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The Study of Treatment of UTIS using Nanomaterials and Nanotechnology

Suryabhan Singh Rathore[1]*, Dr. Manish Gunjan[2]

[1] Ph.D Scholar, Raffles University, Neemrana, Rajasthan, India

Email ID- rathoresuryabhan.pharma@gmail.com

[2] Professor, School of Pharmacy, Raffles University, Neemrana, Rajasthan, India

Abstract - If you have an infection in any of the four parts of your urinary system the kidneys, ureters, bladder, or urethra you have a urinary tract infection. The bladder and urethra, which are part of the lower urinary system, are the most common sites of infection. In comparison to males, women have a higher chance of getting a UTI. A bladder infection may be both uncomfortable and inconvenient. This study delves into several nanoparticles (NPs) used for the treatment of urinary tract infections (UTIs), including organic NPs, chemical NPs, and inorganic NPs that are green synthesized.

Keywords: urinary tract infection therapies, composite materials.

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INTRODUCTION

In both community and healthcare-associated settings, urinary tract infections (UTIs) are among the most prevalent clinical issues. Most women will have a urinary tract infection (UTI) at some point in their lives, and among those women, community-acquired uncomplicated UTIs (uUTIs) are more prevalent. Repeated urinary tract infections (rUTIs) affect a sizeable percentage of women (25–40%), with some women experiencing months or even years of repeated infections. People with complex urinary tract infections (cUTIs) and silent bacteriuria (AB) are two more important clinical issues related to UTIs. Common causes of nosocomial bacteremia, nosocomial UTIs reflect catheter-associated infections and account for 20-30% of all infections acquired in hospitals. Recently, the rise of antibiotic resistance among uropathogens, especially those responsible for community-acquired UTIs, has been a major factor influencing UTI therapy. While antibiotics are currently effective in treating and preventing UTIs, uropathogens are becoming more resistant to these drugs, which might eventually restrict our capacity to treat and prevent these infections.

It is common for urine to be sterile. It contains fluids, salts, and waste materials but is typically devoid of bacteria, viruses, and fungus. A urethral infection develops when microscopic organisms, most often bacteria, attach themselves to the entrance of the urethra and start to proliferate. The majority of gastrointestinal illnesses are caused by the same kind of bacterium, often found in the colon: E. coli. Enterobacteriaceae, Proteus mirabilis, Pseudomonas aeruginosa, Streptococcus faecalis, Staphylococcus aureus, Klebsiella pneumoniae, Mycobacterium tuberculosis, Actinomycetes, Nocardia, Candida, and many more species may cause UTIs and are most usually linked with catheters. Sexually transmitted infections may also include Chlamydia and Mycoplasma. The aetiology, microbiology, prevention, diagnosis, and treatment of different UTI syndromes are just a few of the many topics that the Spanish Society of Clinical Microbiology and Infectious Diseases (SEIMC) asked a panel of specialists to update on. The reasons given above show how diverse and complicated these infections can be. These instructions do not cover the related problem of prostatitis. Written in accordance with SEIMC standards for consensus statements and the suggestions made by the Agree Collaboration for assessing the methodological quality of clinical practice guidelines, this statement becomes an official position. The writers met many times to settle on a series of questions that would later serve as the document's foundation. Their suggestions are based on a thorough analysis of the literature, which incorporates, if appropriate, the viewpoint of experts who are members of SEIMC.

LITERATURE AND REVIEW

Rahul Mittal et al (2017) The process of drug distribution is crucial when dealing with the treatment of diseases. In the face of long-standing challenges, new approaches and technology have a great chance to shine. Therapeutic potential and patient outcomes may be improved using delivery methods that have synergistic antibacterial properties,

targeted targeting, and increased bioavailability. Many of these ways of administration have therapeutic use in urology, particularly in the management of UTIs, and provide benefits over more traditional approaches. This review article aims to talk about the current ways that UTIs are treated and how technology has improved medicine delivery recently. We zero in on the problems that keep cropping up with UTI medication delivery, such as obstacles to antimicrobial penetration, drug resistance, biofilm development, and constraints on particular targeting. We provide an outline of possible treatments, with a focus on those using nanoparticles, and talk about how new approaches address these concerns.

Sarfraz et al (2022) A number of bladder illnesses may be treated with intravenous drug administration, a method of direct medication delivery. The urine bladder is a formidable obstacle for any harmful substance attempting to enter the circulation due to its unique architecture. The urothelium's structure as a semi-permeable barrier is the source of the bladder's screening function. However, the normal function of the bladder may be changed by a number of bladder-related disorders, including cancer, interstitial cystitis, overactive bladder syndrome, urinary blockages, and urinary tract infections. As a result, these disorders may be efficiently treated using the intravesical method of drug administration, which provides site-specific medication activity with minimal adverse effects. A urethral catheter is used for intravenous drug administration, which is the direct injection of medical medications into the urine bladder. Nevertheless, there are a few drawbacks to this kind of medication administration, such as the possibility of therapeutic agent washout due to frequent urination. In addition, the medicinal drugs are diluted before penetration occurs in the urinary bladder because of their poor permeability, which compromises their efficacy. Intravesical medication delivery makes use of a variety of nanomaterial-based delivery technologies to improve drug penetration and retention at the intended location. The several nanomaterials that have been used for the transport of drugs into the body's blood vessels, as well as their potential applications in the future, are discussed in this comprehensive overview article.

Hossam H. Tayeb et al (2021) A new danger to world health is the rise of viral infections. The worldwide effects of the coronavirus disease (COVID-19) caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) are substantial. Vaccines against SARS-CoV-2 that were recently authorised for emergency use need more testing to determine their efficacy, dose, and safety. We urgently want safe and effective vaccinations or treatments against SARS-CoV-2 as there is currently no medication that effectively combats COVID-19. Emerging as advanced, protective, and therapeutic platforms are oil-in-water nanoemulsions (O/W NEs). The adjustable surfaces and encapsulation capabilities of NEs make them potential instruments for medicinal applications, since they provide superior drug pharmacokinetics. The breakthroughs in medication delivery and the difficulties in drug development highlight the promise of NEs in combating developing illnesses such as COVID-19. In this review, we compile what is known about COVID-19 and talk about O/W NEs' composition, stability, preparation, characterisation, and biological destiny. In addition, we shed light on the structural-functional characteristics of NE, which might help in the search for therapeutic or prophylactic measures against COVID-19.

Atinderpal Kaur et al (2017) We have developed an intravaginal delivery system for the treatment of urinary tract infections using a nanoemulsion based gel that contains polyphenon 60 (P60) and cranberry (CRB). The study included loading cranberry and polyphenon 60 into a single nano-emulsion gel (NBG) using an ultra-sonication process. The NBG was then analysed for growth curves, in vitro release, rheological characteristics, and particle size. In order to conduct in vivo pharmacokinetic experiments in animals, P60+CRB NBG were radiolabeled using technetium pertechnetate (99mTc). The finalized NE's droplet size was 58±1 nm, according to the results. Simulated vaginal fluid showed an in vitro release of 90.92 ± 0.6% in 8 hours for P60 and 99.39 ± 0.5% in 6 hours for CRB. The inhibitory activity of the nano-emulsion based gel was shown by the E. coli growth curve at the fifth hour after inoculation. Research using gamma scintigraphy on Sprague-Dawley rats revealed the passage of a gel containing nano-emulsions from the vaginal canal into the bloodstream. In addition, radiolabeled P60+CRB NBG demonstrated a markedly increased absorption of radio labelled actives by the kidney (3.20±0.16) and urine bladder (3.64±0.29) in biodistribution tests conducted intravaginally. Findings demonstrated efficient distribution in organs affected by urinary tract infections and indicated that 99mTc-P60+CRB NBG might be delivered via the vaginal canal to target organs.

Mahipal Reddy Donthi et al (2022) One new drug delivery technology that has the potential to improve the efficacy of lipophilic medicines is nano-emulgel. Low oral bioavailability, variable absorption, and poor solubility are only a few of the disadvantages of lipophilic formulations. To address these restrictions, nano-emulgel is an amalgamation of many technologies. By combining nano-emulsion with gel, a new method is created that enhances stability and allows for controlled release and fast drug administration. Targeted deliveries, simplicity of administration, safety profile, lack of gastrointestinal degradation, and first pass metabolism have all contributed to nano-emulgel's rising prominence. Topical drug delivery using nano-emulgel is the subject of this review, which also delves into its pharmacokinetics and safety aspects.

NANOTECHNOLOGY USED AS A DIAGNOSTIC METHOD AND IN ANTIMICROBIAL TREATMENT

Pathogens cause a wide variety of diseases, and many of these diseases are highly contagious. In

order to pinpoint the origin and spread of an illness and to treat patients appropriately, rapid and precise pathogen diagnosis is crucial. Diagnosis might be challenging due to the complexity and diversity of infections as well as the incubation time before the first signs of the disease appear. High sensitivity and repeatability are hallmarks of modern diagnostic technologies like ELISA and PCR. The time it takes to prepare samples and get definitive findings is two drawbacks of these approaches.
Rapid, low-cost methods for detecting infections caused by a wide variety of pathogens are within reach, thanks to nanotechnology's promise of improved sensitivity and specificity.

Diagnosis of UTIs by Nanotechnology

At some point in their life, about half of the population will have a urinary tract infection (UTI), making it one of the most prevalent bacterial diseases. Deadly repercussions could result from undetected and improperly treated UTIs. In the clinical phase, it might be very beneficial to establish a quick, early, and dependable way to identify uropathogens. Because of its many possible uses in biomedicine, nanoscience is a flourishing field that has attracted a great deal of attention from scientists. By combining nanomedicine with these methodologies, we may improve the treatment of UTIs and solve the issues posed by standard diagnostic procedures. When compared to more conventional approaches, nanostructures provide significant cost savings while also improving toxicity and resistance prevention. Figure 1 displays the existing state of the art in UTI detection techniques and nanotechnological approaches.

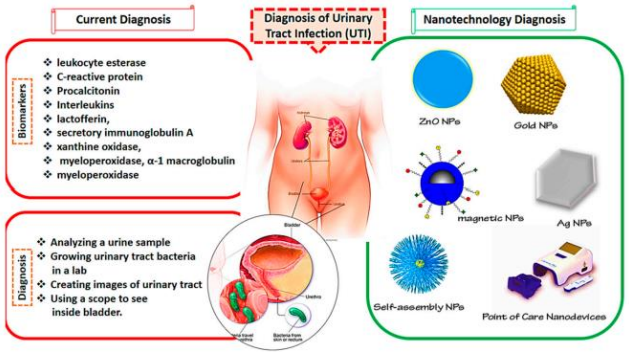

Figure 1. Current methods and nanotechnology approaches for the diagnosis of urinary tract infections (UTIs).

Previous discussion established that current urinalysis methods are laborious, inaccurate, and time-consuming. More and more people are interested in photoluminescence (PL)-based biosensors because of its increased accuracy, rapid reaction time, and other desirable qualities.
Genomic analysis makes use of a wide range of nanomaterials, including magnetic and fluorescent gold nanoparticles, among others. The potential diagnostic use of these inorganic nanoparticles stems from their adaptability and the variety of target molecules or microbes with which they interact. Because these nanoparticle-based diagnostic approaches rely on the identification of distinct sequences in the bacterial genome, it is important to stress that no novel strains have been detected. Nanotechnology must develop new methods of detecting the existence of infections as well as their susceptibility to antibiotics, as resistant types of bacteria and viruses are constantly appearing. The needs for a quick way to diagnose UTIs are high on the list of priorities. A number of techniques for detecting UTIs have been developed since 1980. One of them is dipping a strip in urine to measure the esterase that leukocytes and nitrites create. Modern automated analyzers built on the flow cytometry concept enable the quick identification of various substances such as bacteria, leukocytes, erythrocytes, epithelial cells, crystals, and more. The microbiological diagnostic and antibiotic susceptibility of microbes cannot be provided by this technology, notwithstanding its speed. Collecting and transporting the biological sample is one of several stages that make up the conventional method for identifying UTIs. It is the policy of every clinical laboratory to tell the doctor when the findings are ready, and the doctor is then responsible for informing the patient. Time is of the essence, and all these necessary procedures might postpone the delivery of efficient therapy. The advent of biosensors built on micro- and nanotechnologies has opened the door to the prospect of very effective molecular diagnostics.

In a biosensor, two primary components work together: a bioreceptor, a sensitive biological element that can identify a target substance in a complex environment when attached to a support, and a physicochemical system that records the bioreceptor's response to the target substance and converts it into an electrical signal. Enzymes, cellular organelles, microbes, and even tissues are examples of catalytic (metabolic) bioreceptors; antigens and antibodies are examples of non-catalytic (affinity) bioreceptors. There are a lot of moving parts when making a biosensor to detect UTIs. In order to do the relevant analyses for UTIs, one must follow these steps: procedure for preparing samples—pipetting, centrifugation, and cleanliness. Several variables, including matrix effects and nonspecific binding, may impact the biosensor's sensitivity. A urinary tract infection sensor should be able to detect infections, analyse them quickly, automatically prepare samples with little to no intervention from technicians, identify pathogens, and be sensitive enough to antimicrobials to identify different pathogens in different infections. A new danger to human health is the rise of bacteria and other microbes that are resistant to antibiotics. Both harmful microbes and the effects of antibiotic resistance on human health have been the primary foci of research on this phenomenon.

From a clinical standpoint, it is crucial to address the issue of antibiotic resistance since it threatens the

efficacy of infection treatments. Because of mutations, the acquisition of antibiotic-resistant genes, the misuse and overuse of medications, and the absence of new treatments, bacteria were able to evolve resistance shortly after antibiotics were introduced for human therapy. A species' or genus's inherent resilience is an identifying feature. The chromosome ensures that it may be passed on to future generations. Therefore, the antibiotic-resistant phenotypes of wild-type bacterial species are defined by natural resistance. In contrast to inherent resistance, acquired resistance is specific to a changing percentage of a given species or genus's strains. Acquired resistance develops when a particular resistance phenotype—different from the wild one—is determined by the accumulation of one or more resistance mechanisms. A bacterial resistance to antibiotics may develop via one of three types of processes. The first one manifests as an increase in efflux systems or a decrease in permeability, both of which reduce the quantity of antibiotic that reaches the target. In particular, Gram-negative bacteria exhibit reduced permeability due to partly or totally closed pores, or even the absence of pores altogether. Some mutations may impede the crossing process, making antibiotics less accessible to the pores beyond the outer membrane. Another way is to employ outflow systems, which use a proton-motor force to evacuate the antibiotic from the bacterial cell as soon as it arrives.

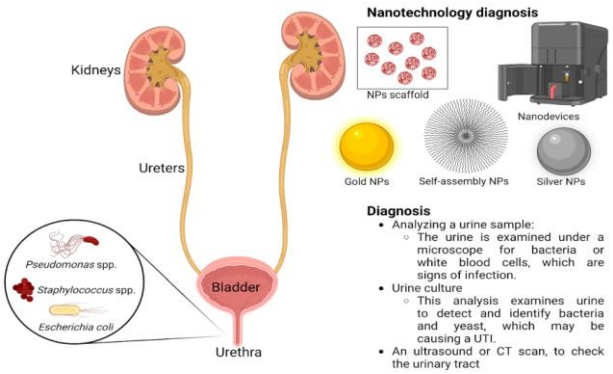

Figure 2. Diagnosis of urinary tract infections.

Table 1. Most commonly used nanoparticle (NP)-based sensors for the diagnosis of UTIs.

Nanosensors	Application
bacteria-grabbing nanochip-based on SERS	detection of *Proteus mirabilis* PRM1, *Escherichia coli* CFT 073, and *Pseudomonas aeruginosa* PAO1 uropathogens
nanopaper-based systems	detection of LE (LE-PAD) as a proof-of-concept for UTI quantitative testing
MNPs identification of	*Pseudomonas aeruginosa* in vivo

Abbreviations: SERS, surface-enhanced Raman scattering; MNPs, magnetic nanoparticles; LE, leukocyte esterase; LE-PAD, leukocyte esterase-paper-based analytical device; UTI, urinary tract infection.

An additional mechanism that bacteria can acquire resistance to antibiotics is the modification of the antibiotic target. This can happen through mutations in the genes that encode the antibiotic target, the acquisition of foreign genes, or, most commonly, the inactivation of the antibiotic. This last mechanism is most commonly seen in infectious pathology. The production of enzymes that break down or alter antibiotics, such β-lactamases, is a crucial resistance mechanism that continues to pose a major risk to antibiotic efficacy.

By improving the stability and physicochemical properties of antibiotics and antibiotic release, as well as by providing a means for biofilm internalisation, nanomedicine greatly augments the efficacy of current treatments. This, in turn, increases the capacity for targeted drug delivery to the site of infection. It was also shown that nano-sized systems not only enhance the therapeutic action of antibacterial drugs, but they also limit the promotion of resistance by overcoming the techniques that bacteria have devised for resistance. The bacterial cell wall may be modified or β-lactamase or efflux pumps can be used in these ways to break down drugs. An enhanced line of defence against antibacterial resistance has been the growing number of nanoparticle variations, because the majority of these particles can bypass these typical resistance mechanisms.

Organic Nanoparticle Therapy Approaches

It is now common knowledge that using organic nanoparticles has many benefits. From improved colloidal stability of tiny medications (such as proteins or nucleic acids) to more accurate targeting of specific tissues or even cells, these nano-sized carriers transformed the idea of contemporary treatment.

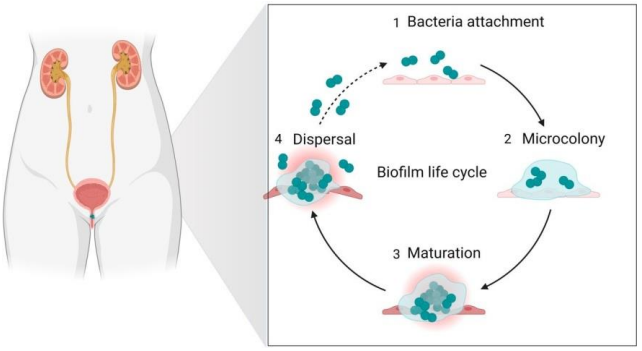

Figure 3. Biofilm infections in the urinary tract.

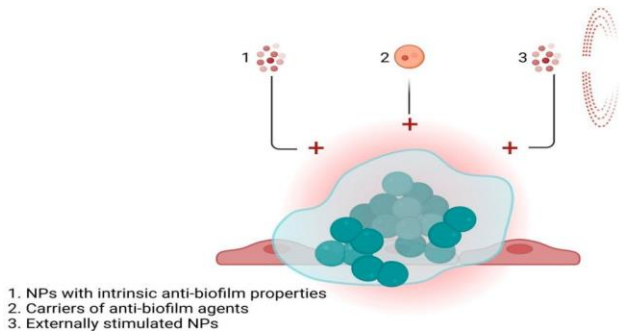

Figure 4. Nanoparticles for treating biofilm infections in the urinary tract.

We provide many encouraging results about the use of nanoparticles in the administration of UTI therapies in light of this matter.

Zingerone, a food sweetener found naturally in ginger, is the first example. Zingerone nanoparticles (ZNPs) were evaluated in vivo on mice as a potential substitute for conventional treatments for Pseudomonas aeruginosa, a kind of biofilm-forming bacterium. After receiving zingerone and ZNPs, the bacterial count in the kidney and bladder tissues of the treated mice was lower than that of the untreated controls. In addition, zingerone and ZNP-treated animals had lower levels of many inflammatory indicators (MDA, MPO, and reactive nitrogen intermediates) compared to control mice; the impact of ZNPs was larger than that of zingerone. Finally, compared to zingerone, ZNPs improved serum sensitivity and phagocytosis of Pseudomonas aeruginosa, highlighting the need of exploring nanoparticle formulations for UTI therapy rather than traditional, straightforward medications.

The increased bioavailability and enhanced retention in the target tissue of nanocarriers led to their consideration as potential treatments for UTIs. An example of this is the formulation of Trimethoprim (TMP) that Brauner et al. suggested: nanospheres based on poly (D,L-lactic-coglycolic acid) (PLGA) that would be further conditioned with wheat germ agglutinin (WGA) and administered intravesically using a catheter. Although transdermal methicillin-polymyxin (TMP) is most often given orally to treat uropathogenic Escherichia coli infections, there have been instances when intratracheal administration was necessary to achieve the desired local concentration and prevent systemic side effects. In addition, WGA is used to imitate the function of Escherichia coli type 1 fimbriae (FimH), which shares the same elevated binding activity for the bladder epithelial area. Immortalised human uroepithelial cells were used to evaluate PLGA-coated TMP nanospheres with and without WGA added to the surface. The scientists found that nanoparticles with a higher WGA density had more adhesions after the urothelium was washed again and again following the first application of the formulations. In general, it did not seem that adding TMP affected the adherence of nanoparticles. Nanoparticle adherence to the urothelium was enhanced by longer incubation periods and lower pH values.

Antibiotic resistance is a big problem all around the globe, but there are solutions that employ organic nanoparticles to stop some bacteria from becoming resistant. For instance, there are a number of ways that Amikacin (AK) resistance might develop, including mutations in the 30S ribosomal subunit, aminoglycoside-modifying enzymes (AME), changes in plasma membrane lipid content, and efflux pumps. In addition, there are significant systemic side effects and limited therapeutic indices for antibiotics such as Amikacin. Improving bioavailability and targeting particular tissues are both possible with the help of nanocarriers in these situations. Liposomes, developed by scientists to address this problem, contain a variety of antibiotics (including Amikacin) and may fuse with the cell membrane of bacteria, allowing them to transfer their contents directly to bacteria that are resistant to antibiotics. The liposome encapsulates the antibiotic molecule and keeps it outside the cell, where it is safe from AME

In case the previous approach doesn't work, it's worth noting that surfactants like Poloxamine 908 may affect absorption in certain organs (lowering liver uptake and boosting spleen uptake, for example). Like Amikacin-bearing PLGA nanoparticles, which have a higher absorption in Peyer's patches than plain Amikacin, certain polymeric nanoparticles may enhance uptake in a particular tissue, further aiding in site targeting of the intended infection.

Finally, Song et al. developed a copolymer (LGseseTAPEG) comprising PLGA, elenocystamine, and methoxypoly(ethylene glycol) tetraacid that is responsive to local oxidative stress, taking into account the fact that UTI localization might be difficult to ascertain at times. Organic nanoparticles have several potential uses, such as medication carriers and disease detectors. Cranberry proanthocyanidins (PAC) are a nano-sized UTI detection system that may interact with extra-intestinal Escherichia coli fimbriae. We evaluated the electrochemical changes generated by the interaction between PAC and Escherichia coli by creating PAC-polyaniline (PANI) nanocomposites and using them on screen-printed electrodes (SPE). With a linear electrical response to Escherichia coli concentrations ranging from 1 to 70,000 CFU/mL, the resultant PAC-PANI nanocomposites on SPE were able to quantify a concentration as low as 1 CFU/mL, which is far lower than previous methods reported in the literature. Additionally, the strategy was likewise unique to Escherichia coli as the electrical response varied among various infections.

Lastly, in a similar vein, nanoparticles might be used to develop noninvasive urine-based diagnostics for non-urinary-systemic disorders. Patients with HIV who had toxoplasmic encephalitis (TE)-specific neurological symptoms were evaluated in a clinical trial using qPCR in addition to NPs of poly-N-isopropylacrylamide coloured with reactive blue-221. Next, the NPs were tested using western blot immunoassay to see if they had successfully caught and concentrated the appropriate antigens from the urine. Unfortunately, the authors couldn't calculate the specificity and sensitivity of the NP-based method presented since there isn't a gold standard test (qPCR has a sensitivity of less than 70%).

Inorganic Nanoparticle Therapy Approaches

To address the new obstacles in UTI treatment, inorganic nanoparticles could be a safer and more effective option. Furthermore, it is worth noting that several NPs include antibacterial characteristics, which may help decrease bacteriuria in infections

caused by both common and multi-drug resistant (MDR) bacteria. As a result, these NPs may be particularly useful in the treatment of UTIs. This is why we're making an effort to provide a more thorough presentation of inorganic NPs' role in UTI treatment.
Biogenic selenium nanoparticles (Se NPs) have been synthesised in two ways: first, by utilising Penicillium chrysogenum filtrate in biogenic synthesis; second, by combining Se with Gentamicin (CN) under gamma radiation in green synthesis; both approaches are part of the ongoing quest for novel and effective treatments for UTIs caused by multidrug-resistant bacteria. The Se NPs-CN, which were combined with CN, showed antibacterial properties against several bacteria and yeasts, including Candida albicans, Staphylococcus aureus, Bacillus subtilis, and Pseudomonas aeruginosa. Biogenic Se NPs were efficient against S. aureus, Candida albicans, and Pseudomonas aeruginosa. The antibacterial activity outshone that of the sodium selenite precursor, the fungal filtrate, Gentamicin monotherapy, and other conventional antimicrobials. The Se NPs-CN also showed better activity than the biogenic Se NPs. When it came to the activity of the Se NPs, Gram-negative bacteria were much more vulnerable than Gram-positive bacteria. Antibiofilm action against Staphylococcus aureus, Pseudomonas aeruginosa, and Escherichia coli was also noted to be shown by Se NPs-CN. According to Figure 5, the Se NPs work by using selenium's ability to produce superoxide radicals. These radicals lead to a thiol shortage in the bacteria, which ultimately leads to cell death. It should be mentioned that tested mice had persistent harmful effects at doses more than 1.8 mg/kg.

Metal NPs are promising new treatments for UTIs because they do not try to modify metabolic pathways, which means they cannot activate the mechanisms that bacteria use to fight their effects. However, there are concerns that the manufacturing process of these devices might harm the environment and cause patients to experience negative effects. In order to address these problems, M. Abd Elkodous et al. investigated sol-gel-produced zinc oxide nanoparticles (ZnO NPs). We tested the nanoparticles against UTI-causing bacteria that are multidrug-resistant. In addition to their anti-corrosive qualities, the ZnO NPs demonstrated excellent chemical and thermal stability. Producing pure particles, the sol-gel technique is an easy production procedure. The antibacterial activity of the synthesised ZnO NPs was shown against several UTI pathogens. In addition to Bacillus subtilis, they were efficient against Pseudomonas aeruginosa and fungus like Candida tropicalis. Antimicrobial activity was much greater in the ZnO NPs compared to zinc nitrate and other agents. The sensitivity of Gram-negative bacteria to ZnO NPs was shown to be higher than that of Gram-positive bacteria. The anisotropic nature, large surface area, small crystal size, and high porosity of the ZnO NPs contribute to their enhanced effectiveness. Candida tropicalis, Pseudomonas aeruginosa, and Bacillus subtilis were the microorganisms tested for antibiofilm activity. In the first step, known as the irreversible adhesion stage, ZnO NPs prevent biofilm development. The failure of Bacillus subtilis to build the biofilm is ultimately caused by the ZnO NPs' inhibition of exopolysaccharide synthesis. Additionally, ZnO NPs were shown to possess anticancer characteristics; specifically, they exhibited a cytotoxic impact on Ehrlich ascites carcinoma (EAC) in vitro. Additionally, the persistent decrease of zinc ions provided further evidence of the antioxidant properties of the ZnO NPs. In addition to their powerful anticancer effects, ZnO NPs have shown promise in treating urinary tract infections (UTIs) and fungal infections. These benefits make ZnO NPs an interesting candidate for future study into their characteristics and potential uses in sectors such food processing, medicines, and cosmetics.

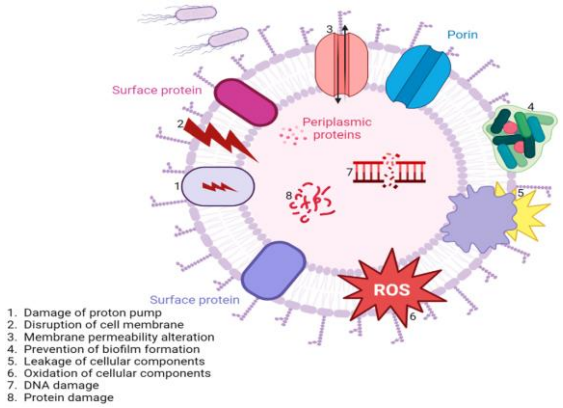

Figure 5. Nanoparticles—common mechanisms of action against UTIs.

Mixed Nanoparticle Therapy Approaches

Researchers aimed to provide effective, long-lasting solutions to the problem of UTIs by combining the best features of organic and inorganic NPs while avoiding their respective disadvantages. So, for example, Gupta et al. functionalized fluoroquinolone drugs into Au-NPs, which led to a minimum inhibitory concentration of the antibiotic that was up to sixteen times lower on Gram-positive and Gram-negative bacteria. Saha et al. also conducted experiments on Staphylococcus aureus, Micrococcus luteus, and Escherichia coli to determine the efficacy and stability of Au-NPs conjugated with Streptomycin, Kanamycin, and Ampicillin. The inhibitory effects of streptomycin on Micrococcus luteus were greater than those of kanamycin Au-NPs on Staphylococcus aureus and Escherichia coli, respectively. In contrast, neither free Streptomycin nor their Au-NP derivatives were able to limit bacterial growth due to Staphylococcus aureus's resistance. In general, functionalized NPs outperformed their traditional counterparts in terms of activity after heat shock exposure or room temperature storage.

Daghian et al. also generated hybrid silver-talc nanocomposites (Ag/Tlc NCs), which are NPs manufactured from mixed materials. The chitosan-capped complexes (Ag/Tlc/Csn NCs) showed remarkable antibacterial and cytotoxic activities as well as wound healing evaluations in mice.

Antibacterial activity was lower in the standard talc preparation, but there was no statistically significant difference between the Ag/Tlc NCs and the Ag/Tlc/Csn NCs compared to the talc-containing composites. At the same concentration, Ag/Tlc and Ag/Tlc/Csn were just as effective as vitamin C in the antioxidant activity tests, but talc had a much lesser impact. The Ag/Tlc/Csn NCs exhibited the greatest antibacterial action and the lowest total tissue bacterial count compared to the Ag/Tlc and Tlc formulations, respectively.

Finally, we couldn't overlook the growing market for mobile biosensors, which, intriguingly, have found use in the treatment of UTIs as well. The presence of Escherichia coli in urine samples taken from anonymous individuals is assessed punctually utilising cellulose base built as origami to help in assembling all the essential analytical steps. The nanoparticles, antibody-decorated (Ab-AuNPs), are employed in this process. A dose-dependent reddening of the NPs' colour occurs when a droplet of dried Escherichia coli urine is moved from one paper fold to another that contains Ab-AuNPs. The next step was to calibrate a smartphone app so that it could detect the concentration of Escherichia coli by taking a picture of the paper filled with Ab-AuNPs. As a result, these biosensors have shown promise for the rapid and cost-effective identification of UTIs at the point of treatment.

Table 2. Most commonly used NP-based delivery approaches for therapy against UTIs.

NPs		Pathogens	Properties
metallic NPs	Ag	*Escherichia coli*	MIC of 7.5 mg/mL, 97% reduction of biofilm formation, 80% destruction of matured biofilms
	Copper	*Escherichia coli, Klebsiella pnemoniae, Pseudomonas aeruginosa, Proteus vulgaris, Staphylococcus aureus, Proteus mirabilis*	high zone of inhibition against UTI pathogens, low cytotoxicity of the NPs
	ZnO	*Escherichia coli, Escherichia hermannii*	anti-bacterial effects at 10 and 40 µg/mL (*Escherichia coli, Escherichia hermannii*), low MIC
polymeric NPs (chitosan-based NPs)		*Candida albicans*	high therapeutic efficacy and targeting of pathogenic microbe-laden cells, low cytotoxicity
hybrid NPs		*Escherichia coli*	high potency (inhibition of bacterial growth within 8 h at 0.156 mg/mL)
carbon-based NPs		*Staphylococcus epidermidis*	prevention of biofilm formation on Foley catheter by graphene-nano Ag nanolayers

Abbreviations: NPs, nanoparticles; Ag, silver; ZnO, zinc oxide; MIC, minimum inhibitory concentration; UTI, urinary tract infection.

CONCLUSIONS

This review is structured and written on the assumption that urinary tract infections (UTIs) are a major driver of antibiotic use in the modern era. Since this fact was mentioned several times in the underlying material of this publication, we chose to trace the history of inventions that replaced traditional antibiotic treatments by simply gavage them. Numerous studies are being conducted on novel compounds with the potential to cure and avoid urinary tract infections (UTIs).

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Corresponding Author

Suryabhan Singh Rathore*

Ph.D Scholar, Raffles University, Neemrana, Rajasthan, India

Email ID- rathoresuryabhan.pharma@gmail.com