

REVIEW ARTICLE

A Comprehensive Review on Plant-derived Bioactive Compounds for Treatment of Urinary Tract Infections

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ABSTRACT

Urinary tract infections (UTIs) are considered one of the most common bacterial infections, affecting millions of people globally, making UTIs a global health threat. These infections are caused by both Gram-positive and Gram-negative bacteria, termed uropathogenic bacteria, but the most predominant causative agent is uropathogenic *Escherichia coli* (UPEC). Due to antimicrobial resistance/antibiotic resistance (AMR/ABR) of these bacteria, the treatment of UTIs in patients using routinely used antibiotics is becoming difficult. In this situation, to test the sensitivity of the antibiotics against bacterial strains, the urine sample of the patients is required. However, the sample is cultured to grow colonies of uropathogens (bacteria/fungus), which takes around 72 h to completely develop the strain in the sample, and the condition of the patients may be severe. Therefore, to reduce AMR/ABR sensitivity, there is a need to identify such types of bioactive compounds of plant origin, which are more effective as compared to antibiotics without side effects on the organs of the body. The present review summarizes the antibacterial activities of medicinal plants against UTI-associated pathogens, as reported by various pioneer researchers. Several medicinal plants have also been commonly used by the pharmaceutical industry to prepare herbal products for the treatment of UTIs. The major medicinal plants and their bioactive compounds are *Vaccinium macrocarpon* (A-type proanthocyanidins), *Boerhavia diffusa* (rotenoids, alkaloids and β -sitosterol), *Tribulus terrestris* (steroidal saponins, alkaloids and flavonoids), *Arctostaphylos uva-ursi* (arbutin and hydroquinone derivatives), *Allium sativum* (allicin and ajoene), and *Phyllanthus fraternus* (phyllanthin and hypophyllanthin). The findings of this review highlight the therapeutic potential of medicinal plants and their bioactive compounds as promising alternative approaches for the treatment and management of UTIs, particularly in the context of increasing AMR. Further studies focusing on the mechanisms of action, standardization of bioactive compounds, and their translation into clinically applicable therapeutic strategies may help facilitate their wider use as alternative or complementary approaches for UTI management. However, further studies focusing on the mechanisms of action, standardization of bioactive compounds, and their translation into clinically applicable therapeutic strategies may help facilitate their wider use as alternative or complementary approaches for UTI treatment and management.

1. INTRODUCTION

A urinary tract infection (UTI) is frequently termed acute cystitis and/or a bladder infection that is characterized by symptomatic inflammation of the urinary system accompanied by significant bacteriuria. A clinical UTI is typically confirmed when a midstream clean-catch urine specimen demonstrates a bacterial load of $\geq 10^5$ colony-forming units/mL.^[1] The urinary tract is an important part

of human physiology that removes bodily waste products and maintains the balance of body fluids.^[2] Physiologically, the urinary tract is divided into an upper urinary tract, which includes kidneys and ureters, and a lower urinary tract, which includes a bladder and a urethra. UTIs are caused by bacterial infections and obstruction in the urinary tract, sometimes due to irregularity in the discharge of urine in certain circumstances. The most common symptoms of UTIs are frequent urination, irregularity in the discharge of urine, painful urination due to dehydration in unfavorable conditions, and sometimes hematuria.^[3] In the present scenario, after COVID-19, UTIs are one of the most common bacterial infections, affecting around 150 million

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people globally.^[4,5] Of these, most of the cases were reported in school-going girls and female staff due to hesitation and, in some cases, due to unhygienic conditions in the institutions and using common washrooms. Microbiologically, Enterobacteriaceae is the most common family associated with UTIs caused by uropathogens *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Citrobacter* spp., and *Enterobacter* spp. Other frequently reported pathogens, including *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Streptococcus bovis*, and the fungus *Candida albicans*, are also among the most common uropathogens reported in UTI infections.^[6,7] Among these, *E. coli* is one of the most important bacterial pathogens responsible for both complicated and uncomplicated UTIs occurring in both men and women; however, women/girl children suffer most (>70%) because their urethra is closer to the anus (as compared to men), which facilitates the spread of gastrointestinal pathogens to the urinary tract.^[8] Most strains of *E. coli* bacteria are harmless and live in the gut, particularly in the large intestine, and are commensal strains of the bacteria that adhere to the mucous layer of the large intestine and are part of the normal microbiota/microflora of the gut, where they constitute about 0.1% of the gut along with other facultative anaerobic bacteria. *E. coli* is a Gram-negative, facultative, and rod-shaped coliform bacterium.^[9-12] Most *E. coli* strains do not cause disease and naturally live in the gut; however, its virulent strains can cause gastroenteritis, hemorrhagic colitis, and UTIs as well. Common symptoms and signs of this type of infection include severe abdominal cramps, vomiting, diarrhea, and sometimes fever. Very young children are more susceptible to infection with *E. coli*; however, healthy individuals of all ages are also at risk of getting infected with *E. coli*.^[13-17] Uropathogenic *E. coli* (UPEC) is one of the main causes of UTIs. It is part of the normal microbiota in the gut and can be introduced in many ways. In particular for females, the direction of wiping after defecation (wiping back to front) can lead to fecal contamination of the urogenital orifices. Anal intercourse can also introduce this bacterium into the male urethra, and in switching from anal to vaginal intercourse, the male can also introduce UPEC to the female urogenital system.^[18]

In pathophysiology, a UTI occurs when uropathogens, most commonly *E. coli*, enter from the gastrointestinal flora and ascend through the urethra, colonize the urinary bladder, and potentially spread to the upper urinary tract region. *E. coli* bacteria contaminate the polyurethral area and adhere to the mucosal cells of the urethra through the pili and/or fimbriae. Uropathogens migrate up into the urinary bladder, attach to the superficial cells, multiply, and form intercellular bacterial communities; due to this bladder invasion, cystitis occurs in UTI patients. In patients, bacterial toxins and cellular damage trigger an innate immune response for recruiting neutrophils to the infected site. This is called an inflammatory response, and this inflammation causes the typical type of lower UTI symptoms, particularly dysuria and urgency. An inflammatory response of the urothelium to bacterial invasion may result in pyelonephritis (kidney infection), urethritis, cystitis (bladder infection), or prostatitis (in males).

If bacteria continue to ascend through the ureters against normal urine flow, they colonize the renal pelvis and parenchyma, leading to severe inflammation and systemic signs of flank pain and fever.

UTIs are usually treated with antibiotics. However, the effectiveness of commonly used antibiotics, such as trimethoprim-sulfamethoxazole, fluoroquinolones, and β -lactams, has decreased because of the increasing number of multidrug-resistant (MDR) uropathogens. Frequent and unnecessary use of antibiotics is an important reason

for the development of antibiotic resistance (ABR). This can lead to treatment failure, increased illness, and higher hospitalization costs. Even short-term exposure to antibiotics can increase the risk of resistant bacteria, especially in patients with severe UTIs, catheter-associated UTIs, and recurrent infections. Unnecessary antibiotic use for asymptomatic bacteriuria, particularly in elderly and catheterized patients, also promotes resistance.^[19] The increasing emergence of antibiotic-resistant uropathogens, particularly *E. coli*, *K. pneumoniae*, and *P. mirabilis*, poses additional challenges to UTI treatment and management and emphasizes the need for alternative or complementary therapeutic strategies.^[20] Therefore, bioactive compounds of medicinal plants are gaining popularity as an alternative approach for the treatment of UTIs. Medicinal plants contain a number of compounds that are medicinally useful for the treatment of UTIs in the form of infusion, decoction, extract, and in powdered form. Chemically, these bioactive compounds are secondary metabolites of plant origin secreted from the plants for their defensive purpose and are of many types: resin, tannin, gum, saponin, flavonoid, glycoside, polyphenol, terpenoid, and alkaloids.

1.1. Aims and Objectives

1. To focus on the growing concern of UTI cases
2. To explore alternative therapeutic approaches for the treatment of UTIs
3. To find out recent advancements in the use of bioactive compounds of plant origin.

2. MATERIALS AND METHODS

Most of the available scientific literature on UTIs and their therapeutic management was retrieved from multiple databases and sources, including PubMed, PubChem, Google Scholar, MDPI, Scopus, Web of Science, Semantic Scholar, ScienceDirect, ResearchGate, Elsevier, National Centre for Biotechnology Information, Taylor and Francis Online, Frontiers, Wiley Online Library, Shodhganga, and ChemSpider. The collected literature was critically reviewed and organized based on the information available on medicinal plants and their reported bioactive compounds, mode of action, and potential to treat UTIs [Figure 1].

3. REVIEW OF LITERATURE

Apu et al.^[21] examined the phytochemical composition and *in vitro* biological activities of aerial-part extracts of *Boerhavia diffusa* Linn. The researchers prepared n-hexane, ethyl acetate, and methanol extracts from the aerial parts of *B. diffusa* and evaluated them for phytochemical constituents and antimicrobial activities using specific *in vitro* assays. The *B. diffusa* extracts were assessed for their antimicrobial effects against three microorganisms: *S. aureus*, *Shigella dysenteriae*, and *C. albicans*. The extracts exhibited concentration-dependent antimicrobial activity against *S. aureus*, *S. dysenteriae*, and *C. albicans*, with greater inhibition observed at 1000 μ g/disc than at 500 μ g/disc. In addition, the extracts showed significant antifungal activity, which was suggested to be associated with the presence of anthraquinones.

Mehta et al.^[22] reported the antibacterial activity of the ethanolic fruit extract of *Phyllanthus fraternus*. The ethanolic extract was tested against several bacterial strains, including *E. coli*, *Bacillus megaterium*, *Corynebacterium glutamicum*, *Bacillus cereus*, *Bacillus subtilis*, *S. aureus*, *Salmonella* Typhi, *P. aeruginosa*, and *Proteus vulgaris* using the disc diffusion method. The ethanolic extract showed maximum

antibacterial activity against *B. cereus* with a zone of inhibition (ZOI) of 28 mm, followed by *C. glutamicum* and *S. Typhi* with a ZOI of 27 mm and 25 mm, respectively.

Alsedairy et al.^[23] examined the phytochemical composition and bioactive properties of leaf extract (LE) and seed extracts (SE) of *Tribulus terrestris*. The methods included gas chromatography-mass spectrometry (GC-MS) for phytochemical profiling. The antibacterial activity of the *T. terrestris* LE and SE was evaluated using the disc diffusion method against three Gram-positive bacteria: *S. aureus* (MTCC-29213), *Staphylococcus epidermis* (MTCC-12228), and *Bacillus subtilis* (MTCC-10400); and three Gram-negative bacteria: *E. coli* (ATCC-25922), *P. aeruginosa* (MTCC-27853), and *K. pneumoniae* (MTCC-13883). The results showed that *T. terrestris* LE was more potent than SE, with minimum inhibitory concentrations (MICs) of 6.25–25 and 12.50–50 µg/mL, respectively. *E. coli* was the most susceptible strain to the SE, whereas *K. pneumoniae* was the most susceptible to both extracts. In contrast, *S. aureus* and *S. epidermidis* were the most resistant strains to the LE, whereas *B. subtilis* was the most resistant to the SE. Previous studies also reported antibacterial activity of *T. terrestris*, which has been attributed to bioactive constituents such as alkaloids, flavonoids, and saponins. Fruit-derived compounds were also reported to be effective against methicillin-resistant *S. epidermis*.

Cipriani et al.^[24] have reviewed bioactive compounds as alternative approaches for preventing UTIs. Their study highlighted the increasing problem of antimicrobial resistance (AMR) and discussed non-antibiotic preventive approaches, particularly plant-based compounds with antibacterial, anti-adhesion, anti-quorum sensing, and uroepithelial protective activities, for the prevention and management of UTIs. Referring to the European Association of Urology guidelines, the authors reported several interventions for preventing recurrent UTIs. Their study explored various medicinal plants such as *Arctostaphylos uva-ursi*, *Phyllanthus amarus*, *Psidium guajava*, *Premna serratifolia*, and *Trigonella foenum-graecum* L., along with their phytochemical composition, which may exert their antibacterial effects through mechanisms such as bacterial cell wall disruption, interference in metabolic processes, and inhibition of bacterial adhesion and biofilm formation. Vitamins were also assessed for their antioxidant, immunomodulatory, and epithelial-protective roles in prevention and management of UTIs.

Eyasu et al.^[25] examined the antibacterial and antioxidant properties of *Thymus schimperi* (Ts), *Rhamnus prinoides* (Rp), and *Justicia schimperiana* (Js) against MDR uropathogenic bacteria. The highest total phenolic content (TPC), total flavonoid content, and proanthocyanidin content were found in Ts. GC-MS identified 14 bioactive compounds in Ts (predominantly, hexanedioic acid, bis[2-ethylhexyl] ester, thymol, and o-cymen-5-ol), 6 bioactive compounds in Rp, (mainly hexanedioic acid, bis[2-ethylhexyl] ester, β-D-glucopyranoside, methyl, and desulphosigrin), and 5 bioactive compounds in Js (mainly hexanedioic acid, mono [2-ethylhexyl] ester, debrisroquine, and 8,11,14-heptadecatrienoate, methyl ester). The TPC of the extracts showed a strong, statistically significant negative correlation with both 2,2-DiPhenyl-1-PicrylHydrazyl ($r = -0.999$, $P = 0.023$) and 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid) ($r = 0.999$, $P = 0.032$) antioxidant assays. Antibacterial testing demonstrated that Ts showed remarkable antibacterial activity against extended-spectrum β-lactamase-producing *E. coli* and *K. pneumoniae* isolates at 1000 mg/mL, whereas Ts yielded the lowest MICs (4 mg/mL) against reference *E. coli* (ATCC 25922). Overall, Ts and

Rp possess significant bioactive components with antioxidant and antibacterial potential against UTIs.

Braja et al.^[26] studied the antimicrobial property of *Quisqualis indica* L. plant extracts on uropathogenic bacteria. Their evaluation revealed broad-spectrum antibacterial efficacy against *E. coli*, *P. aeruginosa*, *S. aureus*, *K. pneumoniae*, *A. baumannii*, and *Streptococcus pyogenes*. Analysis of 110 urine samples from UTI patients revealed *E. coli* as the most frequently identified strain in collected samples (57%), followed by *P. aeruginosa* (17%), *S. aureus* (15%), and *K. pneumoniae* (10%). Furthermore, *in silico* profiling via the Molsoft platform identified phytol, trans-squalene, and stigmaterol as key bioactive compounds having favorable drug-likeness scores, supporting the therapeutic potential of *Q. indica* as a candidate source for anti-UTI drug development.

Jouaneh et al.^[27] demonstrated that plant-derived catechol-containing polyphenols can reverse the quiescent state (non-proliferating) of UPEC responsible for recurrent UTIs. Testing a library of 114 plant extracts against UPEC strain CFT073 yielded a 69% overall active hit rate, with epigallocatechin gallate and rosmarinic acid emerging as the most potent agents. Ultimately, the outcomes of their study identified a group of metabolites with the potential to target dormant bacteria in recurrent UTIs.

Acharjee et al.^[28] assessed the antibacterial potential of six medicinal plant species: *Sphagneticola calendulacea*, *Enydra fluctuans*, *Chenopodium album*, *Mentha arvensis*, *Mimosa diplotricha*, and *Averrhoa bilimbi* – against primary uropathogens, namely *Staphylococcus* spp., *Proteus* spp., *Pseudomonas* spp., *E. coli*, and *Enterobacter* spp. Methanol extracts of plants demonstrated the strongest single-agent efficacy, with inhibition zones reaching up to 14 mm, whereas ethanol and aqueous extracts showed minimal activity. Combining these plant extracts with commercial antibiotics produced a notable synergistic response, expanding inhibition zones up to 26 mm. Their study concluded that pairing plant extracts with conventional antibiotics provides a far more effective strategy against resistant bacterial strains than monotherapy.

Ahmed et al.^[29] characterized the molecular basis of virulence factors and AMR among bacterial uropathogens associated with human UTIs. They investigated bacterial infections and AMR among UTI patients in a tertiary-care hospital in Lahore, Pakistan. During the 1-year study period, 1899 clinical samples were analyzed, of which 1107 yielded bacterial growth. The identified pathogens included *S. aureus*, *P. aeruginosa*, *E. coli*, and other bacterial species. Methicillin-resistant *S. aureus* (MRSA) constituted 16.93% of the positive isolates and exhibited substantial resistance to antibiotics such as amikacin, clindamycin, fusidic acid, gentamicin, and tobramycin. However, the isolates remained completely susceptible to vancomycin and linezolid. The findings highlighted the growing therapeutic challenge posed by anti microbial resistance (AMR).

Bibi et al.^[30] synthesized gold nanoparticles (AuNPs) using the aqueous extract of the medicinal plant *B. diffusa* L. Formation of AuNPs was verified via ultraviolet-visible spectroscopy, with a surface Plasmon resonance peak at 551 nm. Characterization through Fourier transform infrared spectroscopy, X-ray diffraction, scanning electron microscopy, and dynamic light scattering revealed that the biogenic AuNPs possessed a crystalline structure, spherical morphology, and an average size of 53.17 ± 0.58 nm. The authors investigated the antibacterial activity of BD@AuNPs against a Gram-positive bacterium, *Listeria monocytogenes*, and two Gram-negative bacteria:

Bordetella bronchiseptica and *E. coli*, using the agar well diffusion method. The results showed that BD@AuNPs demonstrated notable antibacterial activity against *L. monocytogenes*, *B. bronchiseptica*, and *E. coli*. Therefore, BD@AuNPs showed considerable antibacterial potential with inhibitory effects comparable to those of the standard antibiotics. In addition, BD@AuNPs also exhibited antifungal properties (against *C. albicans*, *Aspergillus niger*, *Cryptococcus neoformans*, and *Trichophyton rubrum*) notably more potent than the crude extract.

Marouf *et al.*^[31] reviewed the antibacterial property of medicinal plants against UPEC. They highlighted that the growing ABR in UPEC increases UTI recurrence rates and complicates standard care. To address this, the authors demonstrated that phytochemicals can serve as effective non-antibiotic alternatives. These plant compounds target and disrupt essential UPEC virulence mechanisms, including bacterial adhesion, cell motility, biofilm formation, and quorum sensing. They emphasized that plant-based treatments hold significant potential for developing novel pharmaceutical strategies to prevent and manage resistant UTI infections.

Obiri *et al.*^[32] explored the antibacterial potential of crude alkaloidal extract of *P. fraternus* (AEPP) via high-throughput spot culture growth inhibition. The interaction between the crude alkaloids and test microbial strains was assessed by time-kill kinetic assays. A modulation study assessed the potential of crude alkaloids to modify the antimicrobial action of a standard antibiotic. The findings showed that *P. fraternus* alkaloids effectively suppress the majority of pathogenic strains *in vitro*. Time-kill kinetics studies confirmed clear bactericidal action against *S. aureus* and *E. coli*. In addition, the authors showed that AEPP can enhance the efficacy of traditional antibiotics, significantly potentiating tetracycline against *Shigella* species. Liquid chromatography-electrospray ionization-mass spectrometry (LC-ESI-MS) characterization attributed these antibacterial properties to two alkaloids – epibubbialine and ent-nosecurinine found in the crude alkaloid extract of *P. fraternus*.

Hsu *et al.*^[33] reported that UTIs are among the most common bacterial infections affecting women, with recurrent infections being a major concern due to increasing AMR. The authors highlighted plant-based therapies as potential complementary approaches due to their antimicrobial, anti-inflammatory, and immunomodulatory properties. Medicinal plants and phytochemicals such as cranberry, pomegranate, and green tea exhibit anti-adhesive and biofilm-disrupting activities. In particular, cranberry proanthocyanidins and bearberry arbutin have shown promising effects in reducing UTI recurrence. Overall, plant-based interventions may serve as useful adjuncts to conventional UTI treatment, although further clinical studies are required to confirm their efficacy and safety.

Ortega-Lozano *et al.*^[34] highlighted that UTIs – primarily caused by *E. coli* (80–90%) alongside pathogens like *S. aureus*, *E. faecalis*, *P. aeruginosa*, *P. mirabilis*, and *K. pneumoniae* – face significant therapeutic hurdles due to rising ABR and biofilm formation. To address this, the authors reviewed the antimicrobial potential of popular Mexican culinary spices, including cinnamon, clove, cumin, oregano, pepper, and rosemary. Rich in bioactive phytochemicals such as polyphenols, saponins, alkaloids, and terpenes, the essential oils of these spices exhibit direct antimicrobial efficacy against uropathogens and demonstrate synergistic effects when combined with standard antibiotics, underscoring their potential as natural adjunctive therapies for UTIs.

Ramírez-Castillo *et al.*^[35] analyzed 110 UPEC isolates (79 community-acquired, 31 hospital-acquired) from UTI patients in Aguascalientes, Mexico. The study found a 63% MDR rate. Resistance was highest against ampicillin, ampicillin-sulbactam, and trimethoprim-sulfamethoxazole, alongside ciprofloxacin (47.3%), levofloxacin (43.6%), and cephalosporins (27.6%). Fluoroquinolone resistance strongly co-occurred with MDR status, whereas hospital-acquired strains correlated with the MTII_{kps} gene and resistance to nitrofurantoin and third-generation cephalosporins. Dominant virulence genes included Fimbrial Adhesin H (71.8%) and Ferric Yersiniabactin Uptake A (68.2%). Plasmid-mediated quinolone resistance was driven mainly by Quinolone Resistance Gene A (22.7%) and Quinolone Resistance Gene B (20.9%), with 12.7% carrying $\text{bla}_{\text{CTX-M}}$ (primarily $\text{bla}_{\text{CTX-M-15}}$). The authors highlighted that high baseline resistance undermines empirical treatment, stressing the need for ongoing local surveillance to guide therapy choices.

Saddam *et al.*^[36] have reviewed herbal approaches for treatment of UTIs. They assessed the possible interactions between bioactive constituents of medicinal plants and UTI pathogenic bacteria. Herbal medicines contain bioactive compounds such as flavonoids and polyphenols, which nullify free radicals and reduce bacterial growth, which is involved in the formation of biofilm. By stopping these processes, herbs reduce cell damage (oxidative stress) and inflammation in the body. Specific herbs known for fighting bacteria and inflammation were tested to see how effectively they can treat UTIs. Their study highlights the notable effects of several key medicinal plants, namely cranberry (*Vaccinium macrocarpon*), bearberry (*A. uva-ursi*), amla (*Embolica officinalis*), garlic (*Allium sativum*), Harad (*Terminalia chebula*), and baheda (*Terminalia bellirica*) against Uropathogens. Their therapeutic effects are associated with different mechanisms, including inhibition of bacterial biofilm, inhibition of bacterial adhesion to uroepithelial cells, diuretic potential, elimination of bacteria and toxins from the urinary tract, alteration of bacterial enzymatic activity and cellular metabolism, modulation of inflammatory pathways, and inhibition of bacterial growth.

Ilangage *et al.*^[37] studied the antibacterial activities of ten medicinal plants *in vitro* against uropathogens and evaluated the toxicity by brine shrimp lethality assay. The methods in their study include the Agar well diffusion and broth microdilution to assess the antibacterial potential of the 10 herbal plants against *P. aeruginosa* ATCC27853, *S. aureus* ATCC25923, *E. coli* ATCC25922, as well as UTI-positive bacterial strains isolated from active cultures. The methods also include a brine shrimp lethality assay to evaluate the cytotoxicity of the medicinal plants. *P. emblica* extract was highly effective against *E. coli* strains, whereas *B. diffusa* and *T. chebula* performed best against *S. aureus*. For *P. aeruginosa*, *T. involucrata* excelled against the standard strain, whereas *Zingiber officinale* and the plant mixture were most potent against the UTI strain. Conversely, *Cucumis melo* lacked antibacterial activity, though all tested materials demonstrated cytotoxicity in the Brine Shrimp Lethality Assay.

Gadisa and Tadesse^[38] evaluated the antimicrobial properties of medicinal plants for the treatment of UTIs in Ethiopia's pastoralist community. They conducted an *in vitro* experiment to examine the antimicrobial potential of *Rumex abyssinicus*, *Cucumis pustulatus*, *Discopodium penninervium*, *Lippia adoensis*, *Euphorbia depauperata*, and *Cirsium englerianum*. They also performed a phytochemical screening of the above-mentioned plants. They tested the drug-resistant microbes using plant extracts prepared with 80% methanol. Their susceptibility was tested by the disc diffusion and broth microdilution

methods. Most plant extracts showed antimicrobial activity against two or more drug-resistant bacteria. The extracts showed MIC values of 1–128 µg/mL and inhibition zones of 9–27 mm. Extracts of *C. englerianum* and *E. depauperata* showed strong activity against MRSA and *E. faecalis*. These extracts also inhibited *E. coli* and *K. pneumoniae*. *R. abyssinicus* showed promising antifungal activity against *C. albicans*. The main phytochemicals found in most of these plants are alkaloids, flavonoids, phenolics, and terpenoids. Therefore, the bioactive compounds of these plants that prevent microbial growth can be studied further and may help in the development of plant-based antimicrobial approaches for the management of UTIs.

Saeed et al.^[39] evaluated the phytochemicals and biological activities of *Carissa carandas* using sequential extraction with n-hexane, dichloromethane, and methanol. The antimicrobial activity of sequential crude extracts of *C. carandas* was evaluated against UTI-causing bacteria (*E. coli* ATCC 25922 and *K. pneumoniae* ATCC 13883) and fungi (*C. albicans* BNCC 187382 and *Candida glabrata* BNCC 337348). The methanol extract showed better phytochemical content, antioxidant, anti-inflammatory, and antimicrobial activities. The active fraction was further analyzed using reversed-phase high-performance liquid chromatography and LC-ESI-MS/MS, which identified phenolic acids, flavonoids, and anthocyanins. The methanolic extract showed significant antibacterial activity against *E. coli* and *K. pneumoniae*, with zones of inhibition of 21 ± 0.5 mm and 26 ± 0.5 mm, respectively, at 50 µg/mL. Its activity was compared with ciprofloxacin, a standard antibacterial drug, used at 5 µg/mL. The methanolic extract also showed activity against the fungal pathogens *C. albicans* and *C. glabrata*, with zones of inhibition of 12 ± 0.5 mm and 10 ± 0.5 mm, respectively. Nystatin, used as the standard antifungal drug, showed strong activity against both *Candida* species. These findings suggest that the methanolic extract of *C. carandas* has strong antimicrobial activity against both bacterial and fungal UTI-associated pathogens. Overall, *C. carandas* appears to be a promising medicinal plant, and further research can explore its therapeutic applications and active compounds.

Zhou et al.^[40] reviewed the role of UPEC in UTIs and discussed how these bacteria cause infection. They also assessed different approaches used for their management. In their study, they observed the evolution of UPEC in many ways, namely changes in patterns of invasion, attachment, colonization, and replication in order to attack the urothelium and then survive. They discussed the use of antibiotic therapy for UTI treatment and how the increasing rate of recurrence in UTI cases and elevating AMR have decreased the efficiency of antibiotic treatment of UTIs. Therefore, the growing concern of multidrug resistance globally has stressed the importance of exploring complementary & integrative medicine and also further elucidation of the pathogenic mechanisms of these bacteria.

Tarasadiya et al.^[41] highlighted that UTIs are a major public-health concern due to their high prevalence, recurrent nature, and increasing treatment costs. The authors noted that excessive or inappropriate use of antibiotics has contributed to MDR, whereas biofilm formation further complicates treatment by limiting antibiotic penetration and protecting bacteria from host defense mechanisms. They discussed the potential of nanotechnology-based approaches for improving UTI diagnosis and treatment. Different nanomaterials, including metallic, polymeric, lipid-based, and carbon-based nanoparticles, have demonstrated antimicrobial and antibiofilm properties. Specifically, they indicated that plant extracts, such as *Azadirachta indica* and *Aloe barbadensis* Miller, can serve as eco-friendly reducing and stabilizing

agents in the green synthesis of metallic nanoparticles such as silver nanoparticles. The mode of action of these nanocarriers involves damage to bacterial membranes, generation of reactive oxygen species, controlled antimicrobial release, and improved antibiotic efficacy. Targeted delivery systems, including intravesical and mucoadhesive formulations, may enhance drug localization at infection sites while reducing systemic adverse effects. Overall, the authors emphasized that nanotechnology-based strategies could provide potential approaches for addressing ABR and improving UTI management, although further safety evaluation and clinical validation are required.

Day et al.^[42] explored the potential impacts of traditional plant urologicals in curbing early UPEC infection and their ability to strengthen the innate immune response. They examined the possible mechanism of action of various government-approved herbal preparations which are used in clinical practice, including *Orthosiphon stamineus*, *Betula* spp., *Ononis spinosa*, *Solidago gigantea*, *Solidago virgaurea*, *Agropyron repens*, and *Equisetum arvense*. Liquid chromatography-mass spectrometry profiling showed that aqueous extracts did not directly stop UPEC growth but influenced the initial interaction between UPEC and host cells. A stress-reporter assay was performed, which showed that the extracts specifically induced surface stress in *E. coli* K-12 strain MG1655 through the BaeS-BaeR two-component system, whereas other stress pathways such as osmotic, pH, oxidative, and SOS responses remained unaffected. This surface stress decreased the expression and function of type 1 fimbriae, which led to a notable decrease in adhesion of UPEC strain CFT073 to human bladder cells and reduced intracellular bacterial numbers. However, the bacterial biofilm formation was not adversely affected by the extracts. Further, in an *in vivo* model using *Galleria mellonella* larvae, oral administration of the herbal medicinal product extracts enhanced innate immune responses and improved survival following UPEC infection. The extracts also increased the expression of innate immune genes in human bladder epithelial cells, suggesting enhanced host defense. Overall, the findings indicate that these multi-component herbal preparations may reduce UPEC adhesion and invasion while strengthening host innate immunity. Their findings suggest the possible use as an alternative approach to antibiotic treatment of UPEC infections.

Sharma et al.^[43] investigated *Cyperus rotundus* as a possible source of compounds for treating UTIs. The methods of this study included the disc diffusion method to test the antiuropathogenic activity of crude extract of *C. rotundus*, which demonstrated broad-spectrum antibacterial activity toward uropathogens. The ethanolic extract exhibited MIC values ranging from 2.5 to 10 mg/mL against various uropathogens. Tannins and saponins were identified through phytochemical screening of *C. rotundus*. TLC analysis showed two spots, with thin-layer chromatography (TLC)-bioautography confirming antibacterial activity in the spot having an R_f value of 0.435, demonstrating its bioactive nature. High-performance liquid chromatography analysis confirmed saponins in the active fraction (retention time: 16.102 min), with a quantified concentration of 75.6373 mg/mL in the ethanolic rhizome extract. The findings of this study scientifically support the therapeutic potential of *C. rotundus* for treating UTIs.

Saha et al.^[44] investigated the *in vitro* antibacterial potential of LEs of selected medicinal plants (*Tamarindus indica*, *T. foenum-graecum*, *Clitoria ternatea*, *Dalbergia sissoo*, *Ocimum sanctum*, *Ocimum basilicum*, *Mentha pipertia*, *Z. officinale*, *Curcuma longa*, and *Canna indica*) on bacterial pathogens that cause UTIs in indigenous

communities of Bolangir, Odisha, India. For the identification of UTI-causing bacteria, they used techniques, namely colony morphology, Gram's staining, and biochemical characterization. The antimicrobial activity of the selected antibiotics was evaluated using the disc diffusion technique. The inhibitory effects of the medicinal plant LEs were assessed by the agar well diffusion method. The MIC and minimum lethal concentration were determined using the broth dilution method. Four UTI-associated bacterial species: *E. coli*, *E. faecalis*, *S. aureus*, and *K. pneumoniae* – were isolated and identified. Among these, *E. coli* showed the highest pathogenicity, whereas *S. aureus* exhibited the lowest. Greater susceptibility to UTI was observed in females aged 16–30 years and males aged 61–75 years. The LEs of *T. indica* and *C. ternatea* demonstrated stronger antibacterial activity against the tested pathogens than ceftriaxone and piperacillin [Figure 2].

4. DISCUSSION

This review demonstrates the potential of medicinal plants and their bioactive compounds for the management of UTIs. The increasing resistance to conventional antibiotics, partly associated with mechanisms such as β -lactamase production, has emphasized the need for alternative antimicrobial strategies. Several studies have reported antimicrobial activity of plant extracts against UTI-associated pathogens. As summarized in Table 1, the reviewed literature indicates that medicinal plants and their bioactive compounds exhibit diverse activities relevant to UTI management, including antibacterial, anti-biofilm, anti-adhesive, diuretic, anti-inflammatory, and anti-urolithiatic effects. For instance, quercetin from *B. diffusa* has been associated with antibacterial and anti-biofilm effects, while protodioscin from *T. terrestris* has shown activity against UPEC along with diuretic and anti-urolithiatic properties. A different mechanism is suggested by A-type proanthocyanidins from cranberry (*V. macrocarpon*), which may reduce bacterial adhesion. Collectively, these reports indicate that plant-derived compounds may target both bacterial infection and factors associated with urinary tract symptoms. However, differences in plant species, compounds, extraction methods, concentrations, target pathogens, and experimental conditions limit direct comparison among studies. Moreover, much of the available evidence is based on *in vitro* studies, with comparatively limited information on mechanisms of action, standardization, safety, and clinical efficacy. This creates a notable translational gap between laboratory success and real-world clinical application. Future research should therefore emphasize compound characterization, mechanistic studies, standardized preparations, safety assessment, and clinical validation, including evaluation of their potential use alongside conventional antibiotics.

5. CONCLUSION

UTIs pose a significant global health challenge due to their frequent recurrence and the increasing prevalence of AMR among uropathogens. Although antibiotics remain the primary UTI treatment option, their continuous use may be associated with side effects, disruption of the normal microbiota, and the increasing problem of AMR. In this context, medicinal plants have gained attention as potential alternative or complementary approaches because they contain a wide range of bioactive compounds that possess diverse biological activities, including antimicrobial and anti-biofilm effects, which may be beneficial in the management of UTIs. Over the last decade, considerable research has been conducted on medicinal plants and their bioactive compounds, with many studies reporting promising efficacy against UTI-causing pathogens. Several studies also reported enhanced antimicrobial effects when certain plant-derived bioactive

compounds were combined with conventional antibiotics, suggesting synergistic interactions. In addition, plant-mediated nanoparticle-based strategies are also being explored as an emerging avenue for addressing UTIs. These approaches highlight the potential of plant-derived compounds in UTI management. Moving forward, bridging the translational gap through standardized formulations and clinical validation will be essential to establish these natural therapeutics as safe and reliable options for managing recurrent UTIs.

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11. DATA AVAILABILITY STATEMENT

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12. DISCLAIMER/VIEW AND OPINIONS

The opinions expressed in this article are solely those of the authors and do not reflect the views of the International Research Journal of Ayurveda and Yoga or its editorial board.

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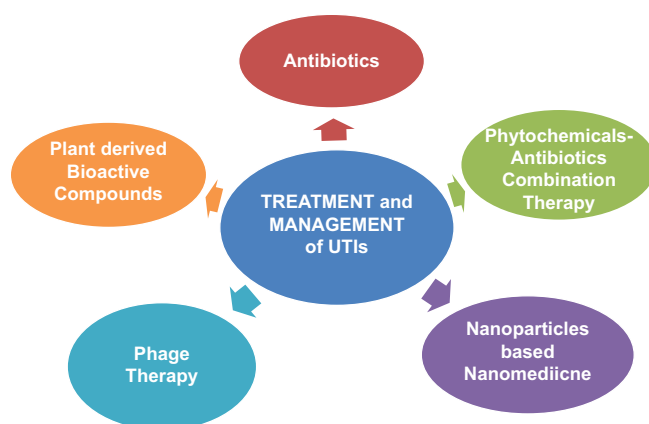


Figure 1: Conventional and alternative treatment and management approaches for urinary tract infections

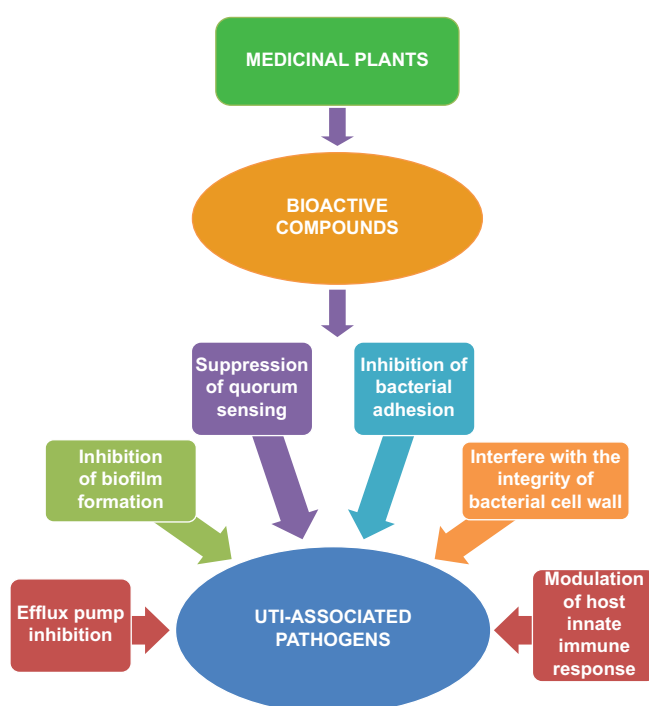
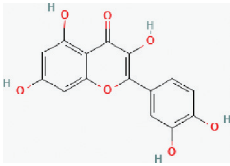
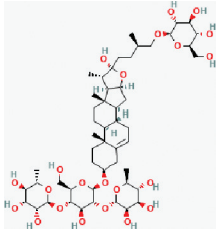
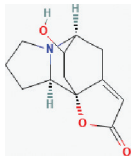
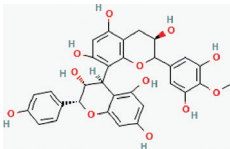
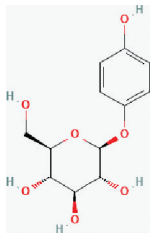
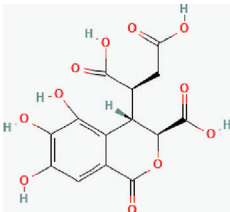
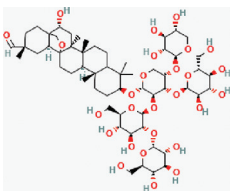
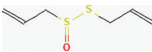


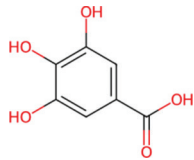
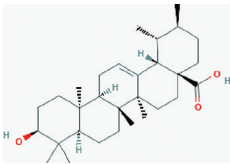
Figure 2: Possible mechanisms of action of plant-derived bioactive compounds against urinary tract infection-associated pathogens

Table 1: List of medicinal plants, bioactive compounds, and the pharmacological properties for the treatment and management of UTIs

Medicinal plants	Bioactive compounds	Structure of compound	Pharmacological properties	Reference
<i>Boerhavia diffusa</i> (Punarnava)	Quercetin		- Exhibits antibacterial and antibiofilm properties - Mild diuretic effect and a potent anti-inflammatory agent.	[45]
<i>Tribulus terrestris</i> (Gokharu)	Protodioscin		- Antibacterial activity and inhibits uropathogenic <i>Escherichia coli</i> - Increases urine output and enhances the excretion of electrolytes - It also possesses anti-urolithiatic properties.	[46]
<i>Phyllanthus fraternus</i> (Bhui-amla)	Epibubbialine		Shows antibacterial activity against common uro-pathogens. Also has anti-inflammatory effects and downregulates inflammatory mediators.	[22,32,47]
<i>Vaccinium macrocarpon</i> (Cranberry)	A-type proanthocyanidins (PACs)		- Condensed tannins found abundantly in cranberries are responsible for anti-adhesion activity - Can induce structural changes or deformation of bacteria.	[48]
<i>Arctostaphylos uva-ursi</i> (Bearberry)	Arbutin		- Acts as a traditional urinary antiseptic and anti-inflammatory agent for UTIs - High tannins in its leaves help in smoothing irritated urinary mucous membranes.	[49]
<i>Terminalia chebula</i> (Harad/Harra)	Chebolic acid		- Displays inhibitory effects against various bacteria, fungi, and viruses - Can neutralize reactive oxygen species and prevent oxidative stress - Also exhibits Anti-inflammatory activity.	[50]
<i>Cyperus rotundus</i> (Nutgrass)	Saponins		- Contain antibacterial properties. The plant acts as a natural diuretic. - Due to its anti-inflammatory and antispasmodic properties, it is used to soothe dysuria and bladder discomfort associated with cystitis.	[43,51]
<i>Allium sativum</i> (Garlic)	Allicin		It shows strong antibacterial activity against multi-drug-resistant bacterial strains isolated from infected human urine.	[52]

(Contd...)

Table 1: (Continued)

Medicinal plants	Bioactive compounds	Structure of compound	Pharmacological properties	Reference
<i>Terminalia bellirica</i> (Baheda)	Gallic acid		• Antimicrobial, anti-inflammatory, antioxidant, and anti-biofilm activity.	[53,54]
<i>Carissa carandas</i> (Karonda)	Carissic acid		• Anti-adhesive properties, Methanol extracts of the plant show antibacterial properties against UTI-causing pathogens • Help soothe the irritated lining of the urinary tract and lower pelvic discomfort.	[39,55]

UTIs: Urinary tract infections