



Emerging Insights Into Microbiome Therapeutics for Urinary Tract Infections: A Narrative Review

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Urinary tract infections (UTIs) are among the most common bacterial infections worldwide, affecting millions annually and posing a significant global health concern. Traditional therapies for UTIs are becoming increasingly ineffective due to rising drug resistance and their tendency to disrupt the host's healthy microbiota, leading to further side effects. Consequently, there is an urgent need to develop alternative therapeutic agents that differ from conventional regimens and have fewer or no side effects. In this context, microbiome therapeutics offer a promising solution, given their demonstrated efficacy against various infectious diseases. Advances in scientific technology, particularly next-generation sequencing, have deepened our understanding of urinary microbiome dynamics, revealing a complex interplay within the urobiome that influences the onset and progression of UTIs. Uropathogenic bacteria do not solely cause UTIs; shifts in the composition of the urinary microbiome and interactions within the microbial community, known as host-microbiota interactions, also play a significant role. Although recent studies underscore the potential of targeting the urinary microbiome to manage UTIs and related complications, this field is still emerging and faces numerous regulatory and technical challenges. Further in-depth and comprehensive research is required to advance this pioneering concept into clinical practice.

Keywords: Urinary tract infections, Microbiome therapeutics, Urobiome, Urinary microbiome dynamics, Host-microbiota interaction

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HIGHLIGHTS

This study explores the vital roles of the human and urinary microbiomes in health and disease, emphasizing their impact on urinary tract infections. It highlights advances in microbiome-based therapeutics—like probiotics, postbiotics, phages, and fecal microbiota transplantation—as promising alternatives to antibiotics.



INTRODUCTION

Urinary tract infections (UTIs) are among the most prevalent bacterial infections, affecting millions globally yearly [1]. The high incidence and recurrence rates significantly contribute to the disease burden, rendering UTIs a significant public health concern [2]. Recent reports estimate that 404.6 million new cases of UTIs occur worldwide, with nearly 236,786 deaths attributed to UTIs in recent years [3]. Currently, UTIs are a leading cause of life-threatening conditions such as sepsis, renal damage, and preterm birth, associated with considerable mortality and healthcare costs [4]. UTIs have also become a principal cause of frequent healthcare-associated infections, frequently linked with high levels of multi-drug-resistant pathogens, posing significant challenges for current treatments [5].

The treatment of UTIs predominantly relies on antibiotics, which can disrupt the host's microbiota balance, leading to dysbiosis, increased susceptibility to reinfection, and adverse health outcomes [6]. Moreover, the widespread use of antibiotics has fueled a concerning rise in antimicrobial resistance, limiting treatment options for managing recurrent and chronic infections [7]. The reduced susceptibility of UTIs to last-resort antibiotics, such as ciprofloxacin, poses a significant threat to patients worldwide as bacterial resistance and recurrence continue to increase [8,9]. These challenges underscore the need for innovative strategies that extend beyond traditional medicines to address UTIs effectively [10].

Recent studies have indicated the potential of human microbiome therapeutics as an alternative to current treatments for UTI [11]. Comprising communities of bacteria, archaea, fungi, and viruses, the human microbiome is essential for maintaining immune homeostasis and overall health [12]. By modulating these microbiotas with therapeutic agents, microbiome-based therapeutics have shown promise in treating various diseases, demonstrated by their ability to alter microbial composition—suppressing antibiotic-resistant pathogens while promoting beneficial bacteria—and improve functionality,

thereby restoring microbial balance and enhancing host health [13,14]. Clinical trials have documented significant reductions in UTI recurrence rates among patients treated with microbiome therapeutics compared to those receiving conventional antibiotic therapy [15]. One study highlighted the effectiveness of microbiome therapeutics in treating recurrent UTIs caused by extended-spectrum β -lactamase-producing *Klebsiella pneumoniae* [16]. These findings indicate that microbiome-based therapeutics can introduce beneficial functions to the human microbiome, thereby inhibiting infections [17].

Recent research outcomes have led the European Medicines Agency (EMA) and the U.S. Food and Drug Administration (FDA) to approve microbiome-based therapeutics as promising candidates for clinical trials and drug development [18]. Consequently, this review aims to summarize current research on microbiome therapeutics as a novel approach to UTIs, exploring their therapeutic potential, mechanisms of action, and future directions for translating these strategies into clinical practice.

THE HUMAN MICROBIOME: INSIGHTS INTO ITS ROLE IN HEALTH AND DISEASE

The human microbiome, comprising trillions of bacteria, fungi, viruses, and other microbes, plays a vital role in numerous bodily functions such as digestion, immune responses, and mood regulation [19]. Disruption of this delicate balance can lead to various conditions, including infectious and metabolic diseases [19]. As research increasingly reveals its role in multiple health issues, interest in the human microbiome has grown rapidly.

These findings have spurred research into understanding the human microbiome and its role in maintaining the balance between health and disease [20,21]. Serious exploration of the human microbiome began in the late 20th century, even though microbes had long been recognized within the human body [22]. Advances in molecular biology and sequencing technologies in the early 2000s enabled researchers to investigate these

microbial communities in greater detail [23]. A key milestone was the Human Microbiome Project (HMP), launched in 2007, which aimed to map microbial communities in healthy individuals and understand their significance for health and disease [24].

As scientific technologies progress, microbiome-based therapeutics have become a central focus within the scientific community for treating various human diseases [25]. Unlike conventional drug regimens that primarily address symptoms, human microbiome therapeutics target the root causes of diseases, offering a safe, reliable, and feasible approach with long-term health benefits.

THE UROBIOME: EMERGING INSIGHTS INTO URINARY TRACT HEALTH AND INFECTIONS

The urobiome, or the urinary tract microbiome, represents a recently recognized component of the human microbiome landscape [26]. Traditionally believed to be sterile in healthy individuals, urine's status led to the urinary microbiome's exclusion from the HMP until 2008 [27]. Recent evidence, however, has uncovered microbial communities within the urinary tract, fundamentally altering the perception of UTIs. Previously perceived purely from an immunological and microbiological standpoint, pathogens like *Escherichia coli* were identified as the main causative agents [28]. However, novel findings in urobiome research have unveiled a complex interaction between microbial communities and host immunity, challenging the conventional view.

Advances in sequencing technologies, including next-generation sequencing and 16S rRNA profiling, have significantly enhanced our ability to characterize the urinary microbiome, leading to the identification of a 'core' urobiome. However, most studies have concentrated on the female urinary microbiome due to the higher prevalence of urological disorders in women [29,30]. Discrepancies in urine sampling methods continue, particularly when voided urine samples are sus-

ceptible to contamination from the post-urethral region [31]. A recent study also underlined differences between bacterial communities in urine samples and those in bladder mucosal tissue samples, underscoring the importance of tissue sampling in conjunction with urine collection for a more accurate representation of the urobiome [32]. Research has further uncovered differences between male and female urobiomes. While both are predominantly characterized by the phylum Firmicutes, the male urobiome typically lacks *Actinobacteria* and *Bacteroidetes*, resulting in a simpler environment than the female urobiome [33]. The male urobiome features a relatively high abundance of *Corynebacterium*, a genus typically associated with the skin microbiome [34]. Other genera commonly found in both male and female urobiomes include *Lactobacillus*, *Streptococcus*, and *Staphylococcus* [35]. Profiling studies reveal that the urobiome can vary based on factors such as age, sex, hormonal status, and health conditions [35]. For instance, *Lactobacillus* species, typically prevalent in the urinary tracts of healthy premenopausal women, are thought to protect by reducing pH and inhibiting uropathogen growth [36]. Reduced *Lactobacillus* levels are associated with recurrent UTIs in postmenopausal women [37]. Similarly, imbalances in *Lactobacillus* levels in premenopausal women have been linked to urinary incontinence [38]. In addition, other frequently detected bacteria include *Gardnerella*, *Prevotella*, *Atopobium*, *Megasphaera* species, and various anaerobes [39]. Interestingly, the urobiome of men over 70 is more diverse than that of women of the same age, which may relate to an increased risk of prostate, kidney, and bladder diseases [40]. A cluster of proinflammatory bacteria, including *Streptococcus anginosus*, *Anaerococcus* spp., *Varibaculum cambriense*, and *Propionimicrobium lymphophilum*, is associated with urological infections [41,42]. Despite advances in taxonomic profiling, the impact of temporal factors on the urobiome remains poorly understood. These urinary microbiota play a critical role in modulating local immune responses, maintaining a healthy urobiome, and providing essential protection against UTIs

through interactions with host immunity [43].

COMPLEXITIES OF THE URINARY MICROBIOME IN UTIs

Recurrent UTIs are generally defined as 2 or more episodes within 6 months or 3 or more episodes within 1 year [44]. These infections recur after clinical resolution of a previous episode, manifesting either as reinfections or relapses, irrespective of treatment [45]. Reinfection implies that a different bacterial strain causes a UTI more than 2 weeks post-treatment. In comparison, relapse denotes the continued presence of the same strain, resulting in a UTI within 2 weeks of treatment [45]. Studies indicate that 50% to 80% of women will encounter UTIs at some point, with 20% to 50% suffering recurrent infections [46]. Specifically, 53% of women older than 55 and 36% of younger women report recurrent infections within one year [44]. Women with recurrent UTIs exhibit significantly higher rates of vaginal colonization by *E. coli*, *Enterococcus faecalis*, *Proteus mirabilis*, and *Klebsiella* compared to controls [45]. Uropathogenic *E. coli* (UPEC) is the most common cause of recurrent UTIs among these pathogens. In a study involving 250 hospitalized and community patients with a median age of 83.5 years, *E. coli* was found to be the most prevalent organism in UTI cases, with a higher incidence in females (83%) than in males (46%) [47].

Polymicrobial UTIs, caused by 2 or more bacterial species rather than a single pathogen, are particularly common in elderly populations, accounting for up to one-third of infections [48,49]. Commonly observed in polymicrobial UTIs are dual-species associations such as *E. coli* and *K. pneumoniae*, *E. coli* and *E. faecalis*, *K. pneumoniae* and *E. faecalis*, and *K. pneumoniae* and *P. mirabilis*, constituting 26%, 10%, 8.5%, and 7% of cases, respectively, especially in elderly patients (mean age, 73 ±10 years) [50]. Additional prevalent pathogens in polymicrobial infections include *Pseudomonas aeruginosa*, *P. mirabilis*, and *Staphylococcus aureus*, which are noted at rates of 23%, 25%, and 10.5% respectively [47]. Among

S. aureus strains confirmed as methicillin-resistant, 9 out of 10 were detected in polymicrobial samples, illustrating that *S. aureus* often occurs in mixed infections [47]. *E. coli* isolates from polymicrobial samples were also significantly more invasive than those from monomicrobial samples [47]. In polymicrobial infections, one pathogen may facilitate the growth of others; for example, in *E. faecalis* and *E. coli* coinfections, *E. faecalis* suppresses nuclear factor-kappa B signaling pathways in macrophages, reducing immune responses and facilitating *E. coli* colonization [51]. This underlines the complexity of treating infections involving multiple organisms compared to those caused by a single pathogen.

Biofilms, composed of microbial communities embedded in a matrix of extracellular polymeric substances, pose significant challenges in treating UTIs [52]. Urinary catheters, commonly made from latex or silicone, are particularly susceptible to biofilm formation on both their inner and outer surfaces by organisms such as *Staphylococcus epidermidis*, *E. faecalis*, *E. coli*, *P. mirabilis*, *P. aeruginosa*, and *K. pneumoniae* [53,54]. *E. coli* is particularly effective at forming biofilms on catheter surfaces, with biofilm formation rates among UPEC isolates reaching 84.6%–24.8% strong, 26.1% moderate, 44.6% weak, and 9.3% nonproducers [46]. *E. faecalis* can enhance the growth and persistence of *E. coli* biofilms under limited iron conditions, likely due to alternative iron acquisition strategies rather than direct competition [55]. Specific less common pathogens, such as *Delftia tsuruhatensis* and *Achromobacter xylosoxidans*, also form biofilms on inert surfaces, promoting *E. coli* adhesion and biofilm development [56]. Despite initial colonization by atypical species, *E. coli* often predominates in mature biofilms due to its faster growth rate and higher siderophore production [56]. *P. aeruginosa* is another potent biofilm former commonly found in polymicrobial biofilms. It can obtain nutrients from competitors through siderophore production and enhance its virulence by sensing peptidoglycan from other bacteria, allowing it to eliminate competitors [57].

LIMITATIONS OF CONVENTIONAL THERAPIES IN TREATING UTIs

Antibiotic resistance has become a significant public health concern, contributing to approximately 700,000 deaths annually, with projections indicating this number could rise to 10 million by 2050 if no new treatments are developed [58]. Although antibiotics remain the primary treatment for UTIs, alternative options are still limited. In a study of uropathogenic *E. coli* strains, the highest levels of antibiotic resistance were observed with ampicillin, tetracycline, nitrofurantoin, and chloramphenicol, with resistance rates of 74.6%, 64.9%, 6.2%, and 8.7%, respectively [46]. Bacteria isolated from mixed cultures show similar resistance levels to front-line antibiotics as those from monomicrobial cultures [47]. Additionally, *E. coli* isolates from mixed cultures demonstrate increased resistance to ciprofloxacin and trimethoprim compared to monomicrobial isolates [47]. Selecting an appropriate antibiotic regimen becomes more challenging when *E. faecalis* and *E. coli* coexist, as *Enterococcus* species exhibit inherent resistance to many antibiotics commonly used to treat UTIs [47].

Antibiotic treatment also risks causing dysbiosis, or an imbalance of normal microbiota, which is associated with various health issues, including obesity, allergies, and autoimmune diseases such as type 1 diabetes and rheumatoid arthritis. Dysbiosis may increase the abundance of pathogens, such as *Clostridioides difficile*, while significantly decreasing beneficial bacteria, like *Lactobacillus* [59]. Furthermore, antibiotics can reduce gut bacterial diversity, disrupting essential metabolic processes governed by the microbiota [59-61]. Frequent reliance on antibiotics increases the risk of resistance and may not address underlying issues, such as urobiome imbalances, leading to recurrent infections after initial treatment [62,63]. The limitations of conventional therapies—particularly given the rise of antibiotic-resistant bacteria and recurrent infections—highlight the urgent need to explore alternative or complementary treatment options.

THE POTENTIAL OF MICROBIOME THERAPEUTICS FOR UTI TREATMENT

Probiotic therapy utilizes beneficial microbes, typically bacteria or yeast, to restore the natural microbiota balance and enhance host health. Recently, probiotic therapy has gained interest as a promising approach for managing gastrointestinal disorders, various infections, the gut-lung axis, and uropathogens [64]. Probiotics exert their beneficial effects through several mechanisms, including competitive exclusion of pathogens, production of antimicrobial compounds (e.g., bacteriocins, hydrogen peroxide), modulation of immune responses, and maintenance of epithelial barrier integrity [65,66]. Among probiotics, *Lactobacillus* species produce lactic acid and hydrogen peroxide, which help eliminate uropathogenic *E. coli* by upregulating stress proteins and reducing biofilm formation in both enteric and genitourinary habitats [67-69]. Additionally, other *Lactobacilli* strains, including *Lactobacillus rhamnosus*, *Lactobacillus reuteri*, *Lactobacillus acidophilus*, and *Lactobacillus casei*, have shown potential in downregulating UPEC virulence factors, interfering with biofilm formation and reducing recurrent UTIs [70,71]. *Lactobacillus crispatus*, a well-studied strain, produces Lactin-V. This live biotherapeutic product has been evaluated in double-blind, placebo-controlled phase 2 trials for its effectiveness against UTIs and bacterial vaginosis [72,73].

In addition to probiotics, postbiotics—a heterogeneous mixture of cellular components and metabolites such as exopolysaccharides, peptidoglycan, bacteriocins, teichoic acids, and short-chain fatty acids (SCFAs)—have emerged as potential UTI treatments. Research suggests that postbiotics may benefit the host by modulating protective mechanisms, strengthening epithelial barriers, and influencing immune responses, potentially reducing UPEC reservoirs in the intestines [74]. The ribosomally synthesized peptide bacteriocins produced by probiotics are gaining attention. For instance, the probiotic strain *Lactobacillus gasseri* produces the bacteriocin gassericin E, demonstrating promising effects against

bacterial vaginosis, a condition that resembles UTIs [75]. Subtilisin, a cyclopeptide produced by *Bacillus subtilis* and *Bacillus amyloliquefaciens*, exhibits antimicrobial activity against various pathogens, including *Gardnerella* species, which can colonize the urinary tract [76,77]. Although bacteriocins are often unstable, bioengineering techniques are being explored to improve their stability and antimicrobial efficacy, potentially enabling their use in intravesical treatments or as engineered probiotics to inhibit uropathogens [78-80].

Asymptomatic bacteriuria (ABU), characterized by significant bacterial presence in urine without symptoms of UTI, is a focus of interest in UTI management. A notable strain associated with ABU is *E. coli* 83972 [81,82], first identified in a young girl who carried it for nearly 3 years without showing infection symptoms [83,84]. While *E. coli* 83972 resembles commensal strains, it is thought to have evolved from a uropathogenic ancestor within the *E. coli* B2 phylogenetic group, which includes UPEC strains [85,86]. Although it contains virulence factors such as colibactin and cytotoxic necrotizing factor 1, mutations like the loss of motility and absence of fimbriae decrease its virulence compared to symptomatic *E. coli* strains [82,85-87]. *E. coli* 83972 may reduce UTI risks by out-competing UPEC strains through bacterial interference. Possible factors include nutrient competition, gene acquisition, and biofilm formation inhibition, though it is not due to competition for attachment sites since *E. coli* 83972 lacks fimbriae [82,88]. The European Urology Guidelines endorse the clinical use of *E. coli* 83972 for intentional bladder colonization as a safe preventive measure [89]. Quorum-sensing inhibitors, which disrupt bacterial communication pathways essential for biofilm formation, represent a promising approach, and when combined with existing microbiome-based therapies, they could enhance therapeutic efficacy and overcome the limitations of traditional methods [88-91].

Microbiota transplantation is being investigated as a potential treatment for UTIs. Fecal microbiota transplantation (FMT) involves introducing stool from a healthy donor into a patient's gut and has demonstrated the po-

tential to restore microbial balance. Recent studies indicate that FMT therapy could help reduce recurrent UTIs by replenishing commensal bacteria in the urobiome. For instance, Tariq et al. [92] reported decreases in recurrent UTIs, increased antibiotic susceptibility, and reduced *E. coli* and *Klebsiella* levels following FMT treatment for recurrent *Clostridium difficile* infection (rCDI). Similarly, Biehl et al. observed a significant reduction in *Enterobacteriaceae* levels, from 8.3% to 0.5%, and an increase in *Lactobacillaceae* levels, from 0.5% to over 50%, within 84 days post-FMT in a 50-year-old female [93]. In a 93-year-old female, FMT reduced symptomatic recurrent UTIs and eradicated rCDI, with *Enterobacteriaceae* levels decreasing from 74% pre-FMT to 0.07% post-FMT [94]. FMT has also been shown to significantly reduce UTI frequency, from a median of 4 episodes before treatment to 1 episode post-FMT ($p=0.01$), and improve antimicrobial resistance patterns in *E. coli* and *Klebsiella* isolates. In contrast, patients treated with standard antibiotics showed no change in UTI frequency or resistance patterns, further emphasizing FMT's potential in managing recurrent infections [92]. The mechanisms underlying the effectiveness of microbiota transplantation in recurrent UTIs include restoring the competitive exclusion of uropathogens by commensal bacteria, enhancing the production of antimicrobial compounds such as bacteriocins and SCFAs, and modulating the host immune response to reduce chronic inflammation and epithelial barrier disruption [95]. The success of FMT in managing rCDI highlights the potential of microbial transplantation from other niches, such as vaginal microbiota transplantation, in treating not only bacterial vaginosis but also UTIs and other urological conditions [96]. Further research into urinary microbiota transplantation is warranted.

Unlike antibiotics, microbiome therapeutics that specifically target and inhibit only the causative pathogens without disrupting the native microbiome represent a promising field, with bacteriophages possessing strain-specific targeting properties showing particular potential for addressing uropathogens [97]. Phage thera-

py for UTIs often involves lytic proteins, phage cocktails, or combinations of phages with antibiotics [98]. For example, Sybesma et al. [99] examined the susceptibility of 9 urine-derived *K. pneumoniae* isolates to the lytic phage v_BR-KpS10, which lysed all isolates. Another study found that the lytic phage VB_ecoS-Golestan inhibited 56% of multidrug-resistant UPEC isolates, although its effectiveness is limited by a narrow host range and the potential for phage-resistant mutants [98,100]. Polyphage therapy, in which multiple phages are administered, has shown potential in reducing bacterial titers and demonstrated safety when delivered intravesically via catheter [101].

ADVANTAGES AND CHALLENGES OF MICROBIOME THERAPEUTICS IN UTI TREATMENT

Microbiome therapeutics offer several advantages over conventional drug regimens. Here, we reflect on some of these benefits. First, conventional treatments for UTIs contribute to issues such as antibiotic resistance, decreased chemotherapy effectiveness, and low drug specificity [11]. These challenges hinder the successful management of UTIs and increase public health risks as resistant strains become global, potentially raising healthcare costs due to associated complications. In contrast, microbiome therapeutics introduce a novel approach that addresses these limitations. A primary advantage of microbiome therapeutics is their capacity to restore the host's microbiome balance, tackling the root cause of the infection rather than merely the symptoms. Unlike conventional antibiotics, this strategy is less likely to induce resistance because it diminishes pathogenic bacterial overgrowth while encouraging the growth of beneficial bacteria [24]. Conventional treatments fail to distinguish between harmful and beneficial bacteria, whereas microbiome therapeutics can selectively target pathogenic strains, enhancing specificity. Moreover, they have fewer side effects than conventional therapies, making them as a safer, more reliable, and viable long-

term UTI management option. These therapies can also be personalized to suit individual microbiome profiles, offering more effective interventions aligned with a person's unique microbial ecosystem and potentially leading to improved health outcomes [102].

While advancements in microbiome science have unlocked new potential for using microbial therapeutics to treat UTIs, significant challenges remain. One major challenge involves navigating regulatory hurdles to ensure the safety and viability of these therapeutics. For instance, therapeutic bacteria may unintentionally escape their intended environment and colonize sites in or outside the body, posing a risk. Another concern is horizontal gene transfer between engineered microbes and native microbiota, which could lead to the spread of genetically modified DNA [103]. Therapeutic microbes might transfer antibiotic resistance genes to pathogenic bacteria, thereby exacerbating the problem of antibiotic-resistant infections. Additionally, maintaining the stability and viability of these live-organism products throughout manufacturing, storage, and distribution presents challenges. Regulatory bodies such as the FDA and the EMA have traditionally focused on chemically defined drugs or single-agent biologics [104]. Microbiome-based therapies, which do not fit these categories, complicate the evaluation of safety, efficacy, and quality control. Furthermore, establishing good manufacturing practices and quality standards for microbial products is difficult, as even minor variations in microbial composition can affect their effectiveness [105]. These challenges highlight the need for new regulatory frameworks to assess microbiome-based therapies accurately.

Another challenge for microbiome-based therapeutics is the difficulty of creating a “one-size-fits-all” solution due to the unique composition of each individual's microbiota [106]. Personalized medicine may offer a solution, but advanced diagnostic tools are required to rapidly and accurately assess each patient's microbial profile. A deeper understanding of factors that shape the microbiome and its interactions with the host is essential for advancing personalized medicine [107]. Developing

these therapies necessitates large-scale, high-resolution datasets that capture the dynamic nature of the microbiome across individuals and over time [108].

FUTURE PERSPECTIVES

The study of the urobiome, a relatively new and expanding field, has substantial gaps in our understanding of its role in health and disease. Although emerging evidence indicates the presence of a distinct microbiome in the urinary tract, the complexity and interactions within this microbial community remain largely unexplored [109]. Our understanding of UPEC, the primary pathogen responsible for UTIs, is minimal [110]. Despite considerable research on UPEC, the detailed mechanisms of its virulence factors and interactions with other urobiome microbes still need to be better understood [110]. Advanced 'omics' technologies, such as metagenomics, metabolomics, and proteomics, are crucial for deepening this understanding, though their application in urobiome research is still early. Bridging these knowledge gaps through improved study designs, optimized sample processing, and multiomics analyses should be prioritized in future research.

Another promising avenue is urinary microbiome transplantation (UMT), which could replicate the success of FMT used for rCDI [111]. UMT involves transferring the healthy urinary microbiome of a donor to a patient with UTIs or urinary dysbiosis to restore microbial balance [112]. Although still largely experimental, UMT has significant potential to provide long-term relief from recurrent infections without relying on antibiotics. As urobiome research and broader microbiome studies advance, commercializing microbiome-based therapies is anticipated to be essential in managing UTIs and associated complications.

CONCLUSIONS

The urobiome, once overlooked, is now acknowledged as a critical factor in the health and disease of the uri-

nary tract, especially regarding UTIs. Advances in scientific techniques have deepened our understanding of the diverse microbial communities within the urinary tract, elucidating their roles in both health and disease. Considering the limitations of conventional drug treatments for UTIs, there is an urgent need to develop alternative therapies that can more effectively manage UTIs and related complications. In this context, microbiome-based therapeutics offer a promising avenue, as they possess the potential to not only eradicate target pathogens but also to restore a healthy microbial ecosystem for long-term health advantages. Nevertheless, further comprehensive and in-depth research is necessary to create effective microbiome-based treatments for UTIs and their associated complications.

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