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REVIEW ARTICLE

Biofilms in Urological Infections: Mechanisms, Diagnostic Advances, and Innovative Management Strategies

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Abstract: Urinary tract infections (UTIs) remain one of the most prevalent infectious diseases worldwide, posing significant clinical and economic challenges. The formation of bacterial biofilms, particularly on indwelling urological devices, is a key factor contributing to the persistence, recurrence, and resistance of infections to conventional antibiotics. Biofilms exhibit complex architectures, altered bacterial phenotypes, and the presence of dormant "persister" cells, all of which limit drug penetration and compromise treatment efficacy. Recent advances in diagnostic approaches, including molecular assays, imaging techniques, and precision metagenomics, have led to improved detection of biofilm-associated pathogens and the ability to assess their pathogenic potential. Therapeutic innovations such as nanotechnology-based drug delivery systems, biofilm-inhibiting compounds, phage therapy, microbiome modulation, and AI-driven precision medicine show promise in overcoming traditional treatment limitations. These strategies emphasize patient-specific interventions and targeted antimicrobial approaches, which are crucial for reducing recurrence, minimizing resistance, and improving clinical outcomes. Integrating biofilm research into routine clinical practice, along with fostering interdisciplinary collaboration among clinicians, microbiologists, and biomedical engineers, is essential to advance diagnostics, therapeutics, and preventive strategies for biofilm-associated urological infections.

Keywords: Urinary Tract Infections, Biofilms, Catheter-Related Infections, Drug Resistance, Precision Medicine

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1. Introduction

Urinary tract infections represent some of the most frequently encountered infectious diseases worldwide, exerting a substantial impact on healthcare systems and patient well-being. Estimates suggest that more than 150 million individuals are affected annually, highlighting their widespread prevalence and underlining the considerable global burden. These infections occur across a spectrum of clinical contexts, ranging from community-acquired UTIs to healthcare-associated infections (HAUTIs), with catheter-related UTIs comprising a large proportion of the latter[1]. Importantly, UTIs account for a major share of outpatient consultations, with lifetime incidence rates reported as 50–60% among adult women, and with recurrence being common, especially in younger and elderly populations [2].

The long-term global trends reflect the persistence and rising challenge of these infections. Between 1990 and 2019, incident cases increased from approximately 252 million to more than 400 million, while mortality nearly doubled, disproportionately affecting older adults and high-income regions [3]. These epidemiological patterns underscore not only the high frequency of UTIs but also their significant clinical burden, including risks of hospitalization, reduced quality of life, and recurrent episodes that strain healthcare resources [2, 3].

Beyond clinical outcomes, UTIs impose a notable economic burden, particularly when antibiotic resistance is involved[4]. Recent cohort data indicate that resistant Escherichia coli infections are associated with 29% higher hospitalization costs and significantly longer lengths of stay compared with susceptible infections [5]. The rising incidence of resistant pathogens magnifies both direct healthcare expenditures and indirect societal costs, reinforcing the

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urgent need for effective prevention and management strategies.

Taken together, these findings underscore that urinary tract infections remain a widespread and persistent challenge with substantial clinical and economic consequences. Their high prevalence, increasing global burden, and escalating costs driven by antimicrobial resistance highlight the urgent need for sustained research efforts and targeted public health interventions.

Bacterial biofilms represent the predominant mode of life for many microorganisms and are recognized as multicellular, structured communities embedded within a self-produced extracellular polymeric substance (EPS). This matrix is typically composed of polysaccharides, proteins, lipids, and extracellular DNA, which provide structural stability and facilitate microbial survival in hostile environments [6]. Unlike planktonic bacteria, which exist as free-floating single cells, biofilm-associated bacteria demonstrate enhanced resilience, particularly against antibiotics and host immune responses, making them responsible for a substantial proportion of human infections [7, 8].

The formation of biofilms follows a multi-step process, beginning with initial adhesion to biotic or abiotic surfaces, followed by microcolony development, EPS production, maturation into three-dimensional architectures with water channels, and eventual dispersion of cells to initiate new biofilms [7, 8]. Regulatory mechanisms such as quorum sensing play a pivotal role in coordinating gene expression during biofilm development, further distinguishing biofilm populations from their planktonic counterparts [7].

Clinically, biofilms are defined not only by their physical properties, such as adhesion, size, and EPS encapsulation, but also by their distinct phenotypic and metabolic traits. These include altered gene expression profiles, the presence of dormant or "persister" cells, and physiological adaptations that enable survival under antimicrobial stress [9]. Importantly, biofilm communities are inherently heterogeneous, with spatial and temporal variability depending on bacterial species and environmental context. While laboratory and environmental biofilms have been extensively characterized, clinical biofilms exhibit distinct features that hinder their detection and eradication, reinforcing their role as a major challenge in the management of infectious diseases [9].

Bacterial biofilms play a central role in the pathogenesis and persistence of urinary tract infections and prostatitis, representing a significant challenge in urology. Uropathogenic Escherichia coli (UPEC), the most common causative agent of both community-acquired and hospital-acquired UTIs, exhibits a complex relationship between antimicrobial resistance and biofilm formation. Studies have shown that isolates with lower antibiotic resistance may compensate by forming stronger biofilms, enabling survival and recurrence despite treatment, emphasizing the importance of assessing biofilm-forming capacity during clinical management [10, 11].

Biofilm-associated infections are particularly problematic due to the enhanced antimicrobial tolerance of the bacterial communities within them. Persistent or dormant cells within biofilms exhibit reduced metabolic activity, further complicating eradication and contributing to relapses and chronic infections [12]. Moreover, biofilms formed on urinary catheters are a leading cause of hospital-acquired UTIs, accounting for a substantial portion of nosocomial Gram-negative bacteremia. This highlights the clinical relevance of biofilms as both virulence and resistance factors in urological practice [13].

Systematic reviews and meta-analyses have confirmed that biofilm-producing strains are significantly associated with multidrug resistance and adverse clinical outcomes, including persistence and higher morbidity, both in UTIs and bloodstream infections [14].The prevalence of biofilm formation in catheter-associated UTIs underscores the need to consider biofilms in prevention strategies, therapeutic planning, and infection control policies. Additionally, biofilms contribute to the recurrence of UTIs and prostatitis syndromes, making them a key factor in the long-term management of urological infections [12, 13]. Taken together, these findings show that understanding biofilm biology in the urinary tract is not merely academic; it is essential for improving treatment efficacy, preventing infection recurrence, and mitigating antimicrobial resistance, which are central goals in contemporary urological care.

This review aims to summarize current knowledge on biofilm biology in urological infections, highlight diagnostic and therapeutic challenges, and discuss emerging strategies for effective management.

2. Methods

Relevant literature was identified through a comprehensive search of PubMed, Scopus, and Web of Science databases covering publications from January 2000 to June 2025. The following keywords and Boolean combinations were used: "urinary tract infection" OR "UTI," "biofilm," "catheter-associated infection," "uropathogens," "nanotechnology," "phage therapy," and "precision medicine." Only peer-reviewed English-language studies, systematic reviews, and experimental papers addressing biofilm-associated urological infections were included. Reference lists of key articles were also screened to identify additional sources.

3. Results

3.1. Biofilm Biology and Pathogenesis

3.1.1 Biofilm Formation and Architecture (Initial Adhesion, Maturation, Dispersal)

Biofilms are complex, structured microbial communities that form on both biotic and abiotic surfaces, encased within a self-produced matrix of extracellular polymeric substances. This matrix, composed of polysaccharides, proteins, lipids, and extracellular DNA, provides mechanical stability, protection from environmental stresses, and enhanced antimicrobial resistance, making biofilm-associated infections challenging to treat [15, 16].

The process of biofilm formation is a dynamic, multi-step sequence beginning with initial adhesion, where planktonic bacteria attach to a surface using physical and biochemical mechanisms. Once adhered, bacteria proliferate and begin producing EPS, which promotes the maturation of the biofilm into a three-dimensional, heterogeneous structure with water channels for nutrient distribution and waste removal [16, 17]. During this stage, biofilm communities display coordinated behavior and resilience, often evading host immune defenses and conventional antimicrobial therapies [17].

Eventually, biofilms undergo dispersal, releasing cells back into the planktonic state to colonize new surfaces. This phase plays a crucial role in the spread of infection and persistence of microbial populations in both chronic and device-associated infections [17, 18]. Advanced imaging techniques have recently enhanced our understanding of biofilm architecture, revealing the spatial organization, microbial interactions, and matrix dynamics that underlie their robustness and resistance [16, 18, 19].

Overall, the structured architecture of biofilms, encompassing initial adhesion, maturation, and dispersal, is central to their role in chronic infections, nosocomial infections, and medical device-related complications. Understanding these stages is essential for developing effective strategies to prevent, control, and eradicate biofilm-associated infections.

3.1.2 Molecular and Genetic Regulation of Biofilm Development

Biofilms represent highly structured microbial communities encased within extracellular polymeric substances, which confer both resilience and persistence in clinical and environmental settings. Their development is tightly regulated at the molecular and genetic levels, enabling bacteria to transition from free-living planktonic states to sessile, multicellular communities.

Research on Pseudomonas aeruginosa has established it as a model organism for dissecting biofilm development. The regulatory processes governing adhesion, quorum sensing, and EPS production are critical for biofilm establishment and persistence. These pathways not only facilitate cell–cell signaling but also enhance bacterial tolerance to host immune defenses and antimicrobial agents, contributing to the development of chronic infections and resistance. Current investigations emphasize the lack of effective antibiotics targeting biofilm-specific mechanisms, underlining the need for novel inhibitors directed at enzymes, adhesion pathways, and quorum-sensing systems to disrupt these processes at different stages of biofilm formation [20].

The resilience of biofilms is largely attributed to molecular adaptations that confer antibiotic tolerance. Their structural complexity and altered gene expression profiles protect bacteria against conventional therapies, especially in device-related infections such as catheter- or implant-associated biofilms. This presents a significant clinical challenge, resulting in prolonged hospital stays and increased treatment costs. To counter these issues, novel molecular approaches have been developed, including nanoparticle-based drug delivery systems, enzymatic degradation of EPS, and advanced surface coatings that prevent microbial adhesion. These strategies represent a growing emphasis on integrating genetic and molecular insights into practical therapeutic innovations[21].

In addition, nanotechnology has emerged as a transformative field in disrupting biofilm dynamics. Engineered nanomaterials, such as multifunctional nanozymes, phage-mimetic structures, and microrobotic systems, have been shown to interfere with biofilm molecular pathways, enhance antibiotic penetration, and restore antimicrobial susceptibility. By directly modulating the genetic and biochemical regulation of biofilm formation, these cutting-edge strategies aim to dismantle biofilm structures and reduce multidrug resistance. The rational design of these nanomaterials highlights the potential of integrating molecular biology with engineering innovations to overcome the challenges posed by biofilm-associated infections [22].

In summary, biofilm development is a highly regulated molecular process involving genetic pathways that enable adhesion, communication, and resilience. Advances in understanding these regulatory mechanisms are now being translated into innovative strategies, ranging from quorum-sensing inhibitors to nanomaterial-based interventions, offering new hope for managing persistent biofilm-associated infections.

3.1.3 Host–Pathogen Interactions in the Urinary Tract and Biofilm-Associated Virulence Factors

Urinary tract infections represent one of the most prevalent bacterial infections globally, involving a variety of Gram-positive and Gram-negative pathogens. Among the most common are Escherichia coli, Enterococcus faecalis, Proteus mirabilis, Klebsiella pneumoniae, and Staphylococcus saprophyticus. These pathogens rely on the expression of

surface-associated virulence factors that mediate adhesion, invasion, and immune evasion within the urinary tract environment. The regulation of these proteins is not only critical for successful colonization but also provides a potential tool for distinguishing pathogen subtypes, thereby contributing to improved diagnostic approaches [23].

Recent advances have expanded our understanding of the host–pathogen interplay during UTI pathogenesis. Structural, microbiological, and immunological studies have highlighted how uropathogens adapt to the host milieu by deploying adhesins, toxins, and biofilm-associated factors that enhance persistence. These insights emphasize a shift away from conventional broad-spectrum antibiotics toward pathogen-specific therapeutics that target the molecular interface between host and microbe [24].

Biofilm formation, particularly in the context of indwelling urological devices such as double-J catheters, adds further complexity to these interactions. Strong biofilm producers such as E. coli and Staphylococcus aureus synthesize robust extracellular matrices that confer enhanced resistance to antimicrobial agents. Mixed microbial populations, including underrecognized genera like Bacillus, can promote synergistic biofilm development, thereby exacerbating infection severity and persistence. Understanding such polymicrobial interactions is therefore critical for improving management of catheter-associated UTIs [25].

Uropathogenic E. coli (UPEC) remains the primary agent of UTIs, relying on a wide array of virulence factors including fimbrial adhesins (FimH, PapG, CsgA), outer membrane proteins such as TosA, and motility structures like flagella. These determinants facilitate colonization and invasion despite host immune defenses, while also supporting biofilm maturation. Genetic diversity within UPEC populations, especially in high-risk lineages such as ST131, further contributes to antibiotic resistance and recurrence. The identification of these virulence factors has opened avenues for novel therapeutic strategies, such as vaccines targeting chimeric adhesin fusion proteins (FimH + CsgA + PapG), offering promise for reducing infection rates across diverse patient populations [26].

3.2. Clinical Relevance of Biofilms in Urological Infections

Urinary tract infections are among the most prevalent infectious diseases, and biofilm formation is a central factor in their persistence. Unlike planktonic bacteria, biofilm-associated pathogens establish chronic infections that are difficult to eradicate. Importantly, biofilm involvement is not limited to typical UTIs but also extends to male prostatitis syndromes, where microbial communities complicate treatment and contribute to relapse. In hospitalized patients, biofilms formed on urinary catheters represent a major clinical concern, as they are directly linked to a high proportion of Gram-negative bacteremia [13].

Indwelling urethral catheters provide an ideal surface for microbial colonization. Long-term use, particularly beyond 28 days, predisposes patients to colonization by species such as Proteus mirabilis, which form crystalline biofilms capable of blocking urine flow. This leads to encrustation, recurrent emergency interventions, and serious complications [27].Moreover, biofilm persistence on catheters explains why conventional antibiotic therapy often fails. Catheter replacement before urine collection has been recommended to improve culture accuracy and enhance therapeutic outcomes, yet no definitive preventive strategies currently exist [28].

Recurrent UTIs present another layer of complexity, as biofilm communities enable horizontal gene transfer, promote resistance, and orchestrate virulence gene expression. This dynamic environment not only ensures bacterial survival but also drives recurrence and chronicity of infections [29].

In high-risk patients, such as those undergoing radical cystectomy, biofilm-associated catheter infections are particularly problematic. Innovative approaches combining conventional antibiotics with antimicrobial peptides have shown promise in reducing biofilm biomass and viability, suggesting potential new strategies to prevent or manage these infections [30].

3.3. Diagnostic Challenges in Biofilm-Associated Urological Infections

3.3.1 Limitations of Conventional Microbiological Methods

Conventional microbiological approaches, particularly culture-based techniques, remain the cornerstone of diagnosing urinary tract infections. However, these methods face significant challenges when biofilm-associated infections are involved. Bacteria within biofilms exhibit altered phenotypes, including reduced metabolic activity, which limits their ability to grow under standard laboratory conditions. This often leads to underestimation of pathogen diversity or even false-negative results. Moreover, routine cultures lack the sensitivity to detect low-abundance or slow-growing organisms and cannot account for the polymicrobial nature of many biofilms in urological settings. As a result, reliance on these techniques frequently delays diagnosis and contributes to inappropriate antimicrobial therapy [31, 32].

3.3.2 Advanced Diagnostic Techniques

In response to the limitations of traditional methods, various advanced diagnostic strategies have been developed. Imaging approaches, such as confocal laser scanning microscopy and electron microscopy, provide valuable insights into biofilm architecture and cellular organization, although their translation to clinical practice remains limited [33]. Molecular techniques, including PCR, 16S rRNA sequencing,

and next-generation sequencing, allow for faster and more precise detection of biofilm-forming pathogens compared to cultures. Multi-omics technologies encompassing genomics, transcriptomics, proteomics, and metabolomics further enhance our ability to characterize biofilms at a systems level, offering opportunities to uncover genetic determinants of resistance and virulence [34-36]. Despite these advantages, significant challenges remain. These include high implementation costs, potential for sample contamination in molecular workflows, limited availability of standardized protocols, and variability in result interpretation across laboratories.

3.3.3 Biomarkers for Biofilm-Associated Infections

The search for reliable biomarkers represents an important step toward improving biofilm-related diagnostics. Several urinary biomarkers, including nucleic acid-associated, metabolomic, and lipidomic signatures, have been identified as potential tools to distinguish between uncomplicated and complicated UTIs [37]. These biomarkers may enable rapid, non-culture-based detection of infections, offering advantages in sensitivity and specificity. However, many remain in the investigational stage, and their clinical application requires further validation in large-scale studies. Integrating biomarkers with molecular and imaging technologies could eventually support more personalized approaches to managing urological infections linked to biofilms [34, 35, 37].

3.4. Antimicrobial Resistance and Treatment Challenges

Biofilm-associated infections in the urinary tract represent a major clinical problem due to their strong link with antimicrobial resistance and treatment failures. Biofilms fundamentally change the physiology of bacteria compared to their planktonic state, making them inherently more tolerant to conventional antibiotics. The extracellular matrix, low metabolic rates, persister cell formation, and efficient horizontal gene transfer within biofilm communities significantly reduce antibiotic penetration and facilitate the evolution of resistance mechanisms. These structural and functional characteristics, along with interspecies interactions in polymicrobial biofilms, contribute to the persistence and chronicity of infections despite antibiotic therapy [38].

Enterococcus species, which account for a significant proportion of urinary tract infections, highlight the seriousness of this issue. Clinical studies demonstrate that most Enterococcus isolates are capable of biofilm production and are simultaneously resistant to multiple antibiotics. In particular, strong biofilm producers exhibit extreme resistance patterns, leaving only a few therapeutic options such as linezolid and tigecycline. Furthermore, these isolates harbor biofilm-associated genes that correlate directly with both biofilm formation capacity and resistance levels. This connection underscores the clinical challenge of treating biofilm-associated infections, where conventional therapies frequently fail [39]. Adding to the complexity, low-dose or subinhibitory antibiotic therapies—commonly employed as prophylaxis can paradoxically worsen the clinical situation. Research indicates that such exposures enhance bacterial virulence by upregulating adhesins essential for urothelial colonization, strengthening biofilm formation, and promoting the establishment of intracellular reservoirs within host tissues. In animal models, subinhibitory treatment not only failed to reduce recurrence rates but also led to more severe and frequent reinfections. Collectively, these findings underscore the risks associated with prophylactic low-dose regimens in the management of recurrent urinary tract infections, as they may promote infection persistence rather than effectively suppress it [40].

From a broader clinical perspective, catheter-associated urinary tract infections further highlight the relationship between biofilm formation and antimicrobial resistance. In hospitalized patients, biofilm-producing E. coli and other uropathogens isolated from catheters showed markedly higher levels of resistance compared to non-biofilm producers. Quinolones were identified as particularly ineffective, while carbapenems and aminoglycosides retained some therapeutic activity. Importantly, the majority of biofilm-forming isolates exhibited multidrug resistance, creating significant treatment challenges and limiting available therapeutic options [41].

Taken together, these studies highlight the multifaceted challenges posed by biofilm-associated infections, encompassing both intrinsic resistance mechanisms embedded within biofilm architecture and clinical practices that may inadvertently worsen disease persistence. Collectively, this body of evidence underscores the urgent need to move beyond conventional antibiotic therapy and develop innovative strategies for the effective management and treatment of biofilm-related urinary tract infections.

3.5. Emerging Strategies for Management

Recent years have seen growing interest in novel strategies to overcome the persistent challenge of biofilm-associated infections, particularly those linked to urological complications. One promising avenue has been the discovery of biofilm-inhibiting compounds, which have shown potential in disrupting both early and established biofilms. These compounds, such as ethacridine, phenothiazine, and fluorene derivatives, not only impair bacterial viability within biofilms but also enhance the effectiveness of conventional antibiotics, suggesting their role as valuable adjuncts in treatment regimens [42].

Alongside chemical interventions, nanotechnology-based

approaches have gained significant attention for their ability to deliver antimicrobial agents more effectively to biofilm sites. Nano-delivery systems, including liposomes, dendrimers, nanogels, and metal–organic frameworks, offer targeted penetration of biofilm structures while minimizing off-target effects. Such nanosystems improve antibiotic concentration at infection sites, providing a more precise and efficient means of combating biofilm-related resistance [43, 44].
In parallel, microbiome modulation and probiotics are emerging as complementary strategies for urinary tract infection management. Advances in sequencing technologies have highlighted the importance of urinary microbiome dynamics, demonstrating that microbial imbalances contribute to infection onset and persistence. Microbiome therapeutics hold potential to restore balance and mitigate disease progression, although the field still faces regulatory and clinical translation challenges [45].
Another area of development is phage therapy, which has been systematically reviewed as a promising alternative for UTI treatment. Phages target specific uropathogens and have shown promising microbiological and preliminary clinical results in preclinical and limited pilot studies. Nonetheless, phage therapy offers a safe and potentially effective addition to the therapeutic arsenal against biofilm-associated and multidrug-resistant infections [46].
Collectively, these emerging strategies, ranging from novel biofilm inhibitors and nanotechnology-based delivery systems to microbiome-targeted interventions and phage therapy, highlight the breadth of innovative approaches under investigation. Together, they represent crucial steps toward overcoming the limitations of conventional antibiotic treatments in managing biofilm-associated urological infections. Recent advances in biofilm-targeted therapy are summarized in Table 1.

4. Discussion

4.1. Future Perspectives and Research Directions

Recent research on urinary tract infections and biofilms highlights the urgent need to bridge existing knowledge gaps and move toward integrated, personalized approaches in clinical practice. Experimental bladder models both in vitro and in vivo have played an important role in advancing the understanding of UTI pathophysiology. While in vitro models provide controlled environments for investigating specific mechanisms and testing interventions, in vivo models reflect disease manifestation and progression in living organisms. The introduction of advanced techniques, such as three-dimensional bladder organoids, further narrows the translational gap and creates opportunities for precision diagnostics and personalized therapies [47].
Despite these advances, significant challenges remain in the clinical management of UTIs. An international multidisciplinary expert panel identified major gaps in current guidelines, particularly regarding the classification of uncomplicated versus complicated UTIs. Divergences between guidelines, along with their complexity, can hinder practical implementation, especially in primary care. The panel emphasized the importance of individualized treatment decisions, physician education, and antimicrobial stewardship to improve patient outcomes [48].
In the diagnostic field, innovative technologies such as precision metagenomics are emerging as transformative tools. Unlike urine culture or PCR, this method identifies a broader spectrum of microorganisms while simultaneously classifying their pathogenic potential. Such approaches enhance diagnostic accuracy and could support more effective, targeted treatment strategies for complex UTI cases[49].
At the therapeutic level, addressing biofilm-associated antimicrobial resistance requires moving beyond conventional antibiotics. Current and emerging approaches target multiple stages of biofilm development, including adhesion, maturation, and persistence. These multifaceted strategies hold promise in overcoming the resilience of biofilm-related infections and reducing treatment failures[50].
Finally, the integration of precision medicine with artificial intelligence (AI) is paving the way for the future of infectious disease management. By analyzing multi-omic data including genomics, proteomics, and microbiomics, AI-driven models are being explored as emerging tools that may eventually support precision diagnostics and therapy once validated in larger clinical datasets. While this paradigm shift offers great potential, its success will depend on further research, ethical frameworks, and cross-disciplinary collaboration [51, 52].
The findings summarized in this review highlight biofilms as a central determinant of persistence, recurrence, and antimicrobial resistance in urological infections. While conventional diagnostics and antibiotics remain essential, they are insufficient when biofilm-associated mechanisms dominate disease progression. Emerging technologies such as precision metagenomics, nanotechnology-based therapeutics, and phage therapy represent a paradigm shift toward targeted and personalized management. However, clinical translation remains limited by regulatory, economic, and methodological barriers, emphasizing the need for standardized protocols and large-scale clinical trials.

5. Conclusion

This review highlights the critical role of biofilms in urinary tract infections, emphasizing their contribution to persistent, recurrent, and treatment-resistant cases. Evidence from recent studies demonstrates how biofilms impair antibiotic

Table 1: Emerging strategies for managing biofilm-associated urological infections, showing evidence level and limitations

Therapeutic Strategy	Stage of Development	Main Advantages	Key Limitations
Biofilm-inhibiting compounds(e.g., ethacridine, phenothiazine)	In vitro / early preclinical	Disrupts early biofilm formation; synergistic with antibiotics	Limited in vivo data
Nanotechnology-based drug delivery	Preclinical / pilot clinical	Improved drug penetration; targeted delivery	Cost, regulatory hurdles
Microbiome modulation / probiotics	Early clinical	Restores microbial balance; non-invasive	Variable efficacy; requires long-term validation
Phage therapy	Preclinical/limited clinical trials	Pathogen specificity; minimal dysbiosis	Narrow host range; regulatory uncertainty
AI-driven precision medicine	Conceptual / pilot	Personalized approach; integrates omics data	Requires large datasets, ethical validation

efficacy through mechanisms such as reduced drug penetration, altered bacterial phenotypes, and the presence of persister cells. Advances in diagnostic approaches including precision metagenomics, molecular assays, and imaging techniques offer promising solutions to overcome limitations of conventional microbiological methods. On the therapeutic front, innovative strategies such as nanotechnology-based delivery systems, anti-biofilm compounds, phage therapy, microbiome modulation, and precision medicine are emerging as valuable alternatives to traditional antibiotic regimens. From a clinical perspective, these findings underscore the urgent need to integrate biofilm research into daily practice, particularly in the management of catheter-associated infections and recurrent UTIs. The therapeutic importance lies in shifting from broad-spectrum, often ineffective treatments toward more tailored, patient-specific approaches that can reduce resistance, improve outcomes, and lower healthcare burdens.

Ultimately, addressing the challenges of biofilm-associated infections requires strong interdisciplinary collaboration. Microbiologists, clinicians, biomedical engineers, and data scientists must work together to translate experimental advances into clinical practice. By fostering cross-disciplinary partnerships, we can accelerate the development of effective diagnostics, personalized therapies, and preventive strategies, ensuring better patient care and long-term control of biofilm-related infections. Future research should prioritize the development of standardized diagnostic protocols, large-scale clinical trials for emerging therapeutics, and the integration of biofilm assessments into clinical guidelines. Practical measures such as routine evaluation of catheter biofilm risk, optimized antibiotic stewardship, and patient-specific prevention strategies are essential for improving clinical outcomes.

6. Appendix

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6.2. Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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6.4. Author's contributions

All authors were involved in the conception, drafting, and revision of the manuscript. All authors read and approved the final version of the manuscript.

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