Al-imad Journal of Humanities and Applied Sciences (AJHAS)
مجلة العماد للعلوم الإنسانية والتطبيقية
ISSN: 0000-0000
Volume 1 – Issue 1 – 2025
Pages 12-15

Antimicrobial Polymers: Mechanisms of Action and Applications in Combating Antibiotic Resistance

Mohamed Salem [1*], Ilyas Salem [2]
[1] Department of Biology, Faculty of Education, Bani Waleed University, Bani Waleed, Libya.
[2] Department of Chemistry, Faculty of Education, Bani Waleed University, Bani Waleed, Libya.
*Corresponding author: mhomar1988@gmail.com

البوليمرات المضادة للميكروبات: آليات العمل وتطبيقاتها في مكافحة مقاومة المضادات الحيوية

محمد سالم[1*]، الياس سالم[2]
[1] قسم الأحياء، كلية التربية، جامعة بني وليد، بني وليد، ليبيا.
[2] قسم الكيمياء، كلية التربية، جامعة بني وليد، بني وليد، ليبيا.

Received: 14-04-2025; Accepted: 28-06-2025; Published: 11-07-2025

Abstract:
Antimicrobial resistance (AMR) poses a catastrophic threat to global health, necessitating innovative alternatives to conventional antibiotics. Antimicrobial polymers (AMPs) have emerged as promising candidates due to their broad-spectrum activity, reduced resistance development, and multifunctionality. This review comprehensively examines the mechanisms of action of AMPs—including membrane disruption, intracellular targeting, and biofilm inhibition—and their applications in medical devices, coatings, wound dressings, and drug delivery systems. Challenges such as toxicity, environmental impact, and scalability are critically evaluated, alongside future directions for clinical translation. The integration of AMPs into antimicrobial stewardship strategies offers a viable pathway to mitigate AMR.

Keywords: Antimicrobial Polymers, Antibiotic Resistance, Mechanism of Action, Biofilm Inhibition, Medical Coatings, Drug Delivery.

الملخص
تُشكل مقاومة مضادات الميكروبات (*AMR*) تهديدًا كارثيًا للصحة العالمية، مما يستلزم بدائل مبتكرة للمضادات الحيوية التقليدية. برزت البوليمرات المضادة للميكروبات (*AMPs*) كمرشحات واعدة نظرًا لنشاطها واسع النطاق، وانخفاض تطور المقاومة، وتعدد وظائفها. تدرس هذه المراجعة بشكل شامل آليات عمل البوليمرات المضادة للميكروبات - بما في ذلك تمزيق الأغشية، والاستهداف داخل الخلايا، وتثبيط الأغشية الحيوية - وتطبيقاتها في الأجهزة الطبية، والطلاءات، وضمادات الجروح، وأنظمة توصيل الأدوية. يتم تقييم التحديات مثل السمية، والأثر البيئي، وقابلية التوسع بشكل نقدي، إلى جانب التوجهات المستقبلية للترجمة السريرية. يوفر دمج البوليمرات المضادة للميكروبات في استراتيجيات إدارة مضادات الميكروبات مسارًا فعالًا للتخفيف من مقاومة مضادات الميكروبات.

الكلمات المفتاحية: البوليمرات المضادة للميكروبات، مقاومة المضادات الحيوية، آلية العمل، تثبيط الأغشية الحيوية، الطلاءات الطبية، توصيل الأدوية.

Introduction

The relentless emergence and global dissemination of antimicrobial resistance (AMR) constitute a critical public health emergency (Salem & Lakwani, 2024). Contemporary epidemiological analyses, notably the comprehensive Global Burden of Disease Study, quantify the devastating human toll, attributing in excess of 1.27 million deaths directly to antibiotic-resistant bacterial infections on an annual basis (Edwards et al., 2019; Fong, 2023; Moriel et al., 2024). This mortality burden starkly underscores the accelerating inadequacy of conventional antimicrobial arsenals. When coupled with the substantial morbidity, prolonged hospitalizations, and escalating healthcare costs associated with treatment failures, this crisis has catalyzed an urgent, multidisciplinary imperative to discover and develop novel classes of antimicrobial agents capable of overcoming resistant pathogens(Salem et al., 2025).Among the most promising strategies being rigorously explored is the engineering and deployment of Antimicrobial Polymers (AMPs). These agents represent a distinct class of synthetic or naturally derived macromolecules specifically designed or modified to exhibit potent biocidal or biostatic activity against a broad

spectrum of pathogens, including bacteria, fungi, and viruses (Salem, 2024). Unlike many conventional, small-molecule antibiotics that often target specific intracellular processes (e.g., protein synthesis, DNA replication), many AMPs exert their primary antimicrobial effect through direct physicochemical interactions with microbial membranes. Mechanisms frequently involve electrostatic attraction to negatively charged microbial surfaces (driven by cationic charges on the polymer), followed by membrane insertion, permeabilization, and ultimately, catastrophic disruption of membrane integrity – a process less prone to rapid resistance evolution compared to single-target drugs.

Crucially, a core design principle and significant advantage of advanced AMPs lies in their inherent potential to inactivate or kill pathogens while simultaneously minimizing the selective pressures that drive the evolution and spread of resistance mechanisms. This resilience stems largely from the non-specific, multi-target mode of action often employed by these macromolecules, making it considerably more challenging for microbes to develop single-point mutations conferring broad resistance (Kadak & Salem, 2020). Consequently, antimicrobial polymers represent a highly active and innovative frontier in the ongoing battle against drug-resistant infections, offering a complementary or alternative approach to traditional antibiotic therapies Unlike small-molecule antibiotics, AMPs exhibit:

- **Multivalent interactions** with microbial membranes.
- **Reduced susceptibility** to resistance mechanisms.
- **Tailorable chemistry** for targeted applications.

This paper reviews AMP mechanisms, applications, and challenges in combating AMR.

2. Mechanisms of Action

AMPs employ diverse strategies to eradicate pathogens:

2.1 Membrane Disruption

Cationic polymers (e.g., quaternary ammonium compounds) electrostatically bind to anionic microbial membranes, inducing permeability and leakage(Carmona-Ribeiro & de Melo Carrasco, 2013).

2.2 Intracellular Targeting

Reactive oxygen species (ROS) generation: Conjugated polymers (e.g., polythiophenes) produce ROS under light, damaging DNA/proteins (Carmona-Ribeiro & de Melo Carrasco, 2013)

Enzyme inhibition: Phosphorus-containing polymers disrupt cell wall synthesis (Kadak & Salem, 2020)

2.3 Biofilm Inhibition

AMPs like chitosan penetrate extracellular polymeric substances (EPS), disrupting biofilm integrity (Aziz et al., 2023).

Table 1 Key Antimicrobial Polymer Classes and Mechanisms.

Polymer Class	*Example*	*Mechanism*	*Target Pathogens*
Quaternary Ammonium	Poly(4-vinyl-N-alkylpyridinium)	Membrane disruption	Gram+/Gram- bacteria
Chitosan Derivatives	N-Carboxymethyl chitosan	EPS degradation, membrane permeabilization	*Candida albicans*, *S. aureus*
Antimicrobial Peptides (Synthetic)	ε-Polylysine	Pore formation, proton motive force collapse	MRSA, *Pseudomonas*
ROS-Generating Polymers	Polythiophene-PEG	Photoinduced oxidative stress	Drug-resistant fungi

Results and discussion

3. Applications in Combating AMR

3.1 Medical Device Coatings

Catheters/implants: AMP-coated surfaces reduce biofilm formation by >90% (Karlsen, 2025).*Example*: Polyurethane functionalized with quaternary ammonium moieties inhibits *Staphylococcus epidermidis* colonization (Cheng, 2008).

3.2 Wound Dressings

Chitosan-polyvinyl alcohol hydrogels accelerate healing in diabetic ulcers by suppressing *P. aeruginosa* biofilms (Yuan et al., 2021).

3.3 Drug Delivery Systems

AMPs enhance antibiotic efficacy:

Poly(lactic-co-glycolic acid) (PLGA) nanoparticles co-loaded with ciprofloxacin and silver ions overcome *K. pneumoniae* resistance (Sartini et al., 2021).

3.4 Agricultural and Water Treatment

Cationic polymers in water filters reduce antibiotic-resistant gene transfer (Manoharan et al., 2023).

4. Challenges and Future Perspectives

4.1 Toxicity and Selectivity

Balancing microbial toxicity and mammalian cell safety remains critical. *Solution*: "Smart" polymers activated by microbial enzymes (e.g., β-lactamase)(Aytar Çelik et al., 2023).

4.2 Environmental Impact

Non-biodegradable AMPs (e.g., polyacrylates) accumulate in ecosystems. *Future Focus*: Biodegradable designs (e.g., polyhydroxy alkanoates; (Wang et al., 2022).

4.3 Scalability and Cost

High-purity synthesis limits clinical translation. *Emerging Approach*: Photo-polymerization for rapid production (Aziz et al., 2023)

Conclusion

Antimicrobial polymers represent a paradigm shift in AMR management. Their multifaceted mechanisms, adaptability across applications, and capacity to evade resistance mechanisms position them as essential tools in future antimicrobial stewardship. Interdisciplinary collaboration—spanning polymer science, microbiology, and clinical medicine—is vital to address toxicity and scalability barriers.

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