation and targeting antibiotic delivery could be a promising solution to MDR bacteria. This comprehensive review illustrates how nanoparticles cope with MDR infections due to antibacterial photodynamic therapy and use as carriers for targeted drug delivery systems. Though the applications of nanoparticles in the field of medicine to treat multidrug resistant infections is a promising solution, however, the challenges persist in translating nanoparticle-based systems into clinical settings. The main hurdles include biocompatibility, minimizing the cytotoxicity, overcoming scalability problems, and addressing regulatory and environmental concerns. This review explains the recent progress in metallic and non-metallic nanoparticles that help to combat antibiotic resistance, highlighting their therapeutic applications, mechanisms of action, and integration into existing antibacterial strategies. Future directions highlight research to enhance efficient, safe, and sustainable nanoparticle-based therapeutics that address the growing antibiotic resistance crisis.

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Introduction

Over the past 50 years, antimicrobial agents, particularly antibiotics, have been vital to human health. In 1928, when looking back to the pre-antibiotic age, Alexander Fleming's accidentally discovered penicillin as a miracle medication that transformed traditional treatment approaches. This was because of its remarkable capacity to treat or avoid dangerous infections, which used to be the primary cause of long-term sickness or death. Fleming did caution against the negative effects of incorrect and excessive penicillin usage.[1] Despite the caution, antimicrobial resistance has emerged as a result of the widespread usage of antibiotics in agricultural, veterinary and clinical settings.[2] Due to this, many pathogens are becoming MDR (multidrug-resistant) pathogens and increasing the global health crisis, rendering many standard treatments ineffective and leading to increased morbidity, mortality, and healthcare costs.[3]

Antimicrobial resistance is one of the world's public health issues, according to WHO it causes at least 4.95 million deaths worldwide each year. According to the CDC, Antibiotic Resistance (AR) Threats Report 2019, approximately 2.8 million illnesses each year in the US is caused only by antibiotic-resistant bacteria, leading to over 35 000 deaths. One of major cause of antibiotic resistance are the biofilm production, which is connected to 65–80% of human illnesses.[4] Drug resistance in biofilms can result from several processes, such as the transfer of resistant genes, decreased intracellular drug levels, lower drug absorption throughout the extracellular polymeric matrix, and slow down the bacterial metabolism.[5]

MDR prevents the organism's innate defenses against infections or reduces the efficacy of treatment. There are many risk factors associated with MDR bacteria including treatment

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failure and high mortality rate as shown in Fig. 1. Patients with impaired immune systems, such as those undergoing organ transplantation, chemotherapy for cancer, immunosuppressive medication, or chronic illness, are more susceptible to MDR infection. Furthermore, the cost of treatment has gone up due to MDR since microbes have become resistant to commonly available antibiotics, necessitating the use of a more costly one.[6] According to recent report, current annual healthcare costs estimated at around USD 66 billion globally against MDR infections and this would be going to increase USD 2 trillion by 2050.[7]

According to recent reports, the development of antibiotic resistant genes (ARG) among infectious microbes has been made through HGT (horizontal gene transfer), a serious common health problem.[8] Genes resistant to antibiotics can spread through mobile genetic elements like transposomes and plasmids.[9] Through various processes, including changes in targeted drug, decreased antibiotic absorption, and antibiotic degradation in bacteria could evolve resistance.[10]

As the number of diseases caused by various infectious bacteria rises, pharmaceutical firms and researchers are attempting to find new antibacterial agents that could chemically replace current antibiotics.[11] Since these bacteria are constantly evolving, therefore present antibiotics offer no therapeutic advantage. As a result, this challenging scenario has motivated researchers to look for longer-term treatment approaches to stop the emergence of bacterial resistance.[12] To address the issue of drug resistance, current studies have focused on using nanoparticles as antimicrobial agents against various infections caused by MDR, as well as serving as antimicrobial delivery vectors targeted at certain tissues.[13,14] Nanotechnology and nanoparticles offer a promising solution to combat bacterial resistance, MDR, and microbial.[15] Nanoparticles are biomaterials that range in size from one to one hundred nanometers (nm). Nanomaterials have drawn a lot of interest because of their extensive use in cosmetics, medicines, drug delivery system, agriculture, and most importantly as antibacterial components. They are now thought to be effective additions to or replacements for the antimicrobials that are currently in use.[16] Nanoparticles are formed of three layers since they are not simple molecules. (a) The first layer is the surface, that functions with a range of metal ions, small molecules, polymers and surfactants. (b) The shell layer, that is entirely distinct chemically from the core; and (c) the core, that is the main part of the nanoparticles and is typically used to refer to the nanoparticles itself.[17] Nanoparticles could be used directly for treatment (*e.g.*, zinc oxide, titanium dioxide, silver nanoparticles) and as vehicle for antibacterial agents (*e.g.*, dendrimers, liposomes, polymeric nanoparticles). There are two common applications of nanoparticles: (1) as anti-microbial agents themselves, or (2) in conjunction with clinically related antibiotics that are currently on the market to improve and alter their physiochemical characteristics to overcome antibacterial resistance property. The main areas of action for antibiotics are the inhibition of the synthesis of nucleic acids, translation or transcription during protein production, and the inhibition of production or rupture of the outer wall of cell.[18] However, it is found that the use of nanoparticle technologies has an impact on the respiration system of bacteria, affecting the antioxidant system and causing the system of ROS (reactive oxygen species). This offers a new treatment strategy to overcome antimicrobial resistance.[19]

This study review explores the potential of nanoparticles in overcoming antibiotic resistance by targeting resistant pathogens and enhancing drug efficacy while addressing challenges such as toxicity, scalability, and regulatory hurdles. It highlights recent advances and future directions for integrating nanoparticles into antimicrobial strategies. Unlike previous studies, this review focus mainly the multiple mechanisms of nanoparticles to mediate antibiotic resistance and it has been divided into different sections systematically covering from antibiotic resistance mechanism to nanoparticles mode of action and then therapeutic discussing challenges and future directions.

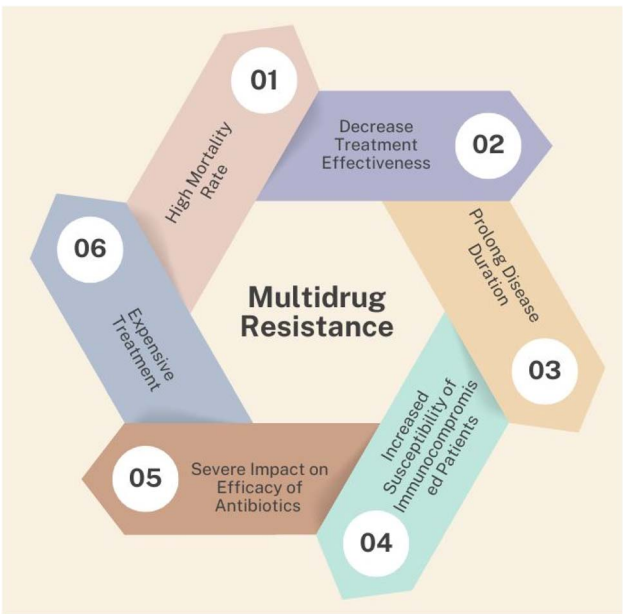

Fig. 1 Risk factors associated with multidrug resistance.

Mechanisms of antibiotic resistance

Antibiotic resistance is a natural and old phenomenon found in bacteria that live in various biological niches, such as forest soil, isolated deep cave networks and marine sediments.[20] Even though bacteria naturally develop resistance to antibiotics, human factors like excessive antibiotic use, improper prescription practices, and widespread agricultural use have enabled the development and spread of MDR bacteria, which exhibit resistance to numerous therapeutically significant drug.[21] The WHO recently released the initial list of 12 MDR infections that are now biggest threats to human wellness for which new medications must be developed immediately.[22] Bacteria develop antibiotic resistance through different mechanisms like efflux pumps, biofilm formation, enzyme production, antibiotic destruction, antibiotic modification,

modifications of antibiotic-activating enzymes, target site alteration, target site protection, and lower the permeability of bacterial cell membrane.[23] Fig. 2 shows the different mechanisms of antibiotic resistance, while some of them are shortly discussed here.

Efflux pump

Bacteria have chromosome-encoded efflux pump genes. Few are constitutively produced, while some may induced or overexpressed in response to specific environmental stimuli or when a suitable substrate is present.[24] Efflux pumps are complicated bacterial systems found on the cytoplasmic membrane that require energy to function and could propel harmful substances from the cell. *Escherichia coli* was the first bacterium to be described with a plasmid-encoded efflux pump that pumped tetracycline outside the cell.[25] Since then, few bacteria have been discovered that contain many efflux mechanisms implicated in antibiotic resistance. Most efflux systems can transfer several unrelated compounds, can result in resistance to multiple drugs.[26]

Biofilm formation

The development of biofilms is another tactic used by bacteria to increase their resistance to antimicrobials. Associations of microorganisms trapped in matrix of extracellular cells that they manufacture themselves are known as biofilms. Through a variety of processes that rely on variables like biofilm composition, architecture, the stage of biofilm development, and growth circumstances, they produce specific habitats that provide bacteria antibiotic tolerance and resistance.[27] The structure of the biofilm prevents antibiotics from penetrating and may also stop bactericidal concentrations from building up throughout the biofilm. Furthermore, the biofilm's gradients in the spreading of oxygen and nutrients produce distinct metabolic states for each cell and promote the growth of bacterial persistence and antibiotic tolerance.[5] Moreover, there are several ways in which biofilms might become resistant to antibiotics. For example, *Staphylococcus aureus* biofilms can colonize within medical instruments like pacemakers, and *Pseudomonas aeruginosa* biofilms cause severe lung problems in people with cystic fibrosis.[28]

Enzymes degradation

Certain enzymes that the bacterium generates precisely render the antibiotic inactive, depriving it of its biological activity. This happens, for example, when beta-lactamases break down beta-lactam medications.[29] Some bacteria develop ESBLs (extended-spectrum-beta-lactamases), that have the same neutralizing action and are difficult to eradicate. Additional enzymes that have the ability to render some antibiotics ineffective include adenyl transferase, phosphotransferase, and acetyl transferase.[4,30]

MDR bacteria and EDR (extensively drug-resistant bacteria) pose a different challenge to public health and the global

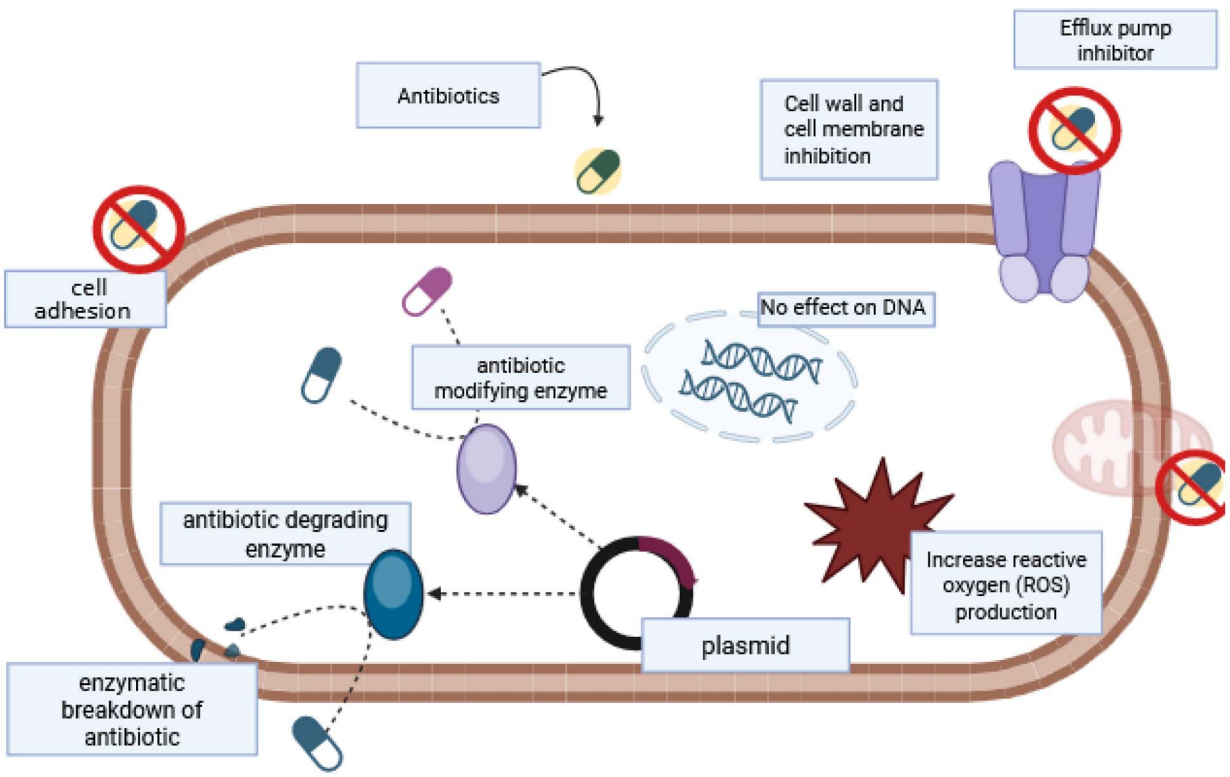

Fig. 2 Various mechanisms of antibiotic resistance, including drug efflux with the help of efflux pump, enzymatic modifications of the antibiotic, enzymatic breakdown of the antibiotics, and modification in the target sites.

healthcare community *etc.* They increase the morbidity and mortality rate, create diagnostic challenges, limit the development of new antibiotics, compromise the medical and surgical interventions, limit the treatment options, cause longer hospital stays, and also cause economic burdens.[4] At least 700 000 deaths worldwide are attributed to MDR per annum, with 23 000 occurring in the US and 25 000 in the EU, according to reports.[31] The WHO says that misuse and overuse of antibiotics are responsible for about 80% of MDR or XDR (extensively drug resistant) bacteria and that these infections have serious side effects.[32] By 2050, 10 million people worldwide are expected to die of bacterial diseases if nothing is done to stop bacterial resistance or develop new medications.[33]

Mechanism of action of nanoparticles

For nanoparticles to have an antibacterial effect, they must encounter bacterial cells. Hydrophobic interactions, electrostatic attraction, receptor–ligand interactions and van der Waals forces are among the recognized kinds of contact.[34] The nanoparticles penetrate the cell membrane, gather within the metabolic route, and alter the structure and functionality of the cell membrane.[35] Subsequently, nanoparticles associate with the fundamental elements of the bacterial cell, including enzymes, DNA, ribosomes and lysosomes. This association results in oxidative stress, heterogeneous alterations, modifications to cell membrane permeability, inhibition of enzymes, imbalances in electrolyte levels, changes in gene expression and deactivation of proteins.[36] According to the latest research, oxidative stress, dissolved metal ion release, and non-oxidative processes are the most often suggested mode of action as in Fig. 3.

The following are the different modes of action of nanoparticles against antibiotic resistance.

Generation of reactive oxygen species (ROS)

Nanoparticles can disrupt the normal metabolic pathways of disease-causing agents through oxidative stress that is due to ROS reactive oxygen species (ROS). The adverse effects of nanoparticles are associated with the generation of reactive oxygen species, such as hydroxyl radicals, superoxide anions and hydrogen peroxide. These ROS hinder DNA replication and protein production, as well as damage cell membranes through lipid peroxidation, affecting membrane permeability and inhibiting oxidative phosphorylation.[37] The quantity of ROS produced by nanoparticles depends on the chemical composition of the nanoparticles.[38]

Disruption of cell membranes

The potential of nanoparticles involves direct contact with the outer wall of bacteria *e.g.* Ag-NPs or ZnO. can permeate the cell wall, leading to alterations in the cell membrane of bacteria. This results in loss of membrane integrity, structural damage, and finally lead to cell die.[39] Nanoparticles also induce the formation of pits in the outer wall of bacteria; for example, Ag-NPs aggregate on the cell surface create small pores in the cell wall move in the cell, and come in contact with fundamental molecules and organelles like DNA and enzyme.[40] On the other hand, TiO_2 produces bactericidal effects by triggering photocatalytic reactions on the membrane of the cell.[41] Anuj *et al.* claim that Ag-NPs have degraded *Pseudomonas aeruginosa* membrane.[42] The perforation of bacterial membranes caused by nanoparticle adhesion permits the nanoparticles to move in to the cell and interact with vital components and organelles including DNA and enzymes.[38]

Destruction of biofilm

Adhesion to the cell surfaces initiates the production of biofilms. However, when cells undergo treatment with nanoparticles, they cannot adhere and establish such a community. This is crucial, particularly when combating pathogenic organisms that generate biofilms.[43] Due to their high surface area-to-volume ratio, nanoparticles interact more effectively with the components of biofilms. This larger surface area makes it possible to contact microbial cells more successfully. Nanoparticles could damage microbial cells by invasion of the biofilm matrix (Fig. 3). Due to their small size, they can more easily penetrate the EPS (extracellular polymeric substance) that envelops biofilm cells and get to the microbial cells that are embedded within ref. 44 Many methods of inhibiting the formation of biofilms include targeting and interfering with quorum-sensing molecules; ZnO-NPs destroy biofilms by releasing Zn^{+} ions.[45] Nanomaterials can damage bacterial membranes and prevent the formation of biofilms, which reduces the microorganism's capacity for life, as numerous studies have shown ref. 46.

Nanoparticles as efflux pump inhibitor

It has recently been discovered that metallic nanoparticles may be able to obstruct bacterial efflux pumps. Nanoparticles attach directly to the pump of the cell membrane, stopping drugs from being whisked away.[18,47] Metal nanoparticles may here act as a competitive inhibitor of antibiotics for the binding site of efflux pumps. Another possible mechanism is through the disruption of efflux kinetics. For Example, the effect of silver nanoparticles for disruption of the efflux kinetics of MDR efflux pump, has already been examined in *Pseudomonas aeruginosa*.[48]

Recent advances in nanoparticle research

Rise of antibacterial resistance has led to significant advancement in nanoparticle-based tactics to combat antibiotic resistance. Here are some recent advances in nanoparticle research for combating antibiotic resistance.

Biomimetic nanoparticle

The application of biomimetic nanoparticles that are altered by artificial or natural cell membranes has improved medication delivery and drawn a lot of interest recently against MDR bacteria.[49] These nanoparticles mimic cell membranes or antimicrobial peptides to evade immune responses and target resistant bacteria. Some of the greatest characteristics of artificial and host nanoparticles are combined in nanoparticles

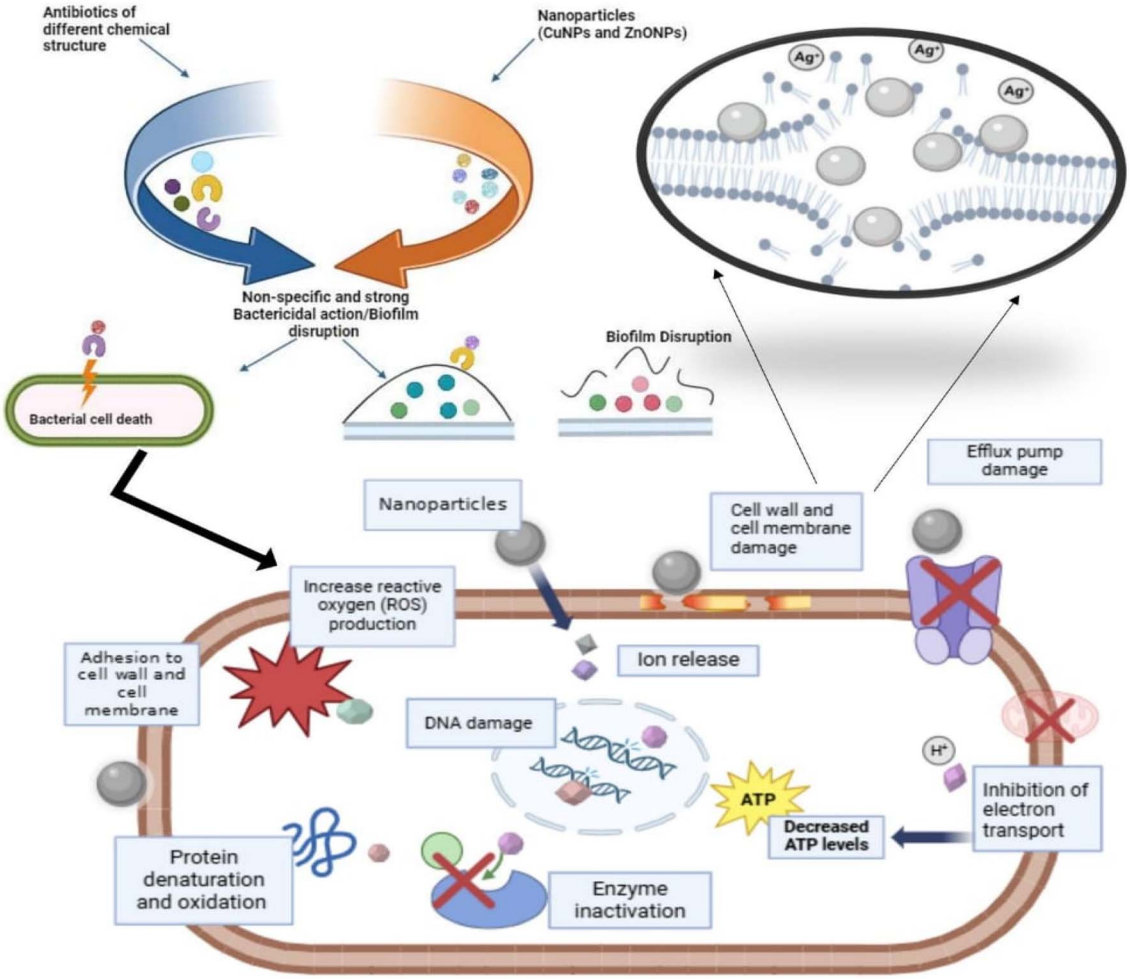

Fig. 3 Primary modes of action for nanoparticles. In addition to activating metal ion release, adhesion, accumulation, and damage to the cell wall and membrane, nanoparticles also show DNA damage, enzyme inactivation, protein oxidation and denaturation, increased reactive oxygen species (ROS) production, and inhibition of electron transport with resulting decrease in ATP level.

that are coated with cell membrane (CM-NPs).[50] Due to their distinct characteristics, including improved targeting ability and immune invasion, CM-NPs offer substantial therapeutic and diagnostic use. Preserving cell membranes' inherent qualities and functions is another advantage of CM-NPs. Because the body views CM-NPs as an integral part of itself, their biocompatibility is quite good. For examples, erythrocyte membrane-coated nanoparticles (RBC-NPs) have been used to improve circulation time and biocompatibility by mimicking red blood cells.[48] It has been reported that Platelet membrane-coated nanoparticles (PNPs) having platelet adhesion properties could target bacteria at sites of injury and interfere the biofilm formation.[51] Consequently, many membrane-coated nanoplatforms have been developed for biomedical devices, primarily focused on cancer therapy.[52] Additionally, it has been documented that CM-NPs can target pathogenic bacteria, neutralize toxins, avoid immune recognition, and deliver medications to treat microbial infections.[53] Currently, CM-NPs can be made using the membranes of erythrocytes, macrophages, platelets, neutrophils, bacteria epithelial cells, and hybrid membranes.[51]

Enzymes mimicking nanoparticles (nanozymes)

Nanozymes also known as enzymes mimicking nanoparticles were first reported in 2007 and are a novel class of synthetic enzymes characterized by distinct physicochemical characteristics and enzymes like properties to disturb bacterial processes.[53] Scientists used the term "artificial enzyme" verbally to describe mimic enzyme models.[54] Compared to natural enzymes, nanozymes offer certain advantages such as low cost and high stability, making them suitable against bacterial pathogens.[55] Medical science has benefited from the use of these nanozymes as many nanozymes have now been used for cancer treatment. As shown in Fig. 4, nanozymes have been known for catalytic activity, ROS production, biofilm disruption and antibacterial activities.[54]

The antimicrobial mode of nanozymes is also based on the production of ROS.POD (peroxidase)-like nanozymes may break

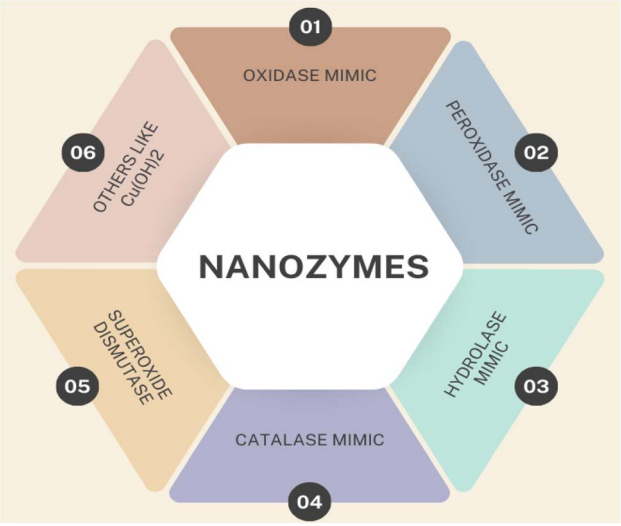

Fig. 4 Catalytic properties of enzyme-mimicking nanoparticles (nanozymes) and their biomedical applications.

down extremely low concentrations of H_2O_2 to form highly oxidative $^{\cdot}OH$, which increases antibacterial activity without endangering healthy tissues.[56] Certain nanomaterials can mimic OXD (oxidase), which is the direct activation of oxygen to produce ROS such as H_2O_2, superoxide anions, and single oxygen on their own. These ROS can kill bacteria and also destroy their biofilm.[57] CuO nanozymes have been found to degrade biofilms formed by *Pseudomonas aeruginosa* through oxidative stress.[58]

Moreover, a variety of nanomaterials demonstrate multi-enzyme-like properties as shown in Fig. 4. For instance, Cu_2WS_4 nanocrystals have outstanding OXD-like and POD-like actions to produce ROS and work as effective antibacterial agents to treat skin infections caused by *Staphylococcus aureus* in mice.[59] MnO_2 and Chitosan nanoparticles could disrupt Gram-negative bacterial membranes like *Staphlococus, Acinetobacter etc* by peroxidase-like action.[60]

Nanoparticle-based antibacterial photodynamic therapy (aPDT)

The merging of nanoparticles in antibacterial photodynamic therapy has improved the efficiency of aPDT, particularly concerning MDR and infections that occur due to biofilms are hard to treat with traditional antibiotics. Nanoparticles enhance delivery, stability, and photodynamic efficiency of photosensitizers, resulting in an increased application of aPDT against bacterial infections. Nanoparticles enhance delivery, stability, and photodynamic efficiency of photosensitizers (PS), resulting in an increased application of aPDT against bacterial infections (Fig. 5). The efficient use of nanoparticles with photosensitizers against wound healing and dental treatment has also been reported.[61] For example, Ag-NPs enhanced the ROS production when combined with rose Bengal (PS) during aPDT against *E. coli*.[62] aPDT is a non-invasive treatment that uses light, photosensitizer, and molecular oxygen together.[63] Meanwhile, it has been found that nanoparticles augment photosensitizers delivery by penetrating into biofilms like chitosan nanoparticles with curcumin (PS) targeted the *Pseudomonas aeruginosa*.[64] ZnO-NPs displayed efficacy against Methicilline resistant *Pseudomonas aeruginosa*.[65] Au and Ag-NPs enhanced ROS production with precise bacterial membrane target in aPDT.[66]

Synergistic effects of nanoparticles with antibiotics

Nanoparticles have capacity to fight bacterial infections by acting as Nano weapons. A promising tactic to fight MDR bacteria is the integration of nanoparticles along with antibiotics to augment their activity. The effects of antibiotics enhance due to nanoparticles beyond their individual action. In fact, against different microbes that are resistant to many drugs, metal oxides and metal nanoparticles have shown encouraging bactericidal activity.[37] When antibiotics are coupled with nanoparticles, antibacterial activity has been enhanced and the adverse results which belong to long-term use of wide-range antibiotics lessened.[67] One of the most promising approaches to address the growing danger of antibacterial resistance is to use nanoparticles in conjunction with antibiotics, as evidenced by their synergistic effects.[40] For example, Synergistic interactions between therapeutically relevant antibiotics and silver nanoparticles, which target the bacterial cell wall, will increase the antibacterial efficacy of the medications. Ag-NPs considerably enhanced the synergistic action of antibiotics (azithromycin, cefuroxime, fosfomycin, cefotaxime, and chloramphenicol) against *Escherichia coli* as compared to antibiotics alone. Nanoparticles can disturb and degrade biofilms that enable the antibiotics to kill bacteria more efficiently. It has been studied that Ag-NPs with penicillin showed increased antibiotic effect against a variety of bacteria.[68] Similarly, Au-NPs with vancomycin, ZnO-NPs with tetracycline, and GO-NPs with ciprofloxacin have showed synergistic antimicrobial activity against MDR bacterial strains.[34]

Nanoparticle-based antibiotic delivery systems

Encasing antibiotics into nanoparticles has emerged, one of the most innovative ways for targeted antibiotic delivery. Nano antibiotics are antibacterial nanoparticles that can enhance the effectiveness of antibiotics.[69] Nanoparticles which are loaded with antibacterial agents also help to combat antibacterial resistance by enhancing (intracellular) uptake, lowering drug-efflux, and inhibiting biofilm development.[70] Nanoparticles-coated antibiotics deliver medications to the target site and simultaneously trigger several antibacterial actions. Because of this combined approach, nanoparticles are superior to single medication or combinations of medication in the treatment of MDR strains.[71] Drug delivery issues are being addressed by nano systems because they can be used to create nano systems that combine the best qualities of the mixture of biomaterials used to create them with the avoidance of their drawbacks.[71] A main aspect of delivery system is its capacity to persist for long time in the circulatory system.[72] Nanoparticles used in delivery systems include a wide variety of types. These include liposomes,

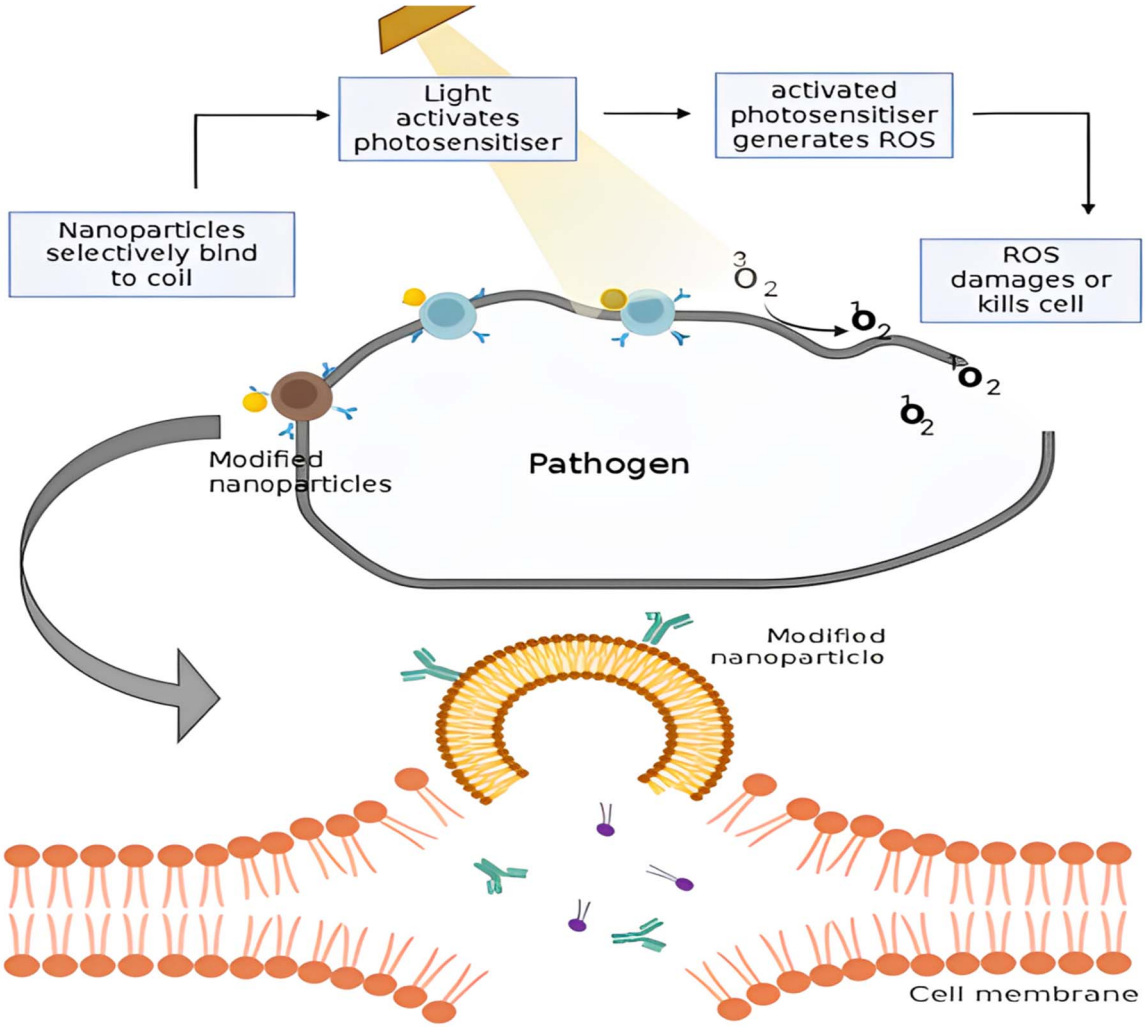

Fig. 5 An overview of nanoparticle-based antibacterial photodynamic therapy (aPDT), illustrating general mechanisms of ROS generation and bacterial inactivation.

organic and inorganic nanoparticles, solid-lipid nanoparticles, and non-toxic biodegradable polymers.[73]

Formulation types of nanoparticles

Here we discuss the nanoparticle types used as antibacterial against MDR (multi drug resistance) bacteria based on metallic and non-metallic forms.

Metallic nanoparticles

Silver nanoparticles. Metallic nanoparticles are either metals or metal oxides.[74] Among metallic nanoparticles, due to its minimal cytotoxicity, silver (Ag) can have antiseptic and antimicrobial properties against various Gram-negative and Gram-positive bacteria.[75,76] Ag-NPs have proven to be successful in treating infectious disorders by inhibiting MDR microorganisms.[8,77] Ag-NPs can destroy plasma membranes and change the structure and metabolism of bacteria because they are small in size and have high ratio of surface area to volume[78] Various techniques based on biological processes has been used to synthesize silver nanoparticles.[79] Because of their nanoscale size (1–10 nm), they can enter bacteria and interfere with intracellular functions, which can hinder the formation of proteins, translation, and transcription.[80] Ag-NPs can cause bacteria's cell membranes to get damaged and produce ROS.[78] Ag-NPs effectively obstruct biofilm development by *Staphylococcus aureus*.[81,82] Ag-NPs have proved to hinder the progress of many microbes, including *Staphylococcus aureus*, *Salmonella typhii*, *Citrobacter koseri*, *Bacillus cereus*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Vibrio parahaemolyticus via* attaching to the molecules present within bacterial cells.[37,38,83]

Gold nanoparticles. Gold nanoparticles block transcription, create pores in cell wall, and bound to Deoxyribonucleic acid.[66] When compared to other metallic nanoparticles, gold (Au-NPs) has not so strong antibacterial effectiveness against both Gram-positive and Gram-negative microbial species. However, Au-NPs smaller than two nanometers exhibit enhanced antibacterial activity, which arises not only from their reduced size but also from the presence of concomitant substances introduced

during synthesis. Compounds such as polyvinylpyrrolidone and ascorbic acid can modify the nanoparticles' reactivity, surface charge, and interactions with bacterial membranes, thereby contributing to the observed antibacterial effects.[84] When used alone, Au-NPs antimicrobial properties are primarily derived from their capacity to disrupt protein formation by blocking capability of transfer RNA to bind ribosome,[85] and to alter the *trans*-membrane potential.[86]

The suppression of ATPase synthesis, which lowers cell metabolism, and inhibiting the ribosome binding component to transfer RNA are associated with the antibacterial activity of AuNPs but they better associate with vaccines, antibodies, and antibiotics.[85] Nicotinamide might be destroyed by Au-NPs, which would then upset the microbial electron transport chain.[84] Au-NPs target microorganisms like *Streptococcus Bovis*, *Staphylococcus epidermidis*, *Enterococcus aerogenes*, *Escherichia coli* and *Pseudomonas aeroginosa*.[78,87,88]

Copper nanoparticles. Copper-containing nanoparticles are efficient against bacteria, decrease MDR biofilms from growing, and function as antimicrobial coating agents. Copper oxide nanoparticles release metallic ions, which can form (ROS) reactive oxygen species and damage the DNA.[38] When CuO-NPs enter bacteria, they impact metabolic activities such as active transport and metabolism.[89] Copper nanoparticles can prevent biofilm formation, inhibit ATP production by interacting with bacterial cells.[90] The combination of Cu_2O nanoparticles with aminoglycoside antibiotics resulted in significant synergistic antibacterial action against *Escherichia coli*.[78] Copper ions exhibit antibacterial activity against several organisms, including *Escherichia coli*, *Clostridium jejuni*, *Salmonella enterica*, *Listeria monocytogenes*, *Staphylococcus aureus* and *Bacillus subtilis*[91,92]

Zinc nanoparticles. Strong, broad-spectrum bactericidal action is demonstrated by ZnO-NPs. They are affordable, biocompatible, and belong to the class of inorganic antibacterial agents. It demonstrates amplification, sensitization, and a synergistic bactericidal activity.[93] ZnO-NPs, are tiny, high surface-area, biosafe, and environmentally benign materials. These NPs have antimicrobial characteristics due to the formation of ROS (hydroxyl radicals and H_2O_2), which enhance cell membrane permeability, internalization of nanoparticles due to force loss, and dissolved zinc ion uptake, which results in a decrease in mitochondrial activity and cell death. They may also cause leakage and bacterial mortality by damaging the bacterial cell membrane's integrity.[38]

Iron nanoparticles. Iron nanoparticles (Fe-NPs) constitute an additional family of antimicrobial compounds. According to several research, altering surfaces activates their antibacterial qualities, which eliminates bacterial biofilms of both Gram-negative and Gram-positive bacteria[94] These have demonstrated as less expensive substitutes in medication solutions, antibacterial coatings, and other applications that aim to limit microbial invasion or eradication since they also hinder the formation of biofilms.[95]

Titanium dioxide nanoparticles. TiO_2 (titanium dioxide) nanoparticles are able to degrade the common food-borne bacteria, *Listeria monocytogenes* biofilms, which can lead to health issues when food is being prepared. Conversely, TiO_2 nanoparticles suppress the proliferation of microbes and reduce biofilms.[96] TiO_2 nanoparticles have a biocidal impact even though it is inert and non-toxic to humans. According to a number of research on the antibacterial properties of TiO_2, when exposed to sunlight or ultraviolet radiation, TiO_2 also produces reactive oxygen species particularly –OH free radicals such as free radicals superoxide ions and hydrogen peroxide which induce tangible harm to the cell walls of microorganisms.[97,98] TiO_2 nanoparticles are also used in hospital environments in antibacterial coatings.

Generally, antibacterial efficiency tends to decrease with increasing particle size, probably because smaller nanoparticles might be capable of passing through the plasma membrane with greater efficacy. In the view of metal nanoparticles, smaller nanoparticles release their metal ions faster if their volume to surface area ratio is larger.[62] These nanoparticles have several special qualities, including increased bioactivity, improved bioavailability, high reactivity with molecules, and novel surface characteristics[99] The antimicrobial activity of various metallic nanoparticles has been summarized in Table 1. The proper incorporation of nanoparticles led to effective interaction with MDR bacteria, leads to the generation of ROS and plasma membrane, which damage and cause the death of the bacterial species.[100]

Non-metallic nanoparticles. Dendrimers are an attractive nano-platform for microbicidal activity and drug delivery because of their large surface area, high (*in vivo*) reactivity, and ability to load both non-polar and polar molecules.[131] Dendrimers have a huge surface region that makes them useful including drug and gene delivery.[132–134] The first and most studied dendrimer for antimicrobial medication delivery is polyamidation, or PAMAM.[135] Certain properties of dendrimers include: its highly branched structure gives a large surface contact-to-volume ratio, leading to exceptional response to microorganisms *in vivo*.[136] Their capacity to load polar and non-polar molecules render them an excellent nano-platform for the delivery of drugs.[131]

Antibacterial activity of dendrimers with a high proportion of (positively) charged sites was greater than that of free antibiotics. This is because the polycationic nature of quaternary ammonium compounds allows them to bind to the (negatively) charged bacterial plasma membrane. This increases membrane permeability, allowing more dendrimers to enter the bacteria, leaking potassium (K^+) ions, and eventually destroying the bacterial cell membrane.[137] In literature, Dendrimers are particularly more efficient against MDR *S. aureus* and *P. aeruginosa*.[138]

Liposomes are spherical nano vesicles that include aqueous compartments or units accompanied by one or more phospholipid bilayers.[139] They have ability to encapsulate medications that are hydrophilic within the aqueous phase or hydrophobic drugs within lipid bilayer distinguishes them from other nanoparticles and significantly expands the range of drugs that may be integrated Fig. 6.[140] According to several studies, liposomal encapsulation increases the safety and stability of antibiotics, extending their bloodstream life and

Table 1 Summarize the various metallic nanoparticles with their mechanism of action and their applications

Nanoparticles used	Targeted pathogens	Nanoparticles mode of action	Applications	Refrences
Silver nanoparticles	*Staphylococcus epidermidis*, *Streptococcus viridans*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Moraxella catarrhalis*, *Proteus mirabilis*	Damage bacterial membranes and trigger the release of (reactive oxygen species) ROS, producing radicals with a strong bactericidal activity	Antiseptic and antimicrobial properties against Gram negative and Gram-positive microbes	101
	Pseudomonas aeruginosa, *Escherichia coli*	Inhibits growth of pathogens by ROS	Drug delivery and have antibacterial activity	102
	Staphylococcus aureus, *Escherichia coli*	Silver ions cause death of bacteria	Used to control growth of bacteria, inhibit cell division, damage the cell envelope	103
	Staphylococcus aureus, *Escherichia coli*, *Citrobacter koseri*, *Pseudomonas aeruginosa*, *Salmonella typhii*, *Bacillus cereus*	Microbicidal effect by producing reactive oxygen	Microbicidal effect against various infections and diseases, and antiseptic efficacy against microbes	90
	Enterococcus faecalis	Generation of ROS	Used in drug design and drug delivery	104
	Staphylococcus epidermidis, *Pseudomonas aeruginosa*, *Staphylococcus aureus*	peroxidation of lipid cytochrome inhibition in electron transport chain		
	Escherichia coli	Reactive oxygen species (ROS) generation	Direct effect on bacterial cell membranes, affect respiration, proliferation and metabolism	38
	Escherichia coli, *Staphylococcus aureus*, *Streptococcus Pneumoniae*	Ribosomal destabilization intercalation of DNA bases	Magnetics, optics, catalysis, mechanics, nanobiotechnology, and nanomedicine, antimicrobial activity, anticancer effects	105
	Klebsiella pneumoniae, *Bacillus cereus*	Proton gradient dissipation leads to lysis	Antimicrobial activities, against MRSA synergistic effect	37
	Klebsiella pneumonia, *Vibrio parahaemolyticus*	Bactericidal activity, damage the membrane of bacteria	Therapeutics, diagnostics, and photovoltaics, as well as catalysts	106
	Proteus sp	Inhibit replication of DNA thus causes death of bacteria	Inhibit DNA replication, act as antibacterial agents, disrupt the cell membrane	107
Gold nanoparticles	*Escherichia coli*, *Pseudomonas aeruginosa*	Antibacterial activity, decrease the level of ATP	Control of diseases, against the cancer cells photothermal therapy, photoimaging	66
	Streptococcus bovis, *Staphylococcus epidermidis*, *Enterobacter aerogenes*, *Escherichia coli*	Bacterial membrane rupture. Bacterial cell wall disruption damage the DNA	Antimicrobial activities against MDR *Escherichia coli*	38
	Staphylococcus aureus, *Bacillus subtilis*, *Kleblesilla pneumoniae*, *Escherichia coli*	Bind to DNA to suppress transcription	Drug & gene delivery systems in cancer therapy, diabetes mellitus, cardiovascular, antibacterial activity	90
	Vibrio cholerae, *Bacillus subtilis*	Loss of membrane potential, inhibit the protein synthesis	Biocidal nano weapons, disrupt the membrane of bacteria, denature the 30 S subunit of ribosome and penetrate inside the cell	37
	Streptococcus bovis, *Staphylococcus epidermidis*, *Enterobacter aerogenes*, *Pseudomonas aeruginosa*	Antimicrobial activities, attach to the cell surface and damage membrane of microorganisms	Penetrate the biological membranes, bactericidal activity, cancer therapy	108
				109

Table 1 (*Contd.*)

Nanoparticles used	Targeted pathogens	Nanoparticles mode of action	Applications	Refrences
	Escherichia coli, *Klebsiella pneumoniae*	Inhibition of ATPase production, disrupt the cytoplasmic membrane	Antimicrobial activity, diagnosis of cancer	
	Escherichia coli	Antibacterial mechanism, attach to the cell wall and penetrate the plasma membrane	Effective against MRSA, antibiofilm and antibacterial activity	110
	Enterococcus faecalis, *Staphylococcus epidermidis*, *Streptococcus pyogenes*, *Enterococcus faecalis and Bacillus*, *Staphylococcus aureus* (MRSA)	Antibacterial and immunological action, generate reactive oxygen species, protein phosphorylation inhibition	Early detection systems, imaging diagnosis, and therapy for diseases specially against drug-resistant microorganisms, immunological characters	111
	Vibrio cholerae, *Escherichia coli*, *Staphylococcus aureus*, *Pseudonomas aeroginosa*, *Enterococcus* species	Antibacterial agents, leads to decrease in the levels of ATP	Biocompatible, non-cytotoxic and used as therapeutic drug delivery vehicles	88
	Pseudomonas aeruginosa, *Escherichia coli*, and MRSA	Antimicrobial activities, attach to the cell surface and damage membrane of microorganisms	Localized surface plasmon resonance (LSPR), role in many applications such as biosensors	112
	Pseudmonas aeruginosa	Interact with the surface of cell, antimicrobial activity	Enhance activity of immune cells against microbes	113
	Escherichia coli, *Staphylococcus aureus*, *Listeris monocytogenes*, *Pseudomonas aeruginosa*	Anti-biofilm and antibacterial activity, breakdown the structures of bacteria, denature the proteins	Prevent biofilm formation, break mature biofilms, and kill many types of Gram-positive	114
Copper oxide nanoparticles	*Escherichia coli*, *Pseudomonas aeruginosa*	Antibacterial effect destruction of cell membrane potential	Gas sensing, hydrogen production, CO (catalytic oxidation), photocatalysis	78
	Bacillus subtilis, *Campylobacter jejuni*, *Listeria monocytogenes*	Inhibit the growth of different pathogenic microbes	Solar cells, gas sensors, conductors and in preservation of polishes and wood	90
	Salmonella enteric, *Klebsiella pneumonia*, *Enterobacter aerogenes*, *Salmonella typhimurium*	ROS production, antimicrobial agents	Biomedical and pharmaceutical sciences	115
	Escherichia coli	Reactive oxygen generation, intracellular content of cell leakage thus causes cell death	High toxicity causes oxidative lesions	37
	Staphylococcus aureus, *Staphylococcus epidermidis*	Binding to DNA disrupts the helix structure, localize into organelles thus disrups the normal functions of cells	To reduce infections in hospitals, burn treatment, prevent microbes and fungi colonization on catheters, vascular grafts, dental materials, eliminate microbes on textile	116
	Staphylococcus aureus, *Pseudomonas aeruginosa*, *Clostridium difficile*, *Escherichia coli*	Result in malfunctions and ultimately kills the bacterial cells, damages the cell and result in the death of cell	Neuropeptide production, cell signaling pathway regulation, antioxidant defence, and immune cell function	117
	Pseudomonas aeruginosa, *Staphylococcus aureus*	Antibacterial activity, decrease the level of ATP, generates the ROS	Semiconductors and heat transfer nanofluids, electronic chips	118
	Staphylococcus aureus, *Escherichia coli*, *Bacillus subtilis*	Disrupt chemical processes within bacterial cells, disrupts the plasma membrane	Field of catalysis, plant pathology therapy, and electrical sensors	92

Table 1 (*Contd.*)

Nanoparticles used	Targeted pathogens	Nanoparticles mode of action	Applications	Refrences
	Pseudomonas aeruginosa, *Staphylococcus aureus*, *Escherichia coli*	Effect metabolic functions of bacteria	Act as antimicrobial coating agents	38
Zinc oxide nanoparticles	*Staphylococcus aureus*, *Mycobacterium tuberculosis*, *Proteus mirabilis*, *Streptococcus pyogenes*	Anti-bacterial activity, generates the reactive oxygen species, damages the membrane of cell	Preservation of food items, cosmetics, wound dressing for fast healing,as an antiseptic ointment, disinfecting agent	119
	Klebsiella aerogenes, *Escherichia coli*	Antimicrobial mechanism, disrupts the plasma membrane, penetrates to the lipid membrane and causes the death of cell	Can be used as potential antibacterial in medicines, biomedical applications, has wide role in addressing drug resistivity issue	115
	Salmonella enterica, *Campylobacter jejuni*, *Listeria monocytogenes*	Enter the bacterial cells and damage them	Act as antibiotic agent for the reduction of coliform bacteria	120
	Listeria monocytogenes, *Salmonella*	Toxic for pathogenic strains along with antibacterial efficacy, generates the reactive oxygen species, damages the DNA	Enhances cell permeability, used as drug delivery vehicle, Act as antibacterial agent	90
	Escherichia coli	Disrupt the microbial plasma membrane, produces the ROS (reactive oxygen species), disrupts the membrane and leads to programmed death of cell	Can be used in photocatalysis, gas sensing, hydrogen production	78
	Staphylococcus aureus, *Pseudomonas aeruginosa*	Inhibition of enzyme lipid and protein damage	Can be used as therapeutic agents, transport of drug to specific site	108
	Escherichia coli, *Staphylococcus aureus*	Inhibit growth of bacterial cells, causes disruption of cell membrane, generates ROS	Antibacterial activity	121
	Staphylococcus aureus, *Streptococcus pyogenes*, *Escherichia coli*, *Klebsiella aerogenes*, *Pseudomonas aeruginosa*, *Proteus mirabilis*, *Mycobacterium tuberculosis*, *Bacillus subtilis*	Antimicrobial activity, ROS production causes oxidative stress, cell death by apoptosis	Anti-bacterial agent, antiseptic ointment, disinfecting agent and for coating of medical devices, water treatment	119
	Pseudomonas aeruginosa, *Vibrio parahaemolyticus*, *Bacillus licheniformis*	Inhibit growth of bacteria, penetrates the bacterial cell, produces ROS	Antibacterial and antibiofilm activity	122
Iron-containing nanoparticles	*Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli*	Bactericidal activity, damage the membrane of bacteria, causes structural damage to cell	Elimination of harmful textile dyes in an environmentally friendly way, effective materials for therapies and have biological applications	115
	Staphylococcus epidermidis, *Staphylococcus aureus*, *Escherichia coli*, *Streptococcus pneumoniae*	Eliminate bacterial biofilms produces oxidative stress, damge the components of cell	Drug solutions and antibacterial coatings and other applications in which microbial elimination occur	90
	Staphylococcus aureus, *Salmonella enterica*, *Pseudomonas mirabilis*, *Escherichia coli*	Antibacterial activity, interferes with the processes of cell, causes death of bacteria	Kill the growth of microorganisms	123
	Bacillus subtilis, *Escherichia coli*, *Staphylococcus aureus*, *Staphylococcus epidermidis*	Generation of ROS, bactericidal activity, effects the transport of ions and molecules	Analytical chemistry, antigen diagnosis, pathogen detection, tissue repair and hyperthermia	124

Table 1 (*Contd.*)

Nanoparticles used	Targeted pathogens	Nanoparticles mode of action	Applications	Refrences
	Salmonella typhimurium, *Staphylococcus aureus*	Bactericidal and antibiofilm activity, act as drug delivery systems, damage the plasma membrane of bacteria	Agriculture, biomedical, and engineering, drug delivery, magnetic resonance imaging, hypothermia therapy in biomedicine	125
	Escherichia coli	Dysfunction of microbial membrane, produces ROS, have antibacterial characteristics	Magnetic resonance imaging	126
	Escherichia coli, *Pseudomonas aeruginosa*	Antibacterial activity, interacts with the iron levels of cell, destroys the cell wall, cause destruction of DNA	Effective against gram positive and negative bacteria	127
Titanium dioxide nanoparticles	*Staphylococcus aureus*, *Escherichia coli*	Inhibit the growth of bacteria, produces hyrdoxyl radicals, superoxide anions	Control the spread and infection of a variety of microbial strains	128
	Enterococcus faecium, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*	Produce oxidixing agents and have antibacterial activity	Utilized in food items such as in chewing gum and sweets, photocatalysts, oxidizing agents	38
	Escherichia coli	Decomposes the membrane, causes the mutuations in DNA, damages the proteins	Photocatalyst, solar cell material, self-cleaning coating material, anti-fogging	129
	Staphylococcus aureus	Reaction with (thioL) group of amino acids (proteins) that occur on bacterial exterior surface and release ions	Antibacterial activity	130
	Pseudomonas aeruginosa, *Enterococcus faecium*, *Klebsiella pneumoniae*, *Staphylococcus aureus*	Damages the DNA thus generates ROS, degrades the proteins and lipids	Semiconductors, and heat transfer nanofluids, electronic chips	114
	Listeria monocytogenes, *staphylococcus aureus*	Minimizing the production of biofilms, damages the DNA, leads to the oxidative stress	Can be used on the surface of medical implants to reduce the rate of contamination by microbes	96

enabling more accurate targeting of infection sites through a variety of delivery methods. This leads to more suitable pharmacokinetic and pharmacodynamics profiles.[141] Aerosolized liposome antimicrobials like ciprofloxacin, tobramycin, amphotericin B and amikacin have been used to treat chronic respiratory tract infections.

Liposomes have a bilayer membrane that mimics cell membranes and can fuse directly with microbes. This allows the liposome's pharmacological payload to be released into the microorganism. Furthermore, liposome surfaces can be easily changed to improve their *in vivo* stability, or to target ligands to enable more selective drug delivery. The use of liposomes as antimicrobial carriers to combat microorganism resistance has grown in research.[131,142]

Liposomes can have antibacterial capabilities, either alone or when encapsulated, which can improve medicine's antimicrobial efficacy. Gram-negative bacteria's outer membrane is a complex barrier that can alter antibiotic interactions with the bacterial wall or block internalization, which makes it a major source of new resistances.[143] However, liposomes may encourage the fusing of bacterial membranes, disrupting the structure and perhaps reversing poor permeability.[143,144] Liposomes have demonstrated activity against MDR bacteria like *Methicillin-resistant Staphylococcus aureus* (MRSA) and *Pseudomonas aeruginosa*.[145]

Another type is polymeric nanoparticles like chitosan, PLGA (Polylactic-Co-Glycolic Acid). They are used as antibacterial against MDR strains and targeted drug delivery.[146] Chitosan having antibacterial properties has been widely used against different bacteria such as *Acinetobacter*, *Escherichia coli*, *Staphylococcus aures*.[147] PLGA nanoparticles were employed to deliver antibiotics (ciprofloxacin and ampicillin) in controlled mannered improved the efficacy against MDR *Klebsiella pneumoniae*.[148] Lipid based nanoparticles (SLNs) are used for sustained release of antibiotics against *Staphylococcus* and *Pseudomonas*.[149] Meso-porous silica nanoparticles (MSN) pores

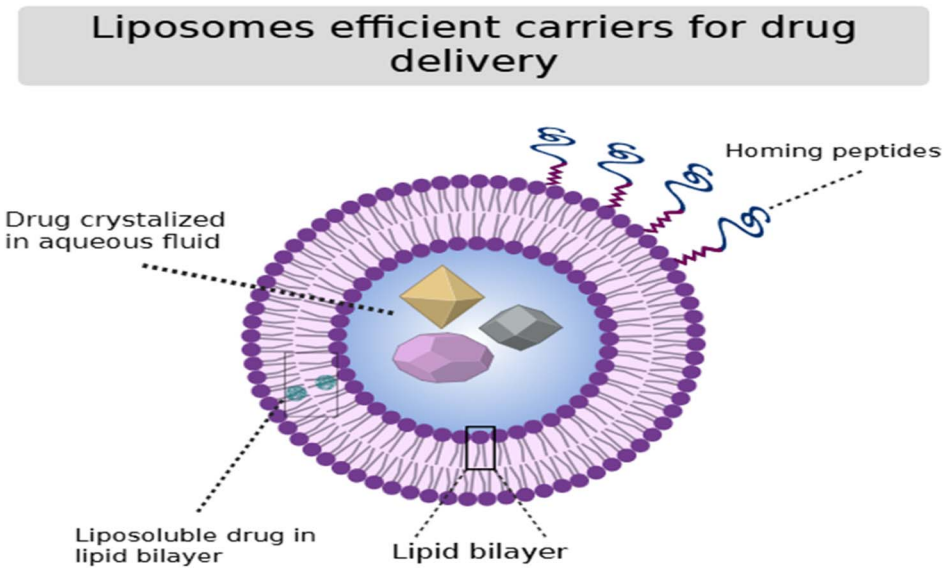

Fig. 6 Liposomal drug delivery systems with entrapped molecules.

allow the encapsulation of antibiotics (tetracycline and gentamicin) and release them at target to control infection caused by *Pseudomonas aeruginosa*[150] (Table 2).

Challenges, limitations and future directions

In the expanding planet, health-related challenges are getting worse. To battle them adequately and sufficiently, the most recent methods are required. The use of nanotechnology and its connection to antibiotic resistance is one of the effective strategies.[165] Though, dealing with nanoparticles has certain limitations. Because of their distinctive size and physical characteristics, nanoparticles provide significant advantages over conventional antibiotics; however, due to this small size characteristic, nanoparticles can breach the physiological barriers of living things and trigger undesirable biological processes.[37] It is evident that nanoparticles can also enter the body *via* skin, intestines, or lungs *etc.* So, long-term exposure could be responsible for threat to public health because of growing worries about the toxicological consequences of these particles.[166] Bioaccumulation of nanomaterials in different tissues leads to toxicity in lungs or kidney. They can also cause cardiac issues, inflammation in the lungs and brain damage.[167]

Sometime, use of organic nanomaterials like liposomes for specific drug delivery leads to premature drug absorption. Also, to develop functionalized organic nanomaterials for targeted delivery is costly and labor-intensive, Scalability and consistent quality in large-scale production remain significant hurdles for organic nanomaterials.[66,168] The development of oxidative stress, DNA damage, and apoptosis by nanoparticles, toxic effects may also result in morphological abnormalities, reproductive problems, and malformations in several non-mammalian animal models.[169]

To date, despite lots of research work on nanomaterials, there is limited possibility of their use against MDR bacteria in clinical settings due to various challenges. The potential toxicity of nanomaterials, which can cause oxidative stress, inflammation, and DNA damage, raises safety issues for human uses.[78,170] Nanomaterials, normally also a subject of great concern for the regulatory authorities. To understand the interactions, between nanomaterials and antibacterial drug is great challenge. Pharmacological assessments are also a concern for nanoparticles due to diverse size range of these nanoparticles. So, uniform pharmacokinetic properties are difficult to achieve for their therapeutic applications. Meanwhile, reproducibility of these nanomaterials at large-scale production is still a limitation factor.[48,141] FDA and European Medicines Agency (EMA) have authorized several nanoparticles for cancer therapy, but guidelines for use these products in soft tissues are still lacking. For the efficient and safe use of nanomaterials, advanced evaluation and detailed regulatory advice is needed. For this, coordination between agencies such as the FDA, WHO, and other health agencies is crucial to develop harmonized risk-assessment protocols, environmental impact guidelines, and post-market surveillance systems for nano-based antibacterial agents.

In the future research should be focused to address the problems faced by the clinicians to apply nanoparticle based system in real life. Therefore, focus on enhancing biocompatibility and reducing cytotoxicity should be preferred. Furthermore, addressing the environmental and regulatory dimensions alongside the development of scalable, eco-friendly synthesis methods will be essential for realizing the full clinical and industrial potential of nanoparticle-based therapeutics against multidrug-resistant pathogens.

Table 2 Summarize the role of non-metallic/organic nanoparticles as antibacterial and in drug delivery system

Nanoparticles used	Targeted pathogens	Nanoparticles mode of action	Applications	References
Liposomes	*Bacillus subtilis*	Liposomes containing antibacterial agents like streptomycin or kanamycin can stop synthesis of protein, thus leads to death of cell	Drug delivery for bacterial infections and antibacterial formulations, also used in cancer therapy and vaccination	151
	Pseudomonas aeruginosa	Bacterial cell membrane disruption can cause lysis of cell when liposomes containing antibacterial drugs such as colistin or tobramycin are present	Antibacterial nanocarriers for controlled release and in cancer therapy	152
	Staphylococcus aureus, *Pseudomonas aeruginosa Saprophyticus*	Act as antibiotic delivery nano-systems, decreasing the selection of resistant strains prolonging the duration of antibiotics in the circulation, enabling more accurate administration of the drugs through different routes to the infection locations	Used in antibacterials that includes antibiotics	145
	Staphylococcus aureus	Vancomycin- or daptomycin-containing liposomes have the ability to stop the formation of cell walls, which kills the cell	Can be delivered directly into microbial membranes, act as drug delivery systems, enhance antibiotic concentration at the site of infection	153
Dendrimers	*Proteus hauseri*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus saprophyticus*, *Staphylococcus aureus*, *Staphylococcus epidermidis*	Antibacterial activity is greater than that of antibiotics, bind to the microbial cell wall, increases the permeability of the membrane, resulting in (k) potassium ion leakage, that eventually leads to the destruction of the microbial plasma membrane	Gene therapy, biomedical applications, biocompatibility and pharmacokinetics, antibacterial agents	136
	Escherichia coli	Antibacterial compounds such as silver or copper found in dendrimers plasma damage bacterial cell membranes, results in lysis and death of cell	Encapsulates the drugs, helps in controlled release of medicines(drugs), deliver the drug safely act as drug delivery systems	146
	Staphylococcus aureus	Cell death may result from dendrimers that contain vancomycin or daptomycin, which block the formation of cell walls	Protects the drugs from degradation, function as non-viral vectors, target specific tissues in the body, promotes differentiation and growth of cell	154
	Bacillus subtilis	Protein synthesis can be inhibited by dendrimers containing antibacterial drugs such as streptomycin or kanamycin, which can ultimately result in cell death	Antbiofilm and antibacterial characteristics	155
SWCNTs (single walled nanotubes)	*Staphylococcus aureus*, *Escherichia coli k12*	The attachment or depositing of bacteria on a bacterial surface. Intracellular fluid leakage	Mechanical, thermal and electrical characteristics used in biosensors and drug delivery	156

Table 2 (*Contd.*)

Nanoparticles used	Targeted pathogens	Nanoparticles mode of action	Applications	References
		and impairment of the cell membrane		
	Escherichia coli, *Bacillus subtilis*	Injuries to the cell wall, seepage of internal fluid, reduction in cell height and volume, and increased roughness on the surface of bacteria	Used in photovoltaics, and nanoelectronics to help in integration into complexed materials	157
f-SWNTs (functionalized single walled nanotubes) with functional groups (–OH, –COOH, $–NH_2$)	*Staphylococcus aureus*, *Bacillus subtilis*, and *Salmonella typhimurium*	While SWNTs functionalized with $–NH_2$ only exhibited antibacterial activity at high concentrations, those functionalized with –OH and –COOH functional groups showed greater microbial inhibition rate (7 log decrease) against certain pathogens	Facilitates the safe delivery of medicines, enhances the specificity such as in MRI and imaging, prevent the growth of bacteria, helps in the repair of tissues	158
SWNTs bound with polyamide WCNmembranes	*Escherichia coli*	Sixty percent of the microbial cells were rendered inactive by the nanocomposite complex after one hour of interaction	Helps in the process of de-salination, importance in separation of gas technologies, helps in development of membranes which can bear high pressure	159
Chitosan nanoparticles	*Escherichia coli*, *Pseudomonas aeruginosa*	Disruption of bacterial membranes due to cationic nature interaction with bacterial cell wall components (*e.g.*, peptidoglycan) ROS generation and inhibition of bacterial enzymes	Drug delivery systems (*e.g.*, antibiotics). Wound healing (chitosan dressings). Antibacterial coatings for medical devices	160
Polymeric micelles	*Escherichia coli*, *Staphylococcus aureus*	Controlled release of encapsulated drugs at target sites enhanced antibacterial efficacy through surface modification	Targeted drug delivery (*e.g.*, cancer, bacterial infections) and coatings for implants and devices	161
Poly (lactic-*co*-glycolic acid) (PLGA) nanoparticles	*Klebsiella pneumoniae*, *Streptococcus pneumoniae*	Controlled release of antimicrobial agents biodegradability and biocompatibility enhancing therapeutic effects	Targeted drug delivery (*e.g.*, to infected tissues) antibacterial and anticancer therapy	162
Polyethylene glycol (PEG)-based nanoparticles	*Escherichia coli*, *Staphylococcus aureus*	PEGylation provides steric stabilization and prevents rapid immune recognition encapsulation of antibiotics for controlled release	Targeted delivery for infections and prolonged circulation time in the bloodstream	163
Polycaprolactone (PCL) nanoparticles	*Staphylococcus epidermidis*, *Pseudomonas aeruginosa*	Encapsulation of hydrophobic antimicrobial agents – slow release over extended periods due to PCL's biodegradability	Controlled release of antibiotics and antibacterial wound dressings	164

Author contributions

Sumreen Hayat: writing – original draft, visualization, investigation, data curation, conceptualization. Asma Ashraf: writing review & editing, Muhammad Hussnain Siddique: writing–review & editing, resources, conceptualization. Bilal Aslam: writing– review & editing, conceptualization, Hamna Shafaqat: writing – original draft, Saba Javed: writing – original draft, resources, Zeeshan Taj: writing– review & editing, Muhammad Hassan Sarfraz: visualization, writing– review & editing, Hafsa Rafiq: visualization, Saima Muzammil: supervision, writing – review & editing.

Conflicts of interest

The authors declare no conflicts of interest.

Data availability

No primary research results and no new data were generated or analysed as part of this review.

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