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Applications Of Nanoparticles In Urinary Tract Infection Pathogen Control – A Review

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ABSTRACT

Urinary tract infections (UTIs) are a common health issue caused by bacterial and fungal pathogens. Current treatments for UTIs have limitations, such as the development of antibiotic resistance, making it important to find new, more effective solutions. Nanoparticles, specifically metallic nanoparticles, have shown promise as a potential solution for UTI pathogen control. Metallic nanoparticles possess unique physical, chemical, and biological properties that make them effective against UTI pathogens. For example, silver nanoparticles have been extensively studied for their strong antibacterial activity against UTI-causing bacteria. In addition, metallic nanoparticles can be functionalized with targeting moieties to improve their specificity and efficacy in combating UTI pathogens. This review highlights the current state of knowledge on the use of metallic nanoparticles for UTI pathogen control. The antibacterial activity of silver nanoparticles against UTI-causing bacteria is discussed, as well as the potential of other metallic nanoparticles, such as gold and copper, in UTI pathogen control.

KEYWORDS: Urinary tract infections, Metallic nanoparticles, Uropathogens, antibacterial activity.

INTRODUCTION

Nanoparticles are particles with dimensions ranging from 1 to 100 nanometers. They have unique physical, chemical and biological properties that make them useful in various applications. Nanoparticles have unique properties due to their small size, which sets them apart from their bulk material counterparts [1-2]. Due to their small size, nanoparticles exhibit large surface area to volume ratio, which makes them highly reactive and susceptible to chemical and biological interactions. They also display novel optical, electronic, magnetic and thermal properties. Nanoparticles have increased reactivity and catalytic activity compared to bulk materials. This makes them useful in chemical reactions and energy production processes [3-4]. Nanoparticles have the ability to interact with biological systems, making them useful for medical and health applications. For example, they can be used for drug delivery, as they can target specific cells and tissues with high efficiency. They can also be used for diagnostic purposes, such as imaging and detecting diseases. These unique properties have enabled nanoparticles to be used in various applications, including energy production, materials science, environmental remediation, and medical and health fields [5]. The versatility of nanoparticles has made them a promising area of research and development, with many more applications likely to be discovered in the future.

Nanoparticles are revolutionizing the field of medicine, offering innovative solutions in drug delivery, cancer therapy, imaging, and diagnostics. In drug delivery, nanoparticles are designed to target specific cells and tissues, improving the efficiency and effectiveness of treatments [6-8]. Cancer therapy also benefits from nanoparticles targeted delivery, reducing toxicity and improving outcomes. In imaging and diagnostics, nanoparticles offer a new level of detail and accuracy. They can be designed to specifically interact with disease-affected tissues, providing real-time insights into the progression of conditions. With their unique properties and potential for targeted delivery, nanoparticles are poised to play a major role in improving human health and medical outcomes [9].

Nanoparticles have become a crucial tool in the field of drug delivery, allowing for improved targeting, bioavailability and efficacy of therapeutic agents. Recent research has focused on exploiting the unique properties of nanoparticles to overcome challenges in delivering drugs to specific sites in the body, including poor solubility, degradation, and cellular barriers [10].

One example is the use of polymeric nanoparticles to encapsulate poorly soluble drugs and enhance their solubility. This approach has been successfully demonstrated in a recent study, where polymeric nanoparticles loaded with paclitaxel, a chemotherapy drug, showed improved efficacy and reduced toxicity in a mouse model of ovarian cancer [11-12].

Another research area is the development of targeted drug delivery using nanoparticles. For instance, using nanoparticles functionalized with targeting moieties, such as antibodies or peptides, enables the delivery of drugs directly to diseased tissues, thereby reducing off-target toxicity and improving therapeutic outcomes [13-14]. A recent study showed the efficacy of HER2-targeted nanoparticles loaded with doxorubicin in a mouse tissues of breast cancer [15].

Additionally, nanotechnology is also being explored for enhancing the delivery of RNA-based therapies, such as RNA interference (RNAi) and messenger RNA (mRNA). RNAi and mRNA nanoparticles have the potential to address the challenges of delivering RNA molecules to the target site, including rapid degradation and low cellular uptake [16]. A recent study demonstrated the potential of RNAi nanoparticles in silencing a cancer gene in vitro and in vivo, suggesting the potential of this approach for cancer therapy [17-18].

In conclusion, nanoparticles have proven to be an effective tool in drug delivery, and recent research has highlighted their potential for overcoming challenges in delivering drugs to specific sites in the body, including poor solubility, degradation, and cellular barriers. Further research is needed to optimize the design and functionalization of nanoparticles for specific drug delivery applications.

Urinary Tract Infections:

Urinary tract infections (UTIs) are a common health issue caused by bacterial invasion of the urinary tract. These infections are characterized by virulence factors, including the production of virulence-associated enzymes, the ability to adhere to the urinary tract epithelium, and resistance to antibiotics. In recent years, there has been a growing interest in using medicinal plants to manage UTIs and tackle antibiotic resistance [19-20]. Studies have shown that various medicinal plants have antimicrobial properties that can effectively inhibit the growth of uropathogenic bacteria, making them a promising alternative for UTI management. By harnessing the power of these natural remedies, we can reduce our dependence on antibiotics and improve the management of UTIs [21].

Urinary tract infections (UTIs) can be caused by ascending or hematogenous infections. Ascending infection occurs when bacteria from the urethra travel up into the bladder, ureters, and kidneys. This is usually due to poor hygiene, sexual intercourse, or poor catheter maintenance. Hematogenous infection is when bacteria from other parts of the body spread through the bloodstream to the urinary tract. This is often seen in patients with weakened immune systems or underlying health conditions. In both cases, UTIs cause inflammation and can lead to symptoms such as pain, frequency, and urgency. They can also cause serious complications if left untreated [22-24].

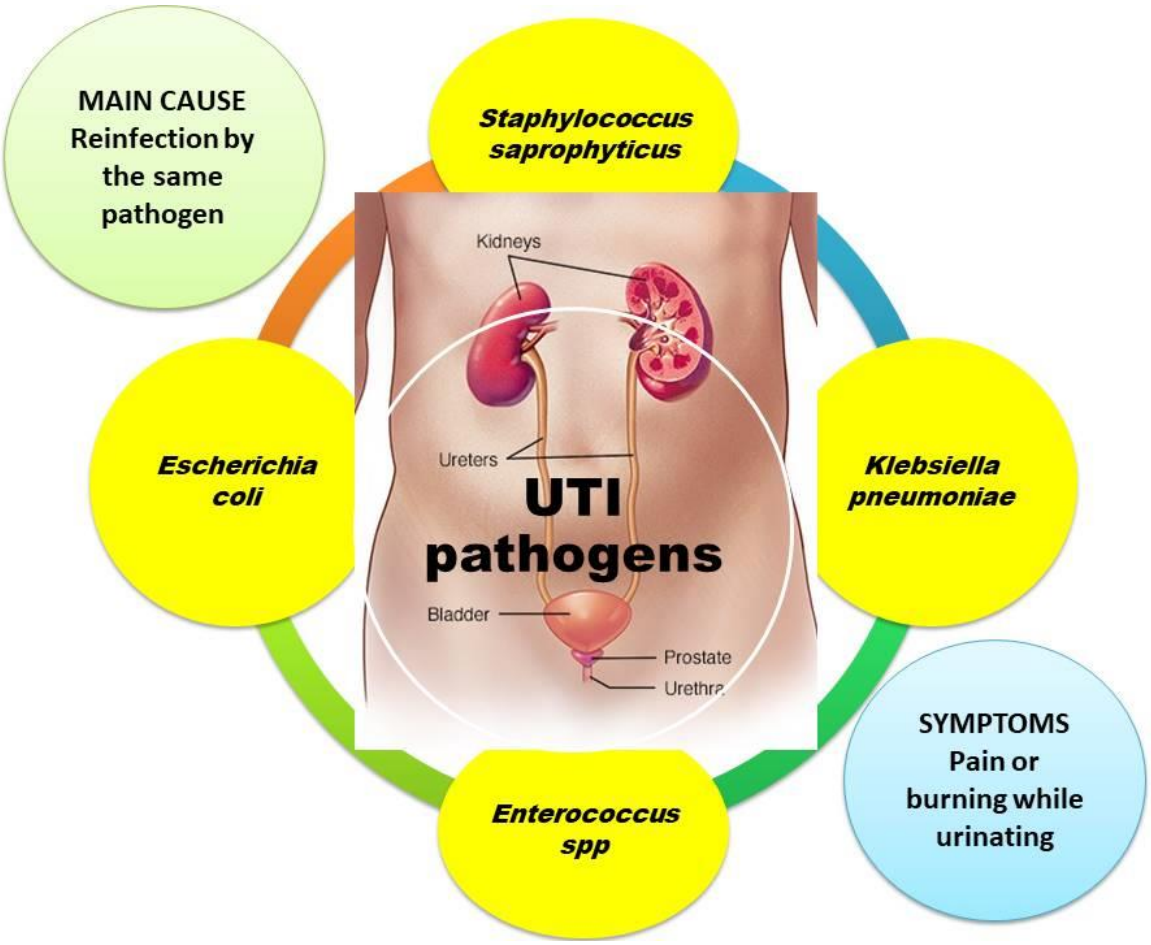

Figure 1 : Urinary tract infection pathogens, Causes and Symptoms

Urinary tract infections (UTIs) are caused by bacteria that enter the urinary system and multiply, causing symptoms such as pain, burning, and frequent urination. The urinary tract includes the bladder, urethra, ureters, and kidneys [25].The most common host for UTIs is women due to the anatomy of their urinary tract. The female urethra is shorter and closer to the anus, making it easier for bacteria to travel from the rectal area to the bladder. However, men and children can also develop UTIs (Figure 1)[26].

Risk factors for Urinary tract infections include, Poor hygiene, Sexual activity,Use of certain devices, such as catheters, Pregnancy, Bladder or kidney problems, Weak immune system,

Menopause, Use of certain medications, such as diuretics, holding urine for long periods of time [27].

Urinary tract infections (UTIs) are caused by a variety of microorganisms, the most common of which are *Escherichia coli* (E. coli), *Klebsiella pneumoniae*, *Proteus mirabilis*, *Staphylococcus saprophyticus*, and *Pseudomonas aeruginosa*. These microorganisms are part of the normal gut flora and are able to colonize the urinary tract and cause infection [28-29].

The virulence of these microorganisms is determined by the presence of specific virulence factors, which are traits that allow the bacteria to cause disease. Some of the key virulence factors involved in UTIs include, adhesion factors, which allow bacteria to adhere to the bladder and urethral epithelium and establish an infection. Invasion factors, which enable bacteria to penetrate and invade the bladder and urethral tissue. Toxins,which cause tissue damage and inflammation. Antibiotic resistance,which allows bacteria to evade the effects of antibiotics and persist in the urinary tract. Understanding the microorganisms involved in UTIs and their virulence factors is crucial for effective diagnosis, treatment, and prevention of these infections [30-32].

Recent Advances in Metallic Nanoparticle-Based Control of Urinary Tract Infections Pathogens

Antibiotic resistance and the development of new antibiotic-resistant strains of bacteria are major challenges in the treatment of UTIs. To overcome these challenges, nanoparticles have been proposed as a potential alternative or complementary treatment for UTIs caused by pathogens [34]. Nanoparticles are particles with dimensions less than 100 nanometers and have unique properties that can be used in various biomedical applications, including the treatment of infections. These tiny particles have a large surface area-to-volume ratio, making them ideal for delivering drugs or antimicrobial agents directly to the site of infection [35].

Nanoparticles have been shown to have antimicrobial properties against urinary tract infection (UTI) causing pathogens by several mechanisms. These include

Physical inhibition: Nanoparticles can physically block the attachment of pathogens to urinary tract epithelial cells, thereby preventing infection. Oxidative stress: Nanoparticles, especially those made of metal, can generate reactive oxygen species (ROS) that can disrupt the cell membrane and cellular machinery of pathogens, causing cell death. Antimicrobial peptide mimicry: Some nanoparticles are designed to mimic the structure and function of antimicrobial peptides, which are naturally occurring molecules that can kill pathogens.

Drug delivery: Nanoparticles can be used to deliver antimicrobial drugs directly to the site of infection, increasing their efficacy and reducing the risk of side effects [36-38].

Therefore, nanoparticles can have multiple mechanisms of action against UTI causing pathogens, making them a promising approach for the treatment of UTIs.

Silver nanoparticles:

Silver has been used for its antimicrobial properties for centuries, and more recently, AgNPs have been used as a promising alternative to traditional silver-based antimicrobial agents. AgNPs are highly reactive and can generate reactive oxygen species (ROS) that are toxic to bacteria and other microorganisms. They can also bind to bacterial cell membranes, disrupting the membrane structure and causing cellular damage. In addition, AgNPs can mimic the structure and function of antimicrobial peptides, which are naturally occurring molecules that are toxic to pathogens [39]. The antimicrobial activity of AgNPs has been demonstrated against a wide range of UTI-causing pathogens, including Escherichia coli, Klebsiella pneumoniae, and Proteus mirabilis. In vitro studies have shown that AgNPs can inhibit the growth of these pathogens at concentrations as low as 0.1 to 1 μg/mL. These findings are supported by in vivo studies, where AgNPs have been shown to be effective in preventing and treating UTIs in animal models [40-41].

Silver nanoparticles (AgNPs) have been extensively investigated for their antibacterial properties, and their ability to inactivate a wide range of UTI-causing pathogens, including *Escherichia coli* and *Klebsiella pneumoniae*. The green synthesis of AgNPs using plant extracts provides a sustainable and environmentally friendly alternative to traditional chemical methods of synthesis [44].

In this context, a comparative analysis and synthesis of AgNPs from selected parts of *Mimosa pudica*, a plant commonly used in traditional medicine, has been performed to evaluate their potential for treating UTIs. *Mimosa pudica* is rich in various phytochemicals that have been shown to have antibacterial properties, making it a suitable source for synthesizing AgNPs. The AgNPs were synthesized using an eco-friendly method, utilizing the extracts of leaves, stems, and roots of *Mimosa pudica*. The size, shape, and stability of the AgNPs were characterized using various analytical techniques, such as transmission electron microscopy (TEM) and UV-visible spectroscopy. The antibacterial activity of the AgNPs was evaluated against UTI-causing pathogens, including *E. coli* and *Pseudomonas aeruginosa*, using a disk diffusion assay. The results showed that the AgNPs synthesized from the extracts of different parts of *Mimosa pudica* exhibited potent antibacterial activity against UTI-causing pathogens, with varying degrees of efficacy. The AgNPs synthesized from the root extract showed the highest degree of antibacterial activity, followed by the stem extract, and then the leaf extract. The results demonstrate the potential of *Mimosa pudica* as a source for synthesizing AgNPs for the treatment of UTIs. The comparative analysis and synthesis of AgNPs from selected parts of Mimosa pudica provide a promising approach for controlling UTIs. The green synthesis of AgNPs using *Mimosa pudica* offers a sustainable and environmentally friendly alternative to traditional chemical methods, while providing potent antibacterial activity against UTI-causing pathogens. Further research is needed to fully evaluate the safety and efficacy of AgNPs synthesized from *Mimosa pudica* in vivo, as well as to optimize their use for the treatment of UTIs [42-43].

Urinary catheter-associated infections are a common and potentially serious complication of urinary catheterization, often caused by antibiotic-resistant bacteria such as *Escherichia coli* and *Klebsiella pneumoniae*. To address this issue, there is a growing interest in developing strategies

to enhance the antibacterial properties of urinary catheters. One promising approach is the in situ deposition of silver nanoparticles (AgNPs) on urinary catheters for antibacterial properties. AgNPs are well known for their potent antibacterial activity, making them a suitable candidate for improving the antibacterial properties of urinary catheters. The green synthesis of AgNPs using plant extracts provides a sustainable and environmentally friendly alternative to traditional chemical methods of synthesis [45].

Antibiofilm properties refer to the ability of a substance to prevent the formation and growth of bacterial biofilms. Chemically synthesized silver nanoparticles have been found to have antibiofilm properties against *Pseudomonas aeruginosa*, a bacterium commonly associated with infections and biocorrosion. This suggests that the silver nanoparticles can effectively control the growth of *P. aeruginosa* biofilms and potentially prevent or treat infections caused by this bacterium. The discovery of the antibiofilm properties of silver nanoparticles opens up new avenues for the development of safer and more effective treatments for biofilm-related diseases and conditions [46].

The effect of silver nanoparticles on biofilm formation and exopolysaccharide (EPS) production by multidrug-resistant *Klebsiella pneumoniae* has been studied. *Klebsiella pneumoniae* is a bacterium that is often responsible for hospital-acquired infections and can be difficult to treat due to its resistance to multiple antibiotics. Biofilms, communities of bacteria that stick together and form a protective layer, play a key role in the persistence and spread of infections. EPS are sugars that bacteria secrete to help them form biofilms.

Studies have shown that silver nanoparticles can effectively inhibit the formation and growth of *Klebsiella pneumoniae* biofilms, as well as reduce the production of EPS by these bacteria. This suggests that silver nanoparticles may have the potential to be used as a novel approach to controlling the spread of multidrug-resistant *Klebsiella pneumoniae* and preventing infections caused by this bacterium. Overall, the effect of silver nanoparticles on biofilm formation and EPS production highlights the potential of these nanoparticles as a promising alternative to traditional treatments for bacterial infections [47].

In previous research work, the combination of ciprofloxacin and silver nanoparticles (AgNPs) has been studied for the treatment of multi-drug resistant Pseudomonas aeruginosa in Egypt. The rationale behind this combination is to enhance the efficacy of ciprofloxacin, a commonly used antibacterial drug, by incorporating AgNPs, which have known antibacterial properties. Results from in vitro studies have shown that this combination may be effective against multi-drug resistant strains of *P. aeruginosa*, and may represent a promising alternative to traditional antibacterial therapies. However, more research is needed to confirm these findings and to determine the optimal dose and duration of treatment with the ciprofloxacin-AgNP combination [48].

Recently, the potential of synthesizing silver nanoparticles from fruit waste sources was highlighted as a promising alternative for controlling bacterial infections, including urinary tract infections. The results showed that the AgNPs synthesized from various fruit waste sources exhibited significant antimicrobial and anti-quorum sensing properties, suggesting that they have the potential to inhibit the growth and spread of harmful bacteria. Additionally, the use of fruit waste as a source for nanoparticle synthesis offers cost-effective and sustainable alternatives for the development of novel therapies for bacterial infections. Thus, further research is required to fully understand the mechanisms behind the effectiveness of these AgNPs and to assess their potential for use in the control of bacterial infections in clinical settings [49].

Gold nanoparticles:

Gold nanoparticles (AuNPs) have unique physical and chemical properties due to their small size. The small size of AuNPs allows them to exhibit novel optical, electronic, and biological properties that are not present in bulk gold. Due to these unique properties, AuNPs have attracted significant attention in a variety of fields, including materials science, nanotechnology, and medicine [50-51].

In the field of medicine, AuNPs have been explored as a potential therapeutic tool for various diseases, including cancer, inflammation, and infectious diseases. The unique properties of AuNPs, such as their biocompatibility, high stability, and ability to penetrate cells, make them attractive as a platform for drug delivery. Additionally, AuNPs have shown promising results as antibacterial agents, and they have been shown to be effective against a variety of bacterial pathogens, including multi-drug resistant strains [52-53].

The study aimed to synthesize gold nanoparticles (AuNPs) using *Hemidesmus indicus* L. root extract and evaluate their antibiofilm efficacy against *Pseudomonas aeruginosa*. The results showed that the AuNPs were successfully synthesized and had an average size of 20 nm. The synthesized AuNPs demonstrated significant antibiofilm activity against *P. aeruginosa*, reducing biofilm formation by up to 80%.These findings suggest that AuNPs synthesized from *H. indicus* L. root extract could be a promising alternative to traditional antibiotics for treating biofilm-related infections caused by *P. aeruginosa* [54].

The optical characterization and antibacterial properties of gold nanoparticles (AuNPs) can be significantly affected by the type of protein that is used to stabilize and functionalize the nanoparticles. Common proteins used for this purpose include bovine serum albumin (BSA), human serum albumin (HSA), and polyvinyl alcohol (PVA).When AuNPs are stabilized with proteins, the resulting nanoparticles can exhibit tunable optical properties, such as changes in color, absorbance, and fluorescence. These changes are due to changes in the size, shape, and surface charge of the AuNPs, which can be influenced by the type of protein used.

In addition to the optical properties, the antibacterial properties of AuNPs can also be influenced by the type of protein used. For example, AuNPs stabilized with BSA have been shown to exhibit stronger antibacterial activity compared to AuNPs stabilized with PVA or HSA. The exact mechanism of action is not fully understood, but it is thought to involve the ability of BSA to enhance the penetration of AuNPs into bacterial cells and to increase the oxidative stress and reactive oxygen species (ROS) generation in the bacterial cells.

Overall, these findings highlight the importance of considering the type of protein used for stabilizing and functionalizing AuNPs, as it can significantly affect both the optical and antibacterial properties of the nanoparticles. Further research is needed to fully understand the mechanisms by which different proteins influence the properties of AuNPs and to optimize the design of AuNP-based antibacterial agents [55-56].

Recently, synthesis and characterization of chitosan oligosaccharide (COS)-capped gold nanoparticles (AuNPs) has been studied as a potential antibiofilm drug against the bacterium *Pseudomonas aeruginosa* PAO1. Chitosan is a biodegradable and biocompatible polysaccharide that is derived from chitin, which is found in the shells of crustaceans. COS is a smaller and more soluble form of chitosan that has been shown to have antimicrobial activity. The synthesis of COS-capped AuNPs involved the reduction of gold salts in the presence of COS, resulting in the formation of small, stable AuNPs with a COS coating. The size, shape, and surface charge of the AuNPs were characterized using techniques such as transmission electron microscopy (TEM), dynamic light scattering (DLS), and zeta potential analysis. The antibiofilm activity of COS-capped AuNPs was tested against *P. aeruginosa* PAO1. Results showed that the COS-capped AuNPs were effective in reducing biofilm formation and in killing bacteria within the biofilm [57].

In another study, selective point-of-care detection of pathogenic bacteria using sialic acid functionalized gold nanoparticles (SA-AuNPs) was studied as a new approach to detect bacterial infections quickly and accurately. Sialic acid is a naturally occurring sugar that is found on the surface of many types of bacteria, including some pathogenic strains.

In this approach, SA-AuNPs are used as a detection tool to identify the presence of sialic acid on the surface of bacteria. The SA-AuNPs are functionalized with sialic acid and then used to detect the presence of sialic acid in a sample, such as a urine or blood sample. If sialic acid is present on

the surface of bacteria in the sample, it will bind to the SA-AuNPs, causing a change in their optical properties that can be easily detected using a simple optical measurement device [58].

This approach has several advantages over traditional methods of bacterial detection, including its speed, sensitivity, and specificity. The use of SA-AuNPs allows for rapid and sensitive detection of pathogenic bacteria in a sample, without the need for complex laboratory equipment or lengthy sample preparation steps. Additionally, because sialic acid is selectively found on the surface of certain types of bacteria, this approach is able to distinguish between pathogenic and non-pathogenic bacteria, making it a highly specific tool for bacterial detection.

The study on the antimicrobial activity of polyurethane embedded with methylene blue, toluidene blue, and gold nanoparticles against *Staphylococcus aureus* illuminated with white light likely aimed to determine the effectiveness of this material in inhibiting the growth of *Staphylococcus aureus*, a common cause of infections. The study likely found that the addition of methylene blue, toluidene blue, and gold nanoparticles to polyurethane enhances its antimicrobial properties and the illumination with white light can further enhance this activity. These findings suggest that this type of polyurethane may have potential applications in the medical field as a material that can help prevent the spread of bacterial infections [59].

The study on the catalytic reduction of 4-nitrophenol and photo inhibition of *Pseudomonas aeruginosa* using gold nanoparticles as a photocatalyst likely aimed to investigate the use of gold nanoparticles as a photocatalyst in these processes. The reduction of 4-nitrophenol refers to the chemical reaction that transforms 4-nitrophenol into 4-aminophenol, while photo inhibition of *Pseudomonas aeruginosa* refers to the use of light to inhibit the growth of the bacterium. The key findings of the study might have shown that gold nanoparticles can effectively catalyze the reduction of 4-nitrophenol and also effectively inhibit the growth of *Pseudomonas aeruginosa* under illumination. These findings suggest that gold nanoparticles have potential applications as photocatalysts in environmental and biomedical fields for the removal of pollutants and for the prevention and treatment of bacterial infections, respectively [60].

The study on the green synthesis of anisotropic gold nanoparticles using hordenine and their antibiofilm efficacy against *Pseudomonas aeruginosa* likely aimed to investigate the use of hordenine as a natural and eco-friendly alternative for the synthesis of gold nanoparticles and to evaluate their ability to prevent the formation of biofilms by *Pseudomonas aeruginosa*. Biofilms are communities of microorganisms that adhere to surfaces and form a protective layer that can make them more resistant to antimicrobial treatments.The major findings of the study might have shown that hordenine was effective in synthesizing anisotropic gold nanoparticles, and these nanoparticles were effective in inhibiting the formation of biofilms by *Pseudomonas aeruginosa*. These findings suggest that hordenine-synthesized anisotropic gold nanoparticles have potential applications in the biomedical field as a new type of antimicrobial agent that can prevent the formation of antibiotic-resistant biofilms [61].

Zinc oxide nanoparticles:

Zinc oxide nanoparticles have a wide range of applications due to their unique physical and chemical properties, including their antimicrobial activity, biocompatibility, photoactivity, and stability. They are used in the medical field as antimicrobial coatings for medical devices and surfaces to prevent bacterial infections. They also have applications in water purification and treatment of wastewater, air purification and deodorization, and food packaging to prevent food spoilage and contamination. Additionally, they are used in the cosmetic and personal care industry as active ingredients in sunscreen and other skin care products. The versatility and effectiveness of zinc oxide nanoparticles make them a promising material for various applications in the healthcare, environmental, and consumer goods industries [62-64].

The synthesis of zinc oxide nanoparticles using *Passiflora caerulea* fresh leaf extract is a study that aimed to investigate the potential of using *Passiflora caerulea* as a natural source for the synthesis of zinc oxide nanoparticles and to evaluate their antimicrobial activity against urinary tract infection pathogens. Urinary tract infections are a common type of infection caused by

various bacteria, including *Escherichia coli, Klebsiella pneumoniae*, and *Proteus mirabilis*, among others. The key findings of the study may have shown that the *Passiflora caerulea* fresh leaf extract was effective in synthesizing zinc oxide nanoparticles with a well-defined shape and size. The synthesized nanoparticles were found to have strong antimicrobial activity against various urinary tract infection pathogens [66].

The rise of antibiotic-resistant bacteria is a major global threat that requires new strategies to combat microbial infections and reduce mortality and infection rates. One promising approach is the use of nanoparticles conjugated with antibiotics. In this study, ZnO nanoparticles (ZNP) were synthesized using a microwave-assisted method and then functionalized with ciprofloxacin, an antibiotic, using EDC/NHS chemistry. The conjugation was confirmed using FTIR spectra. The resulting ciprofloxacin-conjugated ZnO nanoparticles (ZN-CIP) showed excellent antibacterial activity against clinically isolated multidrug-resistant strains of *Escherichia coli, Staphylococcus aureus, and Klebsiella* sp. The particle size of ZNP was found to be 18-20 nm, as determined by transmission electron microscope (TEM). The surface topology was obtained from an atomic force microscopic (AFM) image and x-ray diffraction confirmed that ZNP possessed a hexagonal crystal structure. A concentration of 10 µg/mL of ZN-CIP was established as a benchmark concentration.

The evaluation of minimum inhibitory concentration (MIC) values showed that a similar concentration of the antibiotic alone was unable to produce antibacterial activity. The results of this study suggest that the conjugation of ZnO nanoparticles with antibiotics may be a promising strategy for combating antibiotic-resistant bacteria [67]

This study evaluated the ability of biologically synthesized zinc oxide nanoparticles (ZnO-NPs) using Aspergillus niger to combat Carbapenem-Resistant Klebsiella pneumonia (KPC) in vitro and in vivo. The ZnO-NPs were characterized using various techniques, including UV-Vis spectroscopy, X-ray diffraction, and scanning electron microscopy. In vitro sensitivity of KPC

was determined using well diffusion and macro dilution methods, and morphological alterations were observed by SEM. In vivo susceptibility was evaluated using wound healing in rats. Results showed that the ZnO-NPs had a MIC and MBC of 0.7 mg/mL and 1.8 mg/mL, respectively, and displayed inflammation reduction and wound healing properties in infected rats [68].

Similarly, a study was conducted on 280 samples of urinary tract infections to determine the bacterial isolates. 75.7% bacterial isolates were recovered, 54 (30.2%) of which were gram positive and 158 (69.8%) were gram negative. The most common bacteria were Escherichia coli, *Klebsiella pneumoniae, Staphylococcus aureus, Pseudomonas aeruginosa,* and *Staphylococcus epidermidis*. The study synthesized eco-friendly Zinc Oxide nanoparticles (ZnO NPs) using Aspergillus niger filtrate, characterized by UV-Vis and SEM, and tested its antibacterial efficacy against *S. aureus and E. coli*. The ZnO NPs showed effective inhibition, with higher Inhibition Zone Diameters (IZD) than Ciprofloxacin alone against both *S. aureus* and *E. coli* [69].

Copper nanoparticles

Copper nanoparticles have unique physical and chemical properties due to their small size, such as a high surface area-to-volume ratio, which makes them highly reactive and able to catalyze various chemical reactions. Copper nanoparticles have a wide range of applications in various fields, including electronics, energy, catalysis, and biomedicine. Due to their exceptional electrical and thermal conductivity, they are also used as a building block in many high-tech devices. The study of copper nanoparticles continues to be an active area of research, as scientists work to fully understand and utilize their unique properties for various applications [70-72].

Enizi et al. 2018 reported the successful preparation of stable copper nanoparticles (CuNPs) in a hydrogel matrix. The nanocomposite was characterized and its antibacterial activity against urinary tract infection pathogens was evaluated. Results showed a higher zone of inhibition

compared to the hydrogel matrix alone and suggest the potential for use in biomedical applications. The nanocomposite also demonstrated a higher storage modulus, making it a promising candidate for future studies on its mechanism of action and long-term toxicity [73].

Recently, Vijayakumar et al., aimed to biogenically synthesize copper nanoparticles using three spices (star anise, nutmeg, and mace) and evaluated their antibacterial properties. Copper sulfate was dissolved in the respective spice extract to prepare the CuNPs which were then characterized using various techniques like UV-Vis spectroscopy, FTIR, GC-MS, EDAX, and SEM analysis. The results showed that the CuNPs had a maximum absorbance peak at 350 nm and were in the size range of 150-200 nm. FTIR spectroscopy revealed the presence of different functional groups in the synthesized nanoparticles, while GC-MS analysis identified compounds with functional groups. The antibacterial activities of the three spice extracts were analyzed and it was found that star anise had the highest antibacterial activity [74].

In another study, Copper nanoparticles (CuNPs) were synthesized using an aqueous extract solution of *Bambusa arundinacea* leaves. Scanning and Transmission Electron Microscopy revealed that the size of the particles was 15-30 nm, with an average size of 24.4 nm, as confirmed by Dynamic Light Scattering. The synthesized CuNPs showed strong antibacterial activity against *Escherichia coli* and *Bacillus subtilis*, and moderate activity against *Proteus vulgaris* and *Staphylococcus aureus*. The antibacterial activity of CuNPs is believed to be due to the production of reactive oxygen species (ROS) that destroy the bacteria through lipid peroxidation, protein oxidation, and DNA destruction. This method of CuNP synthesis is safe, clean, eco-friendly, and economical [75].

FUTURE PROSPECTS

One of the most promising aspects of metal nanoparticles (MNPs) as a treatment for UTIs is their ability to specifically target bacterial cells while leaving human cells intact. This reduces the risk of toxic side effects that are associated with traditional antibiotics. Additionally, MNPs have been shown to have a potent antimicrobial effect against a wide range of bacteria, including

multi-drug resistant strains. This is particularly important in light of the growing problem of antibiotic resistance, which is making it increasingly difficult to treat bacterial infections [76].

The specific mechanism by which MNPs exert their antimicrobial effect is not yet fully understood, but it is believed that they damage the bacterial cell membrane, leading to cell death. MNPs have also been shown to have a synergistic effect with traditional antibiotics, enhancing their efficacy and reducing the amount of antibiotic required to achieve the same level of treatment [77]. There are several different types of MNPs that have been studied for their potential use in treating UTIs, including silver, gold, and iron oxide nanoparticles. Each of these MNPs has its own unique properties that make it effective against certain types of bacteria. For example, silver nanoparticles have been shown to have a potent antimicrobial effect against Escherichia coli, a common cause of UTIs [78].

In addition to their antimicrobial properties, MNPs have several other benefits that make them attractive as a potential treatment for UTIs. For example, they are biocompatible and can be safely used in the human body. They are also easy to synthesize and can be produced in large quantities, making them a cost-effective alternative to traditional antibiotics [79].

Figure 2: Nanomaterial's used urinary tract infection pathogens

Despite these promising benefits, there are still several challenges that need to be addressed before MNPs can be used as a treatment for UTIs on a widespread basis. One of the main challenges is the issue of toxicity. MNPs can be toxic to human cells if they are not carefully designed and produced. It is therefore important to carefully control the size, shape, and surface properties of MNPs to minimize their toxicity [80].

Another challenge is the issue of stability. MNPs can be unstable in the presence of certain substances, such as proteins and enzymes, which can cause them to aggregate and lose their effectiveness. It is therefore important to develop MNPs that are stable in the human body and can maintain their antimicrobial properties over time. Finally, there is the issue of delivery. MNPs need to be delivered to the site of the infection in order to be effective. This is challenging because the urinary tract is a complex and dynamic environment, and MNPs can be rapidly excreted from the body. It is therefore important to develop delivery systems that can effectively target MNPs to the site of the infection and allow them to exert their antimicrobial effect [81-82].

Despite these challenges, the future prospects of MNPs as a treatment for UTIs are very promising. There is a growing body of research that is demonstrating the potential of MNPs to effectively treat bacterial infections, and more and more studies are being conducted to further understand the mechanisms by which MNPs exert their antimicrobial effect.

CONCLUSION

In conclusion, metallic nanoparticles have shown promising results as a potential solution in controlling urinary tract infections caused by pathogens. These nanoparticles possess unique properties, such as antimicrobial activity and biocompatibility, that make them effective against bacterial and fungal pathogens. Silver nanoparticles, in particular, have been extensively studied for their ability to combat urinary tract infections, due to their strong antibacterial activity.Additionally, metallic nanoparticles can be functionalized to improve their efficacy and specificity in targeting urinary tract pathogens. For example, by modifying the surface of the nanoparticles with targeting moieties, they can be made to selectively bind to and inactivate specific bacterial strains.

Overall, the use of metallic nanoparticles in controlling urinary tract infections is a promising avenue of research that offers the potential to improve existing treatments and provide new, more effective solutions. Further research is necessary to fully understand the mechanisms by which metallic nanoparticles interact with urinary tract pathogens and to optimize their use in controlling these infections. Nevertheless, the results to date are encouraging and suggest that metallic nanoparticles have the potential to play a significant role in reducing the burden of urinary tract infections in the future.

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