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Targeted Antibiotic Delivery Using Nanoparticles In The Diagnosis And Treatment Of Bacterial Infections

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Abstract : Diseases caused by bacterial infections, especially drug-resistant bacteria have threatened human health throughout the world. It has been predicted that early diagnosis and therapy will efficiently decrease the mortality rate caused by bacterial infections. Therefore it is urgent to develop effective methods for the early detection for bacterial infections and treat them as soon as possible. Some bacteria can be used for the treatment of bacterial infections such as Escherichia coli (E. Coli), Staphylococcus aureus, Pseudomonas aeruginosa, Salmonella spp, Klebsiella pneumoniae, Mycobacterium tuberculosis, Streptococcus pyogenes, Enterococcus faecalis, Helicobacter pylori. Nanotechnology-driven approaches using nanoparticles can selectively target and destroy intracellular pathogenic bacteria, overcoming conventional drug delivery challenges. Nanoparticles are increasingly being effective for the treatment of bacterial infections due to their unique properties, such as high surface area-to-volume ratio and the ability to be functionalized for targeted delivery. Nanoparticles like polymeric micelles, nanoliposomes, and metal nanoparticles enhance drug bioavailability, stability, and targeting, improving therapeutic effectiveness and minimizing side effects. Even nanoparticles like Silver Nanoparticles (AgNPs), Gold Nanoparticles (AuNPs), Zinc Oxide Nanoparticles (ZnO NPs), Copper Nanoparticles (CuNPs), Iron Oxide Nanoparticles (Fe3O4 NPs), Chitosan Nanoparticles, Titanium Dioxide Nanoparticles (TiO2 NPs), Graphene Oxide Nanoparticles, Silica Nanoparticles, Polymeric Nanoparticles can also be very useful for treatment of bacterial infections as they can encapsulate antibiotics or antimicrobial agent to provide sustained release and targeted delivery to bacterial infections (Xu et al., 2019).

Keywords: Bacterial infections, Drug Delivery, Nanoparticles, Antibiotic agents, Drug targeting.

I. INTRODUCTION

The treatment of infections caused by intracellular bacteria poses several unique challenges. Recent advancements indicate that a nanotechnology- based approach utilizing nanoparticles to specifically target and eliminate pathogenic bacteria can be effectively employed. This nanotechnology strategy aims to address the limitations of traditional drug delivery systems through the design and creation of nanostructures. However, challenges related to drug efficacy, toxicity, stability, pharmacokinetics, and regulatory oversight persist. Localized conditions such as infections and inflammation often feature compromised blood vessels and the overexpression of certain epitopes or receptors, which can serve as potential targets for treatment. Consequently, nanomedicines can be strategically directed to these affected areas. A variety of nanoparticulate systems have been explored as viable drug delivery mechanisms, including biodegradable polymeric nanoparticles, polymeric micelles, nanocapsules, nanogels, fullerenes, solid lipid nanoparticles (SLN), nanoliposomes, dendrimers, metal nanoparticles, and quantum dots. These nanoparticles have proven beneficial in developing systemic, oral, pulmonary, transdermal, and other administration routes, facilitating drug targeting, enhancing drug bioavailability, and preserving drug bioactivity and stability. In recent years, the encapsulation of antimicrobial agents within nanoparticle systems has surfaced as a novel and promising approach that improves therapeutic efficacy while reducing the adverse side effects associated with these drugs. This chapter examines nanoparticle-based drug delivery systems and their clinical applications in the treatment of various bacterial infections, as well as their potential uses in the realms of medicine and biology (Salouti & Ahangari, 2014). Moreover combining nanoparticles with antibiotics help us in providing a complementary approach to target multi drug resistant bacteria by avoiding the regulatory issues associated with some bioconjugate system and thus improve current therapeutic strategies (Gupta et al., 2017). The fast emergence of drug resistance continues to outpace the development of new antibiotics in effectively treating bacterial infections (Selvarajan et al., 2020).

II. NANOPARTICLES

Nanoparticles are defined as solid particles whose size is less than 100 nm. Despite of their small size, the nanostructures exhibit a unique physicochemical and biological feature that make them a commendable material for various biomedical applications (Kumar et al., 2017). Among the different types of nanoparticles, Metallic nanoparticles, especially those made from gold, silver, and copper, have shown strong antimicrobial properties. Gold nanoparticles are used for biomedical applications due to their biocompatibility, storage stability, and ease of surface functionalization. These nanoparticles have unique physical and chemical properties which is useful for drug delivery systems, bioimaging, and anticancer therapy. The surface of gold nanoparticles can

adsorb drug molecules which allows targeted delivery of active ingredients to specific sites in the body of the affected individual. Additionally, gold nanoparticles can be conjugated with antimicrobial agents such as antibiotics, antibacterial peptides, and surfactants to enhance their bactericidal activity (Yeh et al., 2020). Silver nanoparticles are another type of metallic nanoparticle known for their broadspectrum antibacterial properties, including effectiveness against drug-resistant bacterial strains. Silver nanoparticles are more effective as antibacterial agents in their nano-sized form compared to their bulk counterparts. By breaking down the bacterial cell wall, they cause the cytoplasmic contents to leak out and the proteins that are in charge of DNA and RNA replication to become inactive, which is how they kill the bacteria (Yao et al., 2012). Superparamagnetic iron oxide nanoparticles are extensively researched for their bactericidal properties, primarily due to their ability to generate heat under a magnetic field, a process known as magnetic hyperthermia. Superparamagnetic iron oxide nanoparticles can be further functionalized with antibodies, antimicrobial peptides, and aptamers to target specific bacteria, making them versatile agents in antibacterial therapy. Additionally, they are effective in penetrating biofilms when triggered by a magnetic field, which is crucial for treating persistent bacterial infections (Gamarra et al., 2011). Nanoparticles for biomedical applications can also be made from natural and synthetic polymers. Antibiotics can be physically integrated into a polymer matrix or covalently linked to a polymer backbone. Nanoparticles derived from biopolymers are highly valuable for their exceptional biocompatibility and biodegradability. Nucleic acids, peptides, proteins, and polysaccharides are few examples of biopolymers (Gopi et al., 2018). Chitosan, a linear polysaccharide, is notable for its antibacterial and antibiofilm properties, which stem from its polycationic nature that disrupts bacterial membranes. Another commonly used biopolymer is alginate, an anionic polysaccharide derived from algae cell walls. Alginate based nanoparticles serve as effective drug delivery nanocarriers and are extensively studied for their biomedical applications. These advancements in nanoparticle technology hold great promise for improving antibacterial therapies, enhancing drug delivery, and overcoming challenges associated with traditional antibiotics, such as drug resistance and toxicity (Yeh et al., 2020). Understanding how cells uptake nanoparticles is vital for nanotoxicology and drug delivery. Factors like nanoparticle properties and cell conditions influence internalization, with variability in delivery shaping predictive models (Rees et al., 2019).

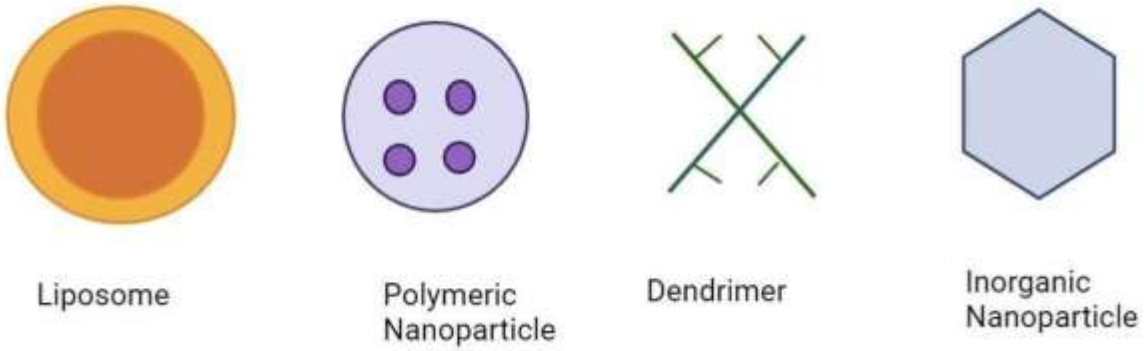

Fig 2.1: Nanoparticle – Based Delivery Platforms for Treating Bacterial Infections

III. Origin Of Nanoparticles

Nanoparticles occur naturally in various environments and have existed long before human intervention. They are formed through a variety of natural processes, including volcanic activity, forest fires, ocean spray, mineral formation and biological formations. Volcanic activity release nanoparticles into the atmosphere. With the advancement of nanotechnology, scientists have developed methods to artificially create nanoparticles for various applications. Techniques like laser ablation, vapor deposition, and ball milling are used to physically create nanoparticles by breaking down bulk materials into nanoscale particles (Jeevanandam et al., 2018). Green synthesis use biological organisms or their extracts (such as plants, fungi, and bacteria) to produce nanoparticles. This approach is often more environmentally friendly and can produce nanoparticles with specific biological properties (Gour & Jain, 2019). The interest in nanoparticles has grown exponentially since the late 20th century, largely due to the unique properties of materials at the nanoscale, which differ significantly from their bulk counterparts. These include increased surface area, quatum effects and enhanced mechanical properties of the nanoparticles (Oberdörster et al., 2007). At the nanoscale, materials can exhibit quantum mechanical properties, such as changes in optical, electronic, and magnetic behaviors (Liu et al., 2016). Nanoparticles often have improved strength, toughness, and durability compared to bulk materials (Guo et al., 2013). Nanoparticles have both natural and synthetic origins, with natural nanoparticles being part of Earth's history and synthetic ones being a product of human ingenuity in nanotechnology. The ability to engineer nanoparticles has led to significant advancements across multiple disciplines, making them a cornerstone of modern science and technology (Palit, 2020).

IV. Advantages

Nano antibiotics offer advantages in overcoming barriers in gastrointestine and enhancing stability, solubility, and oral bioavailability of the drug (Wu et al., 2020). One of the main advantage of nanoparticles is that they are biodegradable. Nanoparticles are also capable of carrying hydrophilic as well as hydrophobic drugs. They also have large surface area which helps them in treating the bacterial infections effectively by allowing great number of drug molecules to be coupled. They can also carry large amount of drugs (Zazo et al., 2016). Some nanoparticles like solid lipid nanoparticles have long term stability and are also of high biocompatibility (Abed & Couvreur, 2014). Moreover in targeted antibiotic drug delivery, nanoparticles cause fewer side effects compared to conventional antibiotics (Zhu et al., 2014).

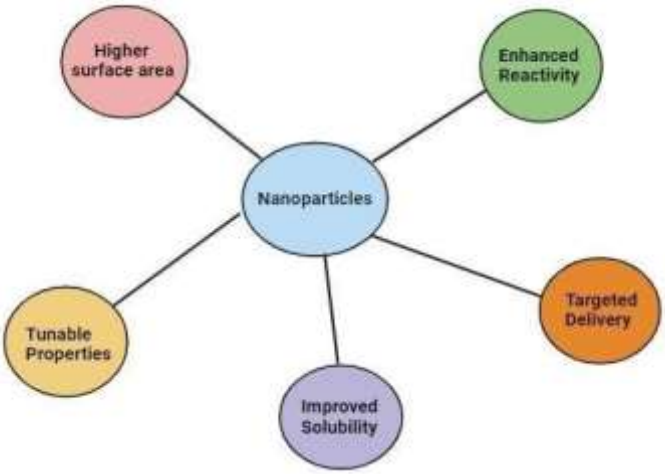

Fig 4.1: Some key advantages of Nanoparticles

Table 4.1: A comparison of Gentamicin drug delivery systems: physicochemical and biological factors of interest (Gamazo et al., 2007).

	Size (µm)	**Controlled release**	**Duration of release**	**Main advantages**	**Main disadvantages**
Liposomes	0.25 - 5.0	No	Days	Good acceptability	Limited stability in biological fluids and during storage and low efficiency
Nanoparticles	0.01 - 1.0	Yes	Weeks	Good stability	Low drug entrapment
Microparticles	1 - 50	Yes	Months	Good stability	The large size can cause embolism

V. TYPES OF NANOPARTICLES

5.1 METAL BASED NANOPARTICLES

Metal based nanoparticles are characterized based upon their size, shape and surface area. All these factors influence their cellular uptake. Generally metal based nanoparticles are small in size so it makes it easier for them to cross boundaries and to easily get absorbed into the bloodstream thereby enhancing the treatment process of the individual (Aderibigbe, 2017). And, metal nanoparticles also release metal ions into the extracellular space, which can penetrate bacterial cells and interfere with their biological processes. Inside the cells, these nanoparticles generate reactive oxygen species, leading to oxidative stress and the oxidation of glutathione. This process diminishes the bacteria's antioxidant defenses against reactive oxygen species (Hosseini et al., 2022).

5.2 GOLD NANOPARTICLES

Gold nanoparticles are suitable for various biological applications like therapeutic and diagnostic applications due to their distinctive physical and chemical properties. (Pissuwan et al., 2010). Gold nanoparticles help detect bacteria by changing their plasmon resonance spectrum upon aggregation, enabling identification of DNA, proteins, and specific bacterial strains (Gao et al., 2014). Gold nanoparticles are also used to convert a weakly binding, biologically inactive small molecule into a multivalent conjugate with enhanced therapeutic potential. (Yaqoob et al., 2020).

5.3 SILVER NANOPARTICLES

Silver in the form of metallic silver, silver nitrate, silver sulfadiazine is found to be beneficial for the treatment of various types of bacterial infections. Metallic silver, have the ability to function as an antibacterial agent. We must treat bacterial infections using silver nanoparticles since many dangerous bacteria have developed resistance to several drugs. Numerous medical applications for silver nanoparticles have also been discovered, including silver-based dressings and silver-coated medical devices such nanogels and lotions (Rai et al., 2009).

5.4 SOLID LIPID NANOPARTICLES

Solid lipid nanoparticles are being used in place of liposomes and polymeric nanoparticles because of their superior qualities. Solid lipid nanoparticles are more viable, sustainable and stable. They can also encapsulate both hydrophilic and hydrophobic medications. By incorporating poorly soluble pharmaceuticals, solid lipid nanoparticles can also improve the solubilization, absorption, and bioavailability of drugs in gastrointestinal tract. In vitro antibacterial activity can be significantly increased and systemic circulation durations can be greatly extended by solid lipid nanoparticles. Additionally, they assist lower dosage and frequency of administration and boost bioavailability (Zhou et al., 2011). Moreover solid lipid nanoparticles are also beneficial in various biological applications such as ocular drug delivery (Chetoni et al., 2016).

5.5 LIPID NANOPARTICLES

Liposomes are tiny spherical vesicles made up of lipid bilayers, often used to deliver drugs in the body. They have the ability to effectively encapsulate drugs, like Gentamicin, according to several factors, like the composition of the liposome (Yadav et al., 2017). Drug entrapment varies according to lipid composition, related to the molar ratio of cholesterol and to the amount of negatively charged phospholipid included, thus, favoring electrostatic interactions with the cationic drug. On the other hand, cationic liposomes seem to entrap Gentamicin more efficiently than comparable anionic vesicles, apparently associated to the vesicle structure (Gamazo et al., 2007).

5.6 PALLADIUM NANOPARTICLE

Palladium is a highly valuable metal known for its exceptional catalytic, mechanical, and electroanalytical properties. Palladium nanoparticles have been developed as selftherapeutic agents with notable antibacterial and cytotoxic effects (Baghayeri et al., 2014). It has been demonstrated that palladium nanoparticles are more effective than Escherichia coli at inhibiting the growth of Staphylococcus aureus, indicating their potential as antibacterial agents, particularly against gram-positive bacteria. Additionally, it was discovered that palladium enhanced the cytotoxicity of different human cancer cell lines when paired with mesoporous silica nanoparticles (Yaqoob et al., 2020).

5.7 ZINC OXIDE NANOPARTICLES

Zinc oxide nanoparticles possess antibacterial properties, capable of inhibiting microorganism growth by penetrating cell membranes and inducing oxidative stress. This oxidative stress can damage lipids, carbohydrates, proteins, and DNA (Sirelkhatim et al., 2015). Lipid peroxidation alters cell membranes, disrupting vital cellular functions. Notably, recent research has shown that this oxidative stress mechanism is especially significant in combating gram negative bacteria. The antibacterial activity of zinc oxide nanoparticles, therefore, holds promise for addressing microbial proliferation, particularly through their impact on cellular oxidative processes (Fadwa et al., 2021).

5.8 ALUMINUM AND COPPER NANOPARTICLES

Aluminium nanoparticles are very beneficial in treating bacterial infections as they can withstand high temperatures and remain stable compared to other nanoparticles (Muzammil et al., 2020). Aluminum oxide nanoparticles also exhibit minute antimicrobial effects primarily by disrupting cell walls, but only at high concentrations. Conversely, aluminium and copper nanoparticles show significant inhibition against bacteria like Pseudomonas aeruginosa and Staphylococcus aureus. For example, copper nanoparticles show superior antibacterial activity against Bacillus subtilis compared to silver nanoparticles and are more costeffective and stable than silver (Huh & Kwon, 2011).

VI. Synthesis And Characterization Of Nanoparticles

6.1 TOP DOWN SYNTHESIS

In this synthesis, destructive method is used. The larger molecules are being decomposed into smaller molecules and then these smaller molecules are transformed into nanoparticles. Some example of Top down synthesis include milling, physical vapor deposition and other destructive approaches (Ijaz et al., 2020). Physical methods of synthesis of nanoparticles include mechanical pressure, high energy radiations, thermal energy or electrical energy to cause material abrasion, melting, evaporation or condensation to generate the nanoparticles. These methods also work based on top down strategy. These methods are advantageous as they are free of solvent contamination and produce even monodisperse nanoparticles (Dhand et al., 2015).

6.2 BOTTOM UP SYNTHESIS

Bottom up synthesis of nanoparticles can be synthesized using various methods. They are as follows:

1. Chemical Reduction: Chemical Reduction method involves the reduction of metal salts using reducing agents to form metallic nanoparticles. It allows for precise control over particle size and morphology but requires careful handling of toxic chemicals (Fiévet et al., 2018).

2. Sol Gel Process: Sol Gel Process involves the transformation of a sol (a colloidal solution) into a gel phase, followed by the formation of nanoparticles. The sol gel process is versatile and allows for the incorporation of different elements into the nanoparticles (Amiri, 2016).

3. Chemical Vapor Deposition: Chemical Vapor Deposition is used to produce highquality nanoparticles by decomposing gaseous precursors onto a substrate. This technique is widely used for producing thin films and coatin

4. Green Synthesis: Recent advancements focus on eco friendly methods, such as using plant extracts or natural polymers as reducing agents. This approach is gaining popularity due to its sustainability and reduced environmental impact (Rana et al., 2020).

6.3 CHARACTERIZATION TECHNIQUES

Characterization of nanoparticles is essential for us to understand about their physical as well as their chemical properties in order to organize them accordingly. Characterization of nanoparticles give us a better understanding about the nanoparticles. Following are the various characterization technique help us in determining the structure, function, capability and many more characteristics about the nanoparticles.

1. Transmission Electron Microscopy: Transmission Electron Microscopy gives us high resolution images of nanoparticles, revealing their size, shape, and structural details. This method help us to study the morphology of nanoparticles (Liu, 2005).

2. Scanning Electron Microscopy: Scanning Electron Microscopy gives us detailed surface images and is also used to study the surface topology and texture of the nanoparticles (Yuan et al., 2018).

3. X-ray Diffraction: X-ray Diffraction is used to determine the crystalline structure of nanoparticles. It gives us information about the phase composition and crystallinity (Moreau et al., 2013).

4. Dynamic Light Scattering: Dynamic Light Scattering measures the size distribution of nanoparticles in a colloidal solution, providing insights into their hydrodynamic diameter (Babick, 2020).

5. Fourier Transform Infrared Spectroscopy: Fourier Transform Infrared Spectroscopy is used to identify functional groups on the surface of nanoparticles, which is essential for understanding their chemical interactions and stability (Mohamed et al., 2017). The methods and techniques outlined above are fundamental for tailoring nanoparticles for specific applications so as to ensure their effective performance.

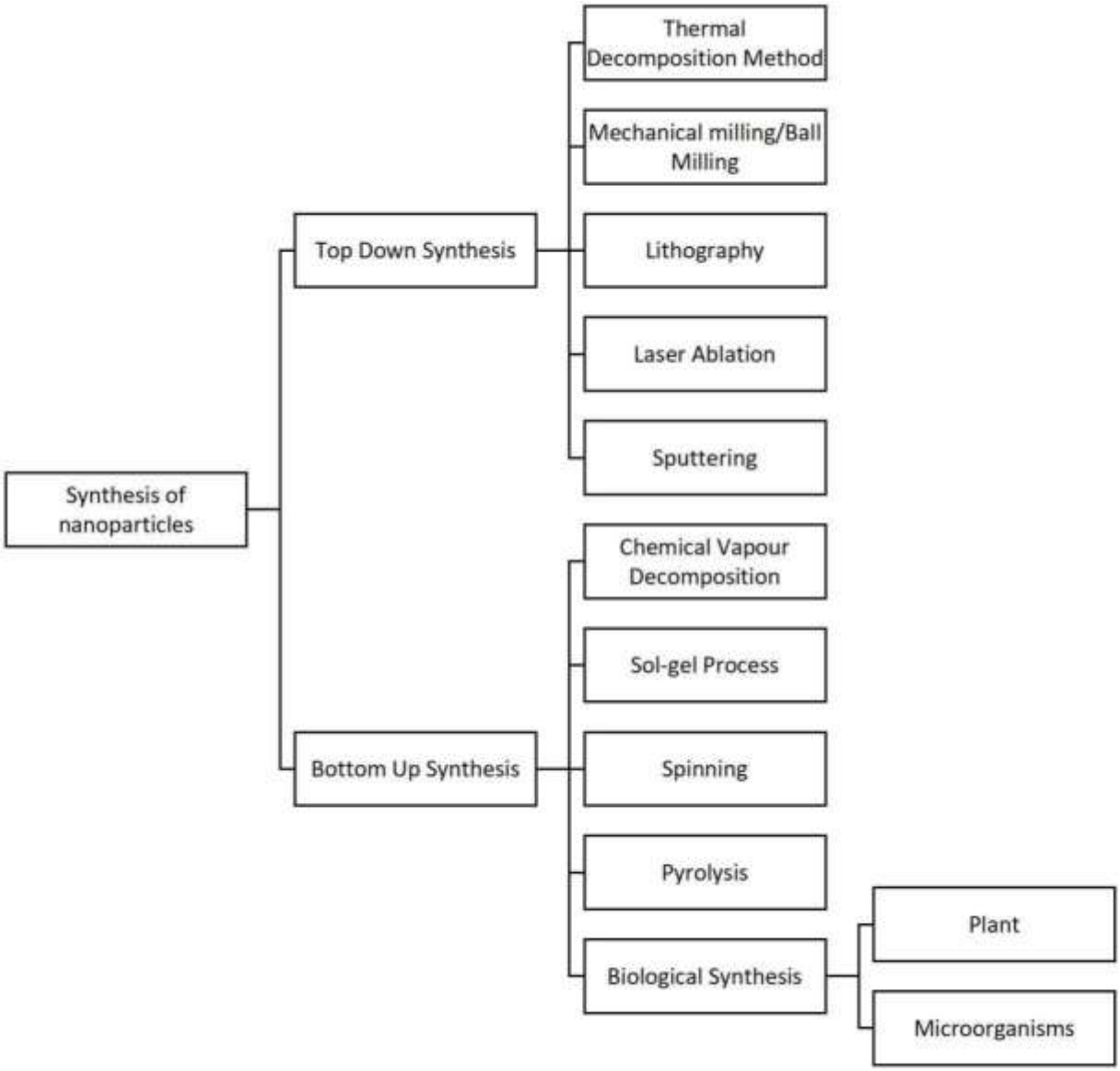

Fig 6.1: Synthesis Methods of Nanoparticles

VII. TARGETED ANTIBIOTIC DELIVERY

The role of antibiotics are mainly based on the treatment of the infectious diseases that were discovered before the early 1980s (Colilla & Vallet-Regí, 2020). Antibiotic delivery and nanoparticles (NP) are important in treating bacterial infections and for a proper systemic delivery, a antibacterial NPs have been developed. Specifically, some methods are made to develop antibiotic delivery and invivo activity by creating drug carrier, they are: Even with the less negative effects, there is an improved results in the treatment, with the lesser possibility of rising of drug resistance from improper drug targeting can cause the drug resistance to develop quickly in unfavorable circumstances, overtaking the mechanisms of drug resistance with long and high local drug concentrations. Nonetheless, creating the antibacterial NPs that would be appropriate for systemic delivery has proven to be a major issue. Significant loss of activity in acidity is known to occur with several antibiotics, and even more concerning, a decrease in localized pH is typically a consequence of increasing disease severity and prognosis just when maximum efficacy is most needed (RadovicMoreno et al., 2012).

Antibiotic resistant bacteria can develop resistance by changing the target's active site, which lowers the drug's binding efficacy, destroying or modifying the antibiotic by certain organisms that make enzymes, or allowing the antibiotic to escape from their cells (Salouti & Ahangari, 2014). These can help the bacteria survive even when antibiotics are used, which is how they develop resistance. This makes infections harder to treat and is a major challenge in healthcare. The antibacterial and antifungal properties of silver nanocomposites, as well as the separate silver nanoparticles, were evaluated through the standard microdilution method, which shows the discovery of the minimum inhibitory concentration (MIC) of an antibacterial agent (Prucek et al., 2011). Antibiotics are released more to treat the bacterial infections if there are more bacteria present at the infection site (Thamphiwatana et al., 2014). Antibiotics are like medicines that treat bacterial infections. When they were first discovered, it quickly became clear that some bacteria could become resistant to them. During his 1945 Nobel Prize address, Alexander Fleming, the man who created penicillin, spoke against the dangers of antibiotic resistance. He said that if people could buy penicillin from stores, there would be a risk. People might take

too little of the medicine, and this could expose the bacteriato a weak dose. The bacteria could then become resistant to the antibiotic, making it less effective in the future (Vassallo et al., 2020).

7.1 ROLE OF ANTIBIOTIC DELIVERY

For the antibiotic treatments, the role is to accomplish in increasing drug concentration at the location of infection place. Recent advancements in stimuliresponsive system development have made it possible for antibiotics to be factorized to the illness site. The medication concentrations attained at the target site may be raised by the antibiotics capacity to release themselves selectively in response to a stimulation. Consequently, this can overcome antimicrobial resistance, minimize medication buildup in healthy tissues and associated side effects, and significantly increase antibacterial efficacy. While antimicrobial nanoparticles are promising substitutes, careful consideration of factors like dosage is necessary when using them in clinical settings to ensure successful therapy. Moreover, these products biocompatibility is a crucial component that is sometimes overlooked when characterizing novel materials and any possible harmful impacts on humans. Any harmful consequences on the environment also need to be taken into account (C. I. Colino et al., 2021). Compounding this issue is the tendency of many bacterial pathogens to form biofilms, which serve as protective barriers that bacteria construct to safeguard themselves. The presence of biofilms complicates the treatment of infections, as they confer an enhanced level of resistance to antibiotics. When bacteria reside within a biofilm, standard antibiotic treatments become significantly less effective, as the biofilm obstructs the penetration of the drug to the bacteria. These developments underscore the pressing necessity for innovative and alternative strategies to address bacterial infections. As the challenge of antibiotic resistance escalates, it is evident that dependence on traditional antibiotics alone is inadequate. It is imperative that we investigate and develop additional methods to effectively combat these resistant bacteria and safeguard public health (Meeker et al., 2018). Metals and metal oxide nanoparticles (NPs) have the potential to be a powerful antibacterial agent which pathogens do not cause resistance. These nanoparticles employ a variety of antibacterial strategies to combat the infections; they can directly damage the cell membrane or produce free radicals. Nanostructured antimicrobial drugs assist reduce toxicity, overcome resistance, and lower cost when compared to traditional antibiotics. Furthermore, there are nanoscale drug delivery systems that can effectively deliver antibiotics by enhancing the pharmacokinetics and therapeutic effects. The development of quick, precise, and affordable diagnostics for the identification of pathogenic microorganisms is aided by nanotechnology as well. The introduction of nanotechnology, in particular nanoparticles (NPs), and their application to drug delivery and infectious disease control is the main goal of this review (Ranghar et al., 2013).

7.2 DRUG RELEASE: The early release of antibiotics would lead to ineffective treatment, making it crucial to minimize premature drug release. If this is not achieved, there may be no significant clinical distinction between the drug that is released freely and the drug that is released uncontrollably from some nanoparticles, potentially failing to reaching the targeted diseased region (Aguilera-Correa et al., 2022).

Prior research has demonstrated that incorporating antibiotics with metal nanoparticles can reduce bacterial susceptibility and enhance the effectiveness of the antibiotic. However, at present, infections caused by resistant bacteria are managed using last-resort antibiotics. These antibiotics are infrequently prescribed and tend to exhibit greater toxicity or adverse effects (Fuller et al., 2020).

VIII. ADVANTAGES IN DRUG DELIVERY

Drug delivery systems involve the creation of nanocarriers that are intended to bind to particular areas in the body so that therapeutic medicines can progressively accumulate there. The goal of this tailored strategy is to limit the delivery of drugs to diseased tissues. In nanomedicine, two main approaches are being investigated at the moment. In the first, certain biologically active chemicals that can recognize and attach to target cell receptors specifically are added to nanocarrier particles. The second plan of action focuses on developing magnetic medication delivery devices that may be applied and manipulated with an external magnetic field to move them to the desired place (Caldera et al., 2022). Because the hydrophobic properties of drug molecules make them less stable for therapeutic usage, the efficacy of antibiotics against these resistant strains is severely impaired, making the advent of bacterial drug delivery resistance a real danger to human society. The antibacterial properties of nanomaterials present promising avenues for addressing bacterial drug resistance. Antibiotic resistance indicates a notable resilience of bacteria that can proliferate in the presence of one or more antibiotics. The overuse and incorrect use of the antibiotics has led to a significant risk to human health in the form of multidrug-resistant bacteria. The insufficiency of effective antibiotics could render common infections, such as bacterial pneumonia, and complex medical procedures, like open heart surgery, increasingly perilous in the future. Factors such as antibiotic overuse, prolonged treatment durations, sub therapeutic dosing, prophylactic antibiotic use, and the misuse of antibiotics for non-bacterial conditions contribute to the limitation of their effectiveness and the emergence of resistance. Consequently, it is responsibility to devise new alternative scheme that are targeted and responsive to stimuli in order to effectively combat bacterial infections (Ahmed et al., 2020).

8.1 USE IN MNPs: The pre determination of drug kinetics and targets is made easier with the use of MNPs, which is essential for preserving the ideal dosage inside the therapeutic window. This approach allows for the administration of reduced drug quantities, thereby minimizing toxicity and lowering the costs associated with pharmaceutical formulations. Furthermore, MNPs can be delivered through a wide range of routes, from local to systemic, enhancing the targeted delivery of pharmaceuticals. This capability may lead to improved bioavailability, continuous drug releasing or extended drug vulnerability. In patients diagnosed with cystic fibrosis (CF), the potential benefits of MNPs have been demonstrated (Tan et al., 2020).

8.2 USE IN NANOCARRIERS: The field of the nanotechnology have been made important into the area of medical treatment, offering advanced methodologies for the design and engineering of nanoparticles that serve as nanoweapons against bacterial infections, surpassing the efficacy of traditional antimicrobial therapies. These nanoparticles are intended to function as targeted nanomedicines for localized applications, providing enhanced antimicrobial effects at reduced dosages, thereby minimizing toxicity

and adverse effects. Among the various types of nanoparticles, some possess intrinsic antimicrobial characteristics, including metal nanoparticles such as silver, gold, etc and metal oxide nanoparticles such as zinc oxide, copper oxide, and titanium dioxide, etc serve as nanocarriers for antimicrobial agents, commonly referred to as nanoantibiotics (Álvarez et al., 2021). The utilization of nanoparticles as a drug delivery system (DDS) remains in the nascent phase of advancement. However, nanotechnology offers a compelling approach to overcome several clinical challenges frequently faced in the development of new pharmaceuticals. Those nanoparticles possess remarkable physicochemical and some biological characteristics that provide substantial benefits for drug delivery. Research has shown their capacity to improve drug solubility, decrease treatment-related toxicity, enhance the precision of drug targeting, and control the release rate of medications (Alavi et al., 2024). It is necessary to consistently evaluate the in vitro antibiotic activity of the medication formulation in nanoparticles with that of the free drug as a control. The pace at which antibiotics are released from nanoparticles and the rate at which the break down of the polymer have been discovered to be substantially linked. An further challenge, especially when using traditional antibiotic therapy, is the inactivity of many intracellular bacteria (Pinto-Alphandary et al., 2000). For the drug delivery, magnetic nanoparticles are a wide scope of biomedical applications. Drug delivery can perform from the higher magnetic point (Kim et al., 2009). When compared to micro particles, NPs offer a larger surface to volume ratio, more precise targeting, and a more controlled and sustained drug release (Rashki et al., 2020). The use of drug delivery has been extremely successful in the past several decades in treating a wide range of bacterial diseases. Antibiotics have historically been widely administered systemically in order to have the benefit of targeting pathogenic germs that are widely dispersed. As an alternative, they have also been applied locally, which is crucial in order to achieve a high medication concentration at the infection site (Gao et al., 2018).

IX. Types Of Bacterial Infections

The diagnosis of bacterial infections and the treatment of infectious diseases are essential for humans health, particularly in light of the emergence of new infectious pathogens, despite significant advancements in the area of medicine (Hasan et al., 2016). Bacterial infections of pathogens which is present in humans can create large health care difficulty (Toti et al., 2011). It has been suggested that in order to treat bacterial infections, an antibacterial agent have been developed that has the ability to fight the issue of antibiotic overuse. The majority of antibiotics used in clinics to treat the bacterial infections break off the intestinal barrier and can cause bacterial resistance (J. Li et al., 2019). The infections on the human beings not only occur on bacteria , also infect on microorganisms like yeasts, viruses and molds in the living environment. The beginning of harmful bacterial resistance to antimicrobial drugs in recent times poses a significant health concern (Shahverdi et al., 2007). Here is some bacterial infections:

9.1 INFECTION ON STAPHYLOCOCCUS AUREUS: The emergence of the bacterial action to antibiotics has required the use of antibiotics that exhibit significant toxic effects. Staphylococcus aureus is recognized as one of the frequent pathogens responsible for invasive infections in both healthcare environments and the general community. Severe and perhaps fatal infections produced by S. aureus can present as sepsis, endocarditis, pneumonia, toxic shock syndrome, and abscesses. This approach has proven to be an effective and unbiased technique for discovering peptides that selectively target various diseased tissues, including tumors, atherosclerotic plaques, and areas of tissue injury (Hussain et al., 2018).

9.2 INFECTION ON ESCHERICHIA COLI: Bacteriophages have been made use as a recognition agents for the detection of bacteria, based on their targeting capabilities and infectivity towardsspecific bacterial strains. In this context, bacteriophages that are capable ofinfecting E. coli have been extensively utilized to functionalize magneticnanoparticles (MNPs) for the purpose of capturing E. coli (Xu et al., 2019). Escherichia coli is a bacterium linked to foodborne illnesses due to thesecretion of a toxin known as Shiga, which leads to diarrhea and significant kidney damage. Recently, nanodecorated electrodes have been created for the purpose of detecting bacteria, E. coli (C. Colino et al., 2018).

9.3 INFECTION ON ENTEROCOCCUS FAECALIS: The main activating agents of pulpal necrosis and periapical lesions are found to be bacteria and the toxins they produce. Infections within the root canal are often caused by various microorganisms, including facultative anaerobes and anaerobes, which are predominantly present in cases requiring root canal therapy and those experiencing post treatment complications. Enterococcus faecalis is frequently isolated from unsuccessful root canal treatments and infections that exhibit resistance. Furthermore, Enterococcus faecalis possesses the capability to evade the lymphocytes located within the root canal system, which can result in the failure of endodontic treatments (Arafa et al., 2023).

9.4 INFECTION ON BRUCELLOSIS: An infectious disease called Brucellosis is linked to the Brucella species. Brucella suis, Brucella melitensis, Brucella abortus, and four other distinct species. Pathogens such as Brucella canis are acknowledged. in humans, each linked to distinct natural host animals. These tiny coccobacilli are primarily found inside of phagocytic cells, complicating treatment efforts, as most antibiotics, despite demonstrating high in vitro efficacy, struggle to penetrate cellular membranes effectively. Over the past twenty years, numerous studies have established substantial evidence regarding antibiotic treatment protocols;however, the optimal antimicrobial therapy for human brucellosis remains a topic of debate. Due to their intracellular positioning, prolonged treatment regimens involving multiple antibiotics are often necessary. Relapses are common, attributed to the limited effectiveness of various drugs and issues with patient compliance. Consequently, alternative strategies, like drug delivery systems aimed at enhancing bacteriakilling activity within cells, warrant consideration. Gentamicin has been tested against B. abortus-infected murine monocyte when it is encapsulated in different liposomal forms with all liposomes demonstrating a reduction in bacterial counts, particularly the stable plurilamellar vesicles (SPLVs), which proved most effective. Rat alveolar macrophages have also been demonstrated to receive the antibiotic in a pH-dependent manner via rifampicin-loaded mannosylated dendrimers (Salouti & Ahangari, 2014).

X. NANOPARTICLE-BASED BACTERIAL INFECTIONS

Accurate tools for identifying pathogens are essential for researchers and clinicians in the fight against the proliferation of infectious diseases. Despite the critical need for precise pathogen diagnosis, the methodologies employed for diagnosing infectious diseases have seen minimal evolution over the past five decades. Traditional diagnostic techniques encompass microscopy, tissue culture, ELISA, and PCR. These methods are often characterized by high costs, limited capacity to distinguish between pathogens, slow processing times, and inadequate detection thresholds. Currently, the focus of molecular disease diagnosis is shifting towards recent advancements in nanotechnology. Nanoparticles' unique electrical, magnetic, luminescent, and catalytic characteristics provide a number of benefits for the quick, accurate, and efficient detection of microbiological pathogens as well as for addressing drug resistance. Nanoparticles are utilized in diagnosing infectious illnesses using three different methods for developing biosensors: assays using lateral flow immunochromatographic, nanoparticle aggregation assays, and nanoparticle labeling of entire pathogens (Al-Awsi et al., 2024). Human health is seriously endangered by the global return of bacterial diseases and the development of antibiotic resistance. Currently, zinc oxide nanoparticles (ZnO NPs) are under extensive investigation owing to their distinctive antibacterial and antifungal characteristics. It is well established that pathogenic bacteria possess cell surface proteins that facilitate adhesion and colony formation (Singh et al., 2020). Before Alexander Fleming's discovery of penicillin, treatments for bacterial and fungal infections primarily relied on metals, metallic oxides, and metallic salts. The advent of antibiotics significantly reduced the use of these substances. However, the new antibiotics and the rise of antibiotic resistances have prompted a renewed interest in these traditional antimicrobial agents. While bacterial cellulose fibers themselves lack antimicrobial property, the introduction of When added to these fibers, silver nanoparticles (Ag NPs) have shown a strong antibacterial impact against of S. aureus and E. coli (Lakshminarayanan et al., 2018). The rise of bacteria resistant to antibiotics bacterial strains exacerbates the severity of illnesses, prolongs hospital stays, and increases mortality rates associated with infections. As a result, there is a growing interest in the process of novel agents and methodologies for the prevention, diagnosis,and the treatment of bacterial infections. It is essential to create molecular imaging probes that are able to evaluate treatment responses, precisely identify bacterial infections, and ultimately assist in clinical decision making. Moreover, the application of contrast compounds specific to bacteria may improve our knowledge of infection pathogenesis. Targeting bacteria using imaging probes would make it easier to monitor the course of infections in vivo and assess how well medications work in animal models. This progress may make the way for the creation of new antibiotics designed to combat bacterial strains that have become resistant to existing treatments. Numerous molecular imaging probes have been developed to far in order to accurately identify bacterial infections. Antibodies, antimicrobial substances, cationic peptides, maltohexose units, and cationic coordination complexes like ZnII dipicolylamine (Zn-dpa) are among the targeting moieties under investigation (Matosziuk et al., 2012). Iron oxide nanoparticles must retain their beneficial magnetic properties in order to function as tailored contrast agents for MRIs characteristics following the application of dendrimer coatings (Landmark et al., 2008).

XI. MECHANISM OF ANTIBIOTIC ON BACTERIAL INFECTION AND NANOPARTICLE

Various nanomaterials exhibit distinct mechanisms for addressing antibiotic resistance. Numerous nanomaterials possess multiple action mechanisms to eliminate antimicrobial resistance, even if it can also be mitigated by incorporating an antibiotic within the same material. Numerous antibiotics operate by inhibiting cell wall synthesis, disrupting essential proteins, and interfering with DNA replication processes. However, bacteria can germinate resistance to these executions. The primary strategy for bacterial infections involves altering the targets of antibiotics, such as the modification of bacterial cell wall components directing to vancomycin resistance, or changes in ribosomal structure resulting in tetracycline resistance. For instance, bacteria may over express enzymes such as aminoglycosides and β-lactams in response to various antibiotics. Furthermore, bacteria can evade the effects ofa number of antibiotics by overexpressing efflux pumps. An instance is Chlamydia pneumonia, which can reside within host cell components, effectively avoiding the action of antibiotics and remaining primarily in the extracellular space. The distinctive physicochemical properties of nanomaterial enable them to counteract antibiotic resistance execution and to implement novel bactericidal path, thereby enhancing antimicrobial efficacy. The cytoplasmic components that leak out of bacteria as a result of bacterial membrane breakdown are what define the action of nanomaterials (Munir & Ahmad, 2022). Nanoparticles (NP) can be designed with fluoroscopes to enhance quantitative discovery capabilities. These characteristics present significant opportunities for investigating bacterial infections. We hypothesized that the attachment of antimicrobic agent to NPs could lead in to the creation of ahighly adaptable tool aimed at more effectively controlling antibiotic resistant (AR) infections. Typically, antibiotics administered in solution reach bacterial cell through with diffusion. While this process outcome in a relatively uniform distribution of molecule throughout tissues, it significantly diminishes the concentration of molecules of antibiotics that can enter any specific sick cell. On the other hand, antibiotics may be able to reach individual bacterial cells with a stronger dosage when they are concentrated on the surface of NPs. This strategy suggests that by specifically delivering less effective antibiotics to resistant bacteria via NPs, their antimicrobial efficacy may be increased (Alabresm et al., 2020).

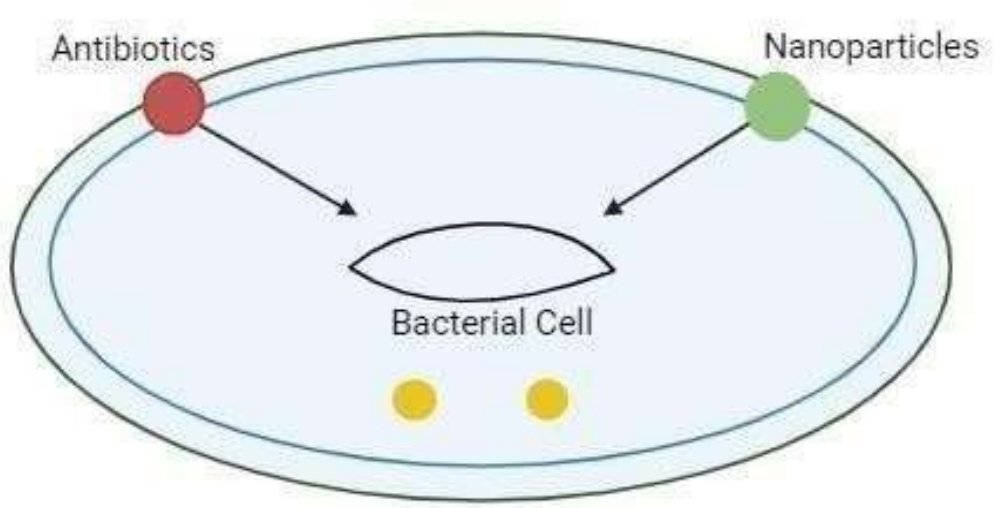

Fig 11.1: Mechanisms of antibiotics on bacterial infections and nanoparticles

Table 11.1 Examples of conjugated MNPs for bacterial detection targeting target molecules (Xu et al., 2019).

TARGETED ANTIBIOTIC	BACTERIA DETECTED	METHOD
PAP1, bacteriophage	*P. aeruginosa*	Colorimetric detection
Amoxicillin	*E. coli*	MALDI MS
Streptavidin	*S.aureus and S. pyogenes*	SERS
Vancomycin and ALP-IgG	*S. aureus*	Fluorescence
Antibiotics	*S. typhimurium*	Colorimetric detection
Vancomycin	*L. monocytogenes*	PCR

XII. Conclusion And Future Perspective

In recent years, the need for better antibiotic treatment has become very crucial as there is a rise in critical bacterial infection cases. According to recent studies and research, it has been found that targeted antibiotic delivery using nanoparticles have given a solution to this problem. In this review we have highlighted on how nanoparticles can help treat various kinds of bacterial infections. We have also explained on how various kinds of nanoparticles deal with different kinds of bacteria. By using nanoparticles the antibiotics can be transported directly to the infection site which makes the treatment and chance of recovery even more easier compared to other traditional methods of treatment. We have also explained about the importance of early diagnosis and detection of the bacterial infection. Early diagnosis and detection of the bacterial infection would help us in treating the disease would help in faster recovery. Additionally early detection of the bacterial infection also help the individual get mentally and physically prepared for the therapy. Recent advancements in nanotechnology have made it easier to identify and cure bacterial infections earlier. The most commonly used drug carriers to date have been nanoparticles such as lipid nanoparticles, polymeric nanoparticles, zinc oxide nanoparticles, gold, silver, and palladium nanoparticles. Because by their unique chemical characteristics in comparison to other medication carriers, this has enabled us to treat the condition more effectively and more efficiently. And every one of these nanoparticles has contributed to the successful treatment of microorganisms like streptococcus, pseudomonas aeruginosa, E. Coli, and others. The bacterial strains have benefited from the targeted medication delivery provided by nanoparticles. Furthermore, it is expected that the nanoparticle will be created in the future and combined with different medicines to treat a wide range of additional bacterial illnesses. Despite these benefits, there are also some challenges that arise by the use of nanoparticles for targeted antibiotic delivery. Certain nanoparticles such as liposomes, even though they have good acceptability, they are less stable compared to other nanoparticles. And some nanoparticles are also less compatible. But these challenges can be tackled by using the suitable nanoparticle for the right bacterial infection. Designing of the nanoparticles is very important as the treatment depends upon the quality of nanoparticles. During the synthesis of nanoparticles it is necessary to ensure that the nanoparticles are stable, compatible and safe for long term use in the body of the individual. The deign of nanoparticle influence their interaction with the cells so it is important to prepare them effectively making sure they do not cause any harm. And clear guidelines are needed to ensure safety and effectiveness of the treatment. In conclusion, targeted antibiotic delivery using nanoparticles has a great potential in improving the treatment of bacterial infections and ensuring that the treatment is effective and efficient.

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