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Review Article

Cationic Antimicrobial Peptides: Current Applications and Future Perspectives in Human Medicine

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Abstract

Cationic Antimicrobial Peptides (CAPs) represent a promising class of therapeutics in the fight against multidrug-resistant infections, offering a novel mechanism of action distinct from traditional antibiotics. These peptides, which exhibit broad-spectrum antimicrobial properties, are involved in immune modulation and tissue repair. CAPs, including defensins, cathelicidins, magainins, and synthetic analogs, have been studied extensively for their potential in treating a variety of infections, such as skin and soft tissue infections, pulmonary diseases, urinary tract infections, and medical device-associated infections. Despite strong preclinical data supporting their efficacy, clinical translation has faced challenges related to peptide stability, toxicity, and manufacturing costs. Ongoing clinical trials have yielded promising results, particularly for topical and localized applications, with peptides such as pexiganan, omiganan, and brilacidin showing encouraging outcomes in treating chronic wounds, catheter-associated infections, and oral mucositis. Moreover, recent advancements in drug delivery systems, such as inhalable formulations and nanoparticle encapsulation, are addressing issues of bioavailability and systemic delivery. However, systemic use remains a critical area of investigation due to concerns about peptide stability and potential adverse effects. This review explores the current state of CAP-based therapies, highlighting ongoing clinical trials, the challenges faced in their clinical integration, and their future perspectives in human medicine, particularly in addressing the growing threat of antimicrobial resistance.

Keywords: Antimicrobial Resistance; Antimicrobial Therapies; Biofilm; Cationic Antimicrobial Peptides (CAPs); Chronic Wounds; Clinical Trials, Drug Delivery Systems; Immunomodulation; Peptides; Peptide Stability; Pulmonary Infections; Skin Infections; Synthetic Peptides; Systemic Delivery

General Introduction to Cationic Antimicrobial Peptides (CAPs)

Cationic Antimicrobial Peptides (CAPs), also commonly referred to as Anti Microbial Peptides (AMPs), are a diverse group of small, positively charged peptides that play a crucial role in the innate immune defense of virtually all living organisms [1]. Typically composed of 12 to 50 amino acids, these peptides are characterized by a net positive charge at physiological pH and an amphipathic structure that allows them to interact with and disrupt microbial membranes. CAPs are evolutionarily conserved across species, underscoring their fundamental importance in host defense mechanisms [1,2]. CAPs are produced by a wide variety of organisms including humans, animals, plants, and even certain bacteria and fungi [1]. In humans, they are expressed by epithelial cells, neutrophils, and other immune cells, and are particularly abundant at sites of host–microbe interaction such as the skin, respiratory tract, and gastrointestinal mucosa. Some of the best-known human CAPs include defensins and cathelicidins, notably the peptide LL-37 [1,3]. These molecules act not only as antimicrobial agents but also as modulators of immune responses,

bridging the gap between innate and adaptive immunity. The growing interest in CAPs stems from their broad-spectrum activity against bacteria (both Gram-positive and Gram-negative), fungi, viruses, and even some protozoa [1,4]. Unlike conventional antibiotics, CAPs often kill microbes through membrane disruption and other mechanisms that are less prone to inducing resistance. This unique mode of action makes them attractive candidates in the fight against multidrug-resistant pathogens, which represent an escalating public health crisis worldwide.

Over the past two decades, extensive research has been devoted to characterizing the structure, function, and potential applications of CAPs. Their versatility includes not only direct antimicrobial activity but also anti-inflammatory, immunoregulatory, and wound-healing properties [1,4]. Despite these promising attributes, clinical translation of CAPs has been limited due to challenges such as peptide stability, toxicity at high concentrations, and cost of production. This article aims to provide a comprehensive overview of CAPs with a specific focus on their relevance to human medicine. We will examine their mechanisms of action, categorize the main types of CAPs under investigation, explore their clinical applications, review ongoing clinical trials, and discuss the challenges and future perspectives for their therapeutic use. The ultimate goal is to assess the viability of CAPs as next-generation antimicrobial agents in an era where antibiotic resistance poses a severe global threat.

Mechanisms of Action of Antimicrobial Peptides

Cationic Antimicrobial Peptides (CAPs) exhibit a range of mechanisms to eliminate or neutralize pathogenic microbes, with their primary mode of action targeting the structural integrity of microbial membranes [1]. Due to their amphipathic and cationic nature, CAPs preferentially bind to the negatively charged components of bacterial membranes, such as Lipo-Poly-Saccharides (LPS) in Gram-negative bacteria or teichoic acids in Gram-positive bacteria [1,3]. This electrostatic attraction facilitates the insertion of the peptide into the lipid bilayer, leading to membrane destabilization, pore formation, and ultimately cell lysis. Several models have been proposed to describe membrane disruption by CAPs, including the "barrel-stave," "carpet," and "toroidal pore" mechanisms [1,2]. In the barrel-stave model, peptides insert themselves perpendicularly into the membrane, forming a pore lined by the peptides. The carpet model suggests that CAPs cover the membrane surface and, upon reaching a threshold concentration, cause membrane disintegration in a detergent-like manner. The toroidal pore model is an intermediate mechanism where peptides induce membrane curvature, forming transient pores lined by both peptides and lipid head groups. Regardless of the exact mechanism, membrane perturbation leads to leakage of cytoplasmic contents and bacterial death [2,3].

Beyond their direct lytic action, many CAPs exert additional intracellular effects. After crossing the microbial membrane, some peptides can inhibit nucleic acid synthesis, protein synthesis, or enzymatic functions essential for microbial survival [4-6]. These secondary mechanisms may enhance the bactericidal efficacy of CAPs and reduce the likelihood of resistance development, as multiple bacterial targets are simultaneously affected. Notably, some CAPs also act synergistically with conventional antibiotics, increasing bacterial permeability and facilitating drug entry. CAPs are not only microbicidal but also play significant roles in modulating the host immune response. They can influence cytokine production, promote chemotaxis of immune cells, and enhance phagocytosis [4,5]. For instance, LL-37 has been shown to induce the release of Interleukin-8 (IL-8) and other pro-inflammatory mediators, while also exerting anti-inflammatory effects depending on the context and concentration. This dual role-combining direct antimicrobial activity with immune regulation-positions CAPs as multifunctional agents in host defense [3]. An important advantage of CAPs is their relatively low tendency to induce microbial resistance [7,8]. Because they target conserved and essential features of microbial membranes and functions, the evolutionary cost for pathogens to develop resistance is high. However, emerging evidence suggests that some bacteria can develop partial resistance through modifications of membrane charge, expression of proteases that degrade CAPs, or increased efflux. Understanding these resistance mechanisms is essential for optimizing CAP design and ensuring long-term efficacy.

Typology of CAPs Studied in Human Medicine

Cationic Antimicrobial Peptides (CAPs) encompass a structurally and functionally diverse group of molecules. In human medicine, CAPs are typically classified into families based on their origin, structural motifs, and amino acid composition. The most prominent classes include defensins, cathelicidins, magainins, bactenecins, and several synthetic or engineered analogs. Each class presents unique properties that influence its therapeutic potential, such as spectrum of activity, stability, and immunomodulatory capacity [1,6]. Defensins are among the most well-studied endogenous human CAPs and are divided into two major subtypes: α-defensins and β-defensins. These peptides are rich in cysteine residues, which form disulfide bridges that stabilize a β-sheet structure. α-defensins are primarily produced by neutrophils (e.g., HNP-1 to HNP-4), while β-defensins (e.g., hBD-1 to hBD-4) are secreted by epithelial cells [1,4,5]. These peptides display broad antimicrobial activity and are also implicated in immune signaling and chemotaxis [6]. Their relatively small size and stable structure make them attractive templates for drug design. Cathelicidins, particularly the human peptide LL-37, are linear α-helical CAPs with potent antimicrobial and immunomodulatory functions. LL-37 is the only cathelicidin identified in humans and is produced by

epithelial cells, neutrophils, and macrophages [1,2]. In addition to disrupting microbial membranes, LL-37 modulates inflammation, promotes wound healing, and neutralizes bacterial endotoxins. Its multifunctional nature has spurred the development of synthetic analogs with improved specificity and stability, such as OP-145 and GF-17 [2,3,5].

CAPs derived from other organisms have also attracted medical interest. Magainins, originally isolated from the skin of the African clawed frog (*Xenopus laevis*), are α-helical peptides that demonstrate broad-spectrum antimicrobial activity with low mammalian cytotoxicity. Similarly, bactenecins, found in bovine neutrophils, exhibit strong bactericidal effects against Gram-negative bacteria. These non-human peptides serve as important models for developing synthetic CAPs and peptidomimetics with enhanced pharmacological properties. To address limitations such as enzymatic degradation, narrow therapeutic windows, and toxicity, numerous synthetic and engineered CAPs have been developed [2-4]. Rational design approaches involve sequence optimization, incorporation of D-amino acids, peptide cyclization, and backbone modifications to improve stability and bioavailability. Peptidomimetics-molecules that mimic the biological activity of CAPs without being peptides-have also emerged as promising alternatives, offering increased resistance to proteolysis and lower immunogenicity. By studying native peptides and designing optimized derivatives, researchers aim to harness the therapeutic potential of CAPs while overcoming the pharmacokinetic and safety challenges that limit their clinical translation.

Clinical Applications Under Investigation or Development

The clinical potential of Cationic Antimicrobial Peptides (CAPs) has been increasingly explored in the context of infections that are difficult to treat with conventional antibiotics, particularly those involving multidrug-resistant organisms or biofilms. Their broad-spectrum antimicrobial activity and immunomodulatory functions make them attractive candidates for a range of therapeutic applications in human medicine Table 1. Several CAPs and their synthetic analogs are being developed for topical, systemic, and localized use in infections of the skin, lungs, urinary tract, and medical devices. Skin and soft tissue infections are among the most advanced targets for CAP-based therapies. Conditions such as infected burns, chronic ulcers, and atopic dermatitis offer a favorable setting for the topical application of peptides, bypassing systemic toxicity concerns. Synthetic peptides like Pexiganan (a magainin analog) have been developed for diabetic foot ulcers and have completed phase III clinical trials. Similarly, omiganan, a synthetic indolicidin analog, has been investigated as a topical agent for catheter-associated infections and skin conditions complicated by bacterial colonization. These peptides not only reduce microbial burden but also promote wound healing and modulate local inflammation.

In pulmonary infections, particularly in diseases like Cystic Fibrosis (CF) and hospital-acquired pneumonia, CAPs have shown promise due to their ability to function in mucus-rich environments and retain activity against biofilm-embedded pathogens. The cathelicidin LL-37, for example, is found in airway secretions and contributes to innate lung defense. Inhalable formulations of CAPs are under investigation to deliver the peptides directly to the site of infection, enhancing efficacy while minimizing systemic exposure. Experimental therapies include nebulized or dry-powder forms designed to combat Pseudomonas aeruginosa and other resistant strains prevalent in CF patients. Urinary and genital tract infections, especially recurrent or catheter-associated types, are another focus of CAP development. The acidic and protease-rich environment of the urinary tract poses formulation challenges; however, modified CAPs with enhanced stability have shown efficacy in preclinical models. Certain peptides also exhibit antiviral activity, making them candidates for treating Sexually Transmitted Infections (STIs), including those caused by Herpes simplex virus or HIV. For example, CAPs have been incorporated into vaginal gels and microbicides to provide local protection against both bacterial and viral pathogens.

A rapidly evolving area of research involves the prevention of infections associated with medical devices such as catheters, endotracheal tubes, and orthopedic implants. CAPs can be immobilized onto biomaterial surfaces to prevent bacterial colonization and biofilm formation. Surface coatings with peptides like LL-37 or synthetic analogs can confer antimicrobial activity while preserving biocompatibility. These approaches are particularly relevant in intensive care settings, where device-associated infections are a major source of morbidity and mortality. Collectively, these clinical applications highlight the versatility of CAPs across multiple domains of human medicine. Their capacity to address unmet therapeutic needs-particularly where resistance or biofilms render antibiotics ineffective-makes them important tools in the development of next-generation anti-infectives. However, successful clinical translation will depend on overcoming formulation, delivery, and toxicity challenges, which remain significant in systemic and long-term applications.

Application Area	Challenges	Examples of CAPs/Analogues	Therapeutic Use
Skin and Soft Tissue Infections	Topical formulation concerns for systemic toxicity- Wound healing promotion	Pexiganan (magainin analog)- Omiganan (indolicidin analog)	Diabetic foot ulcers- Infected burns- Chronic ulcers- Atopic dermatitis
Pulmonary Infections	Delivery through mucus-rich environments- Efficacy against biofilm pathogens	Cathelicidin LL-37- Nebulized or dry-powder CAPs	Cystic fibrosis (CF)- Hospital-acquired pneumonia- Pseudomonas aeruginosa
Urinary and Genital Tract Infections	Stability in acidic and protease-rich environments- Limited antiviral effectiveness	Modified CAPs for enhanced stability- Vaginal gels & microbicides	Recurrent or catheter-associated urinary infections- STIs (Herpes simplex, HIV)
Medical Device-Associated Infections	Preventing bacterial colonization on biomaterial surfaces- Biocompatibility preservation	LL-37- Synthetic CAP analogs	Catheters- Endotracheal tubes- Orthopedic implants

Table 1: Clinical potential of cationic antimicrobial peptides.

Ongoing Clinical Trials and Preliminary Results

Despite the strong preclinical evidence supporting the efficacy of Cationic Antimicrobial Peptides (CAPs), only a limited number have progressed to clinical trials [9-15]. However, the results of early-phase studies have been promising, particularly in topical and localized applications Table 2. These trials provide critical insights into the pharmacodynamics, safety profiles, and clinical efficacy of CAPs in human populations and help identify formulation and delivery challenges for systemic use [15]. One of the most studied CAPs in clinical development is pexiganan, a synthetic analog of magainin developed for the treatment of diabetic foot ulcers. In multiple phase II and III trials, pexiganan demonstrated comparable efficacy to oral antibiotics (e.g., ofloxacin) when used as a topical cream [10]. Although initial FDA approval was not granted due to lack of superiority, subsequent studies supported its safety and non-inferiority, leading to renewed interest in combination therapies or use in resistant infections. Pexiganan's broad-spectrum activity, including effectiveness against Methicillin-Resistant *Staphylococcus aureus* (MRSA), supports its potential as a topical antimicrobial for chronic wound care. Omiganan pentahydrochloride, a synthetic indolicidin derivative, has also been evaluated in clinical trials. It has undergone phase I and II studies for applications including prevention of catheter-associated infections, acne vulgaris, and rosacea [9-12]. In these studies, omiganan was generally well-tolerated and showed moderate efficacy in reducing microbial colonization and inflammatory symptoms. However, some trials reported variable outcomes, possibly due to challenges in peptide penetration and local bioavailability. These mixed results underscore the need for optimized formulations and dosing strategies to maximize therapeutic benefit. A newer class of synthetic CAPs, including brilacidin, has shown promise in both antimicrobial and anti-inflammatory roles [9-14]. Brilacidin has completed phase II trials for oral mucositis in cancer patients and for skin infections. It demonstrated favorable safety and efficacy profiles, with particular effectiveness against Gram-positive bacteria. Brilacidin's ability to modulate pro-inflammatory cytokines and its stability under physiological conditions have positioned it as a potential dual-purpose therapeutic agent, combining antimicrobial action with tissue protection.

CAP	Clinical Applications	Phase of Development	Preliminary Results	Challenges
Pexiganan	Diabetic foot ulcers	Phase II and III	Comparable efficacy to oral antibiotics (e.g., ofloxacin) in topical use.	Lack of superiority for FDA approval initially. Renewed interest in combination therapies for resistant infections.
Omiganan Pentahydrochloride	Catheter-associated infections, acne vulgaris, rosacea	Phase I and II	Moderate efficacy in reducing microbial colonization and inflammation.	Variable outcomes, challenges with peptide penetration and bioavailability.
Brilacidin	Oral mucositis (cancer), skin infections	Phase II	Effective against Gram-positive bacteria, good safety and efficacy profile.	Challenges with formulation, maintaining effectiveness in complex environments.
LL-37 and Derivatives	Inhalable formulations for respiratory infections (Cystic fibrosis, *Pseudomonas aeruginosa*, *Burkholderia cepacia*)	Early-phase trials	Efficacy in complex biological fluids and biofilms, good lung deposition and tolerability.	Delivery challenges, need for optimized inhalation formulations.
Systemic Applications (e.g., Sepsis, Bacteremia, Urinary Tract Infections)	Sepsis, bacteremia, resistant urinary tract infections	Preclinical and early clinical stages	No full regulatory approval yet. Investigations into novel drug delivery systems (e.g., nanoparticles, targeting ligands).	Concerns about peptide stability, potential toxicity, and safe systemic delivery.

Table 2: Ongoing clinical trials and preliminary results for cationic antimicrobial peptides.

Several ongoing clinical investigations are exploring inhalable peptide formulations for respiratory infections, especially in cystic fibrosis patients where multidrug-resistant Pseudomonas aeruginosa and *Burkholderia cepacia* pose serious treatment challenges [11-15]. Peptides such as LL-37 and derivatives are being incorporated into aerosolized delivery systems to directly target pathogens in the lungs. Early-phase trials are assessing lung deposition, tolerability, and microbial clearance, with initial findings suggesting that CAPs maintain efficacy in complex biological fluids and biofilms. Although most clinical efforts have focused on topical and localized infections, some systemic applications are under preliminary evaluation. For instance, systemic use of CAPs for sepsis, bacteremia, or resistant urinary tract infections remains an area of active investigation, albeit with caution due to concerns about peptide stability and potential toxicity [12,14]. Novel drug delivery approaches-such as encapsulation in nanoparticles or conjugation with targeting ligands-are being explored in preclinical and early clinical stages to enable safe systemic delivery. While no CAP has yet received full regulatory approval for systemic use, progress in formulation science and deeper understanding of their pharmacology may soon expand their therapeutic reach. Continued investment in clinical research, particularly for indications involving multidrug resistance and biofilm-related infections, is essential for realizing the full clinical promise of CAPs.

Challenges for Clinical Integration of CAPs

Despite their therapeutic potential, several significant obstacles hinder the widespread clinical use of Cationic Antimicrobial Peptides (CAPs) [16]. These challenges span biochemical, pharmacological, technological, and regulatory domains, each of which must be addressed to ensure successful translation from laboratory to bedside. Understanding and overcoming these barriers is critical to realizing CAPs as viable alternatives or adjuncts to conventional antimicrobial agents [17]. One of the foremost challenges is peptide stability. CAPs are inherently susceptible to enzymatic degradation by proteases present in biological fluids such as blood, saliva, or gastrointestinal secretions [18]. This rapid degradation limits their bioavailability and therapeutic half-life, especially for systemic applications. While local or topical administration can mitigate some of these issues, efforts to improve peptide stability-through D-amino acid substitution, peptide

cyclization, or formulation in protective carriers-are essential for broadening their use. Encapsulation in liposomes, hydrogels, or polymeric nanoparticles has shown promise in enhancing stability and sustained release [17-19].

Another major limitation is toxicity and immunogenicity. CAPs exhibit a delicate balance between antimicrobial efficacy and host cytotoxicity [18,19]. At high concentrations, many peptides can disrupt mammalian cell membranes, leading to hemolysis or tissue damage. Additionally, repetitive or systemic exposure to exogenous peptides may provoke immune responses or allergic reactions. Fine-tuning the amphipathic structure and net charge of CAPs, as well as applying targeted delivery systems, are strategies under investigation to minimize off-target effects and improve therapeutic indices [17]. Manufacturing and production costs also pose a substantial challenge. Unlike small-molecule antibiotics, which are relatively inexpensive to synthesize and scale up, peptide synthesis remains costly and technically complex [16, 18]. The requirement for high purity, stringent sterility, and quality control further increases production expenses. While recombinant DNA technologies and solid-phase peptide synthesis methods are evolving, affordability remains a key barrier to commercialization, particularly for low- and middle-income countries [18]. Economic feasibility will need to be addressed through process innovation and market incentives. Formulation and delivery present additional hurdles, especially for systemic or organ-specific applications. CAPs may interact non-specifically with serum proteins or cell surfaces, reducing their effective concentration at the target site [17-19]. Delivering CAPs to deep-seated infections, such as in the lungs, urinary tract, or bloodstream, requires sophisticated drug delivery systems that protect peptides until they reach their intended target. Routes of administration-including intravenous, inhalable, transdermal, and intravaginal delivery-each carry specific technical and pharmacokinetic challenges [18]. Successful formulations must balance bioavailability, tissue penetration, and patient compliance. Finally, regulatory and clinical development pathways for CAPs remain uncertain. As a relatively new therapeutic class, CAPs often do not fit neatly into existing regulatory frameworks, complicating approval processes. Clinical trial design must demonstrate not only efficacy and safety but also clear superiority or advantage over existing antibiotics, particularly in terms of resistance profiles or therapeutic outcomes [16,18]. Given the urgency of antimicrobial resistance, regulatory agencies may provide accelerated pathways or designations (e.g., orphan drug or fast-track status), but robust clinical data are still essential for approval. Addressing these obstacles is vital for translating the promise of CAPs into practical, effective therapies for infectious diseases in the 21st century.

Future Perspectives in Human Medicine

The future of Cationic Antimicrobial Peptides (CAPs) in human medicine appears promising, particularly in the context of mounting antimicrobial resistance and the urgent need for novel anti-infective agents Table 3 [20,21]. As scientific understanding deepens and technological tools evolve, several innovative strategies are emerging to enhance the clinical utility of CAPs. These advances focus not only on improving antimicrobial activity but also on expanding their role as modulators of host immunity, precision therapeutics, and agents in combination therapy [21,22]. One of the most significant areas of progress is the design of next-generation CAPs with enhanced stability, potency, and selectivity [23]. Techniques such as computer-aided peptide design, high-throughput screening, and machine learning are being employed to generate optimized sequences with desirable properties. Modifications such as D-amino acid substitution, cyclization, lipidation, and the incorporation of unnatural residues have already led to peptides with improved resistance to proteolytic degradation and reduced cytotoxicity [21,23]. These engineered CAPs, including peptidomimetics and hybrid molecules, are paving the way for highly tailored therapeutics suitable for systemic administration. CAPs also hold potential in the field of precision medicine, particularly when integrated with microbiome analysis and host genetic profiling [22]. Individual differences in microbiota composition, immune responses, and susceptibility to infections may influence how CAPs perform in different patients. In the future, CAP-based treatments could be customized based on patient-specific microbial ecology and inflammatory states, enhancing efficacy while minimizing adverse effects.

Future Direction	Description	Key Developments	Potential Applications
Next-Generation CAPs	Design of CAPs with enhanced stability, potency, and selectivity	Computer-aided peptide design- High-throughput screening- Machine learning techniques for optimized sequences	Systemic administration- Increased resistance to degradation and reduced cytotoxicity
Precision Medicine	Customization of CAP treatments based on patient-specific factors like microbiota and genetic profiling	Tailored CAP treatments based on microbiome and immune responses	Chronic infections (e.g., atopic dermatitis, cystic fibrosis)- Personalized therapeutic regimens
Combination Therapy	Combining CAPs with conventional antibiotics to overcome resistance mechanisms	CAPs enhance antibiotic efficacy by disrupting biofilms and increasing membrane permeability	Multidrug-resistant infections- ESKAPE pathogens (e.g., MRSA, P. aeruginosa)
Immunomodulatory and Anti-inflammatory Effects	Exploring CAPs' potential in modulating immune responses and inflammation	Enhanced cytokine release modulation- Influence on cellular signaling- Wound healing promotion	Autoimmune disorders- Cancer immunotherapy- Tissue regeneration
Advanced Delivery Platforms	Integration of CAPs into smart delivery systems for targeted, controlled release	Smart hydrogels- Stimuli-responsive nanoparticles- Implantable devices- Environmental trigger-based release	Targeted delivery for chronic wounds- Cancer therapies- Infection management

Table 3: Future perspectives for Cationic Antimicrobial Peptides in human medicine.

This approach could be particularly valuable in managing chronic infections or inflammatory conditions such as atopic dermatitis, inflammatory bowel disease, or cystic fibrosis [24]. Another promising direction is the combination of CAPs with conventional antimicrobials. CAPs can potentiate antibiotic efficacy by increasing membrane permeability or disrupting bacterial biofilms, thereby overcoming resistance mechanisms [20,23]. This synergy could allow for reduced dosages of traditional antibiotics, limiting toxicity and slowing the development of resistance. Combinatorial regimens may become a cornerstone of future treatment strategies for infections caused by multidrug-resistant organisms, particularly the so-called ESKAPE pathogens (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter species*) [15,23]. Beyond infectious diseases, CAPs are being investigated for their immunomodulatory and anti-inflammatory effects, which open new therapeutic avenues in non-infectious diseases. Their ability to modulate cytokine release, enhance wound healing, and influence cellular signaling cascades suggests applications in autoimmune disorders, cancer immunotherapy, and tissue regeneration [1,2]. For example, CAPs have shown promise in enhancing antitumor immunity and may serve as adjuvants in cancer vaccines or checkpoint inhibitor therapies. This functional versatility expands their relevance beyond antimicrobial therapy alone. Finally, the integration of CAPs into advanced delivery platforms-such as smart hydrogels, stimuli-responsive nanoparticles, and implantable devices-will likely transform how they are administered. These technologies enable targeted, controlled release in response to environmental triggers (e.g., pH, enzymes, infection markers), enhancing therapeutic precision and patient compliance [22,23]. As biotechnology continues to evolve, these platforms will facilitate broader clinical adoption of CAP-based therapeutics across a wide range of indications. While challenges remain, the progress made in understanding and harnessing CAPs has laid a strong foundation for their emergence as a novel class of bioactive therapeutics with broad clinical impact [24].

Conclusion

Cationic Antimicrobial Peptides (CAPs) represent a promising frontier in the ongoing battle against infectious diseases, especially in an era where antimicrobial resistance threatens the efficacy of conventional antibiotics. As naturally occurring molecules with broad-spectrum activity, CAPs offer a unique therapeutic profile that combines direct microbial killing with immunomodulatory functions. Their mechanisms of action-primarily membrane disruption and intracellular targeting-are distinct from those of traditional antibiotics and render them less susceptible to resistance development. Clinical interest in CAPs has expanded significantly over the past two decades, leading to the development of several synthetic and engineered analogs. Topical and localized applications, such as treatment for chronic wounds, skin infections,

and catheter-related biofilms, have shown the most clinical success to date. Ongoing trials of agents like pexiganan, omiganan, and brilacidin have demonstrated acceptable safety profiles and encouraging efficacy. Nonetheless, systemic use of CAPs remains limited by challenges such as enzymatic degradation, cytotoxicity at high concentrations, and formulation complexity.

These barriers are not insurmountable. Advances in peptide engineering, drug delivery technologies, and bioinformatics are creating opportunities to design more stable, selective, and efficacious CAP-based therapies. The development of peptidomimetics, conjugates, and targeted delivery systems is already broadening the potential applications of CAPs. Furthermore, the integration of CAPs into precision medicine frameworks and their use in combination with existing antibiotics may enhance treatment outcomes, particularly for multidrug-resistant infections and biofilm-associated diseases. The road to full clinical integration of CAPs will require interdisciplinary collaboration, sustained funding, and supportive regulatory pathways. Robust preclinical and clinical data, standardized evaluation protocols, and scalable manufacturing solutions are essential to translate these peptides from laboratory tools into routine medical treatments. Given the global health crisis posed by antimicrobial resistance, investment in CAP research is not only scientifically justified but also strategically imperative. In summary, Cationic Antimicrobial Peptides hold substantial promise as a new class of multifunctional therapeutics. Their ability to combat resistant pathogens, modulate immune responses, and integrate with emerging biomedical technologies positions them as key players in the next generation of anti-infective strategies. With continued innovation and clinical validation, CAPs may soon transition from experimental agents to essential components of modern medicine.

Conflict of interest: The author declares no conflict of interest.

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