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Bacteriocins: A "Narrow-Spectrum" Biological Alternative to Traditional Chemical Antibiotics — Mechanisms, Applications, and Future Perspectives

Muthanna M. Bahlool [1*] ***Dhafar N. Al-Ugalili*** [2]

[1,2] Department of Molecular and Medical Biotechnology, College of Biotechnology, Al-Nahrain University, Baghdad, Iraq.

*Corresponding author: **Muthanna.mukdad.bio25@ced.nahrainuniv.edu.iq**

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Abstract

Bacteriocins are a new way to treat infections caused by bacteria through the use of narrow-spectrum antimicrobial agents that provide a biological alternative to standard antibiotics. The focus of this review article is to describe the modes of action, classifications, and applications for bacteriocins against uropathogenic Escherichia coli (UPEC), primarily as a result of the global epidemic of antimicrobial resistance (AMR). As of now, AMR was associated with an estimated 4.95 million deaths in 2021 alone, according to the 2024 Lancet global burden analysis due to bacterial pathogens that have become resistant to antibiotics. Yet the development of new antibiotics is very limited. Bacteriocins are ribosomally produced antimicrobial peptides derived from bacteria that provide narrow-spectrum antimicrobial action; this enables the targeted treatment of specific pathogens while preserving the normal functioning of the host commensal microbiota. This review selectively details the structure (Classes I–IV), mechanism(s) of action, and bacteriocin species (e.g., Class IIb microcins, which utilize a multifaceted and complex "Trojan horse" mechanism via siderophore receptors) utilized against UPEC. This report gives detailed attention to UPEC-associated urinary tract infections (UTIs) that are the most common bacterial infections on the planet, and how microcins can use UPEC iron-acquisition siderophore receptors as points of entry, while at the same time inhibit the production of siderophores and biofilms in UTIs. The ten areas of comparison for assessing the comparative advantages of bacteriocins over traditional antibiotics have been evaluated, including specificity of target organisms, compatibility with the microbiome, risk of resistance development, and inhibition of biofilm formation. Possible new translational approaches, such as engineered live biotherapeutics products (eLBP) and nanoencapsulation, have also been discussed. The body of evidence presented in this report demonstrates the scientific validity, biological complexity, and potential for bacteriocins to serve as transformational antimicrobial platforms for the future of therapeutics in the post-antibiotic era.

Keywords: Bacteriocins; Antimicrobial peptides; Uropathogenic *Escherichia coli*.

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Introduction

The emergence and global dissemination of multidrug-resistant (MDR) bacterial pathogens constitutes one of the most formidable public health challenges of the twenty-first century. The World Health Organization has unequivocally declared antimicrobial resistance a global health emergency, with the 2024 *Lancet* analysis estimating that approximately 4.95 million deaths were associated with bacterial AMR in 2021 — a single-year burden, not an annual recurring rate, of which 1.27 million were directly attributable to resistant infections — a burden that now surpasses that of HIV/AIDS and malaria combined.[1] Without decisive corrective interventions, AMR-associated mortality is projected to reach 10 million deaths annually by 2050.[2]

The number of new antibiotics in the clinical pipeline has not experienced meaningful investment or development for many years. The 2023 WHO antibacterial clinical pipeline analysis showed that only 12 of the 97 agents being studied for evaluation have met at least one of the innovation criteria. As a result of the continued stagnation in development, along with the rapid evolutionary adaptability of bacteria, there is an urgent need to explore new antimicrobial paradigms.

In Iraq, the antimicrobial-resistant infection burden is an immediate public health priority. Numerous studies conducted in Iraqi clinical settings have extensively documented MDR UPEC strains and their contribution to both community-acquired and hospital-acquired UTIs, with the rate of resistance to first-line agents being documented at greater than 60% in Karbala (Al-Mayahie & Al-Kuriashi, 2023) and comparable resistance patterns reported in Baghdad, Basra, and other governorates in parallel clinical surveys. These realities throughout the country create an essential need to identify and develop antimicrobial agents that are microbiome-preserving and targeted towards the treatments of these infections; therefore, developing such alternatives immediately becomes a matter of national clinical urgency.

Urinary tract infections (UTIs) represent the most prevalent bacterial infections encountered in both community and healthcare settings, affecting approximately 150 million individuals annually worldwide.[5] Uropathogenic *Escherichia coli* (UPEC) is responsible for more than 80% of community-acquired UTIs and over 50% of catheter-associated UTIs.[6] The virulence of UPEC is substantially mediated by its sophisticated iron-acquisition machinery — a network of siderophores including salmochelin, aerobactin, and yersiniabactin — that allow the bacterium to scavenge iron from host proteins in the iron-depleted environment of the urinary tract.[7] Notably, UPEC phylogroup B2 strains harbor siderophore-microcin gene clusters that provide both virulence traits and competitive advantages within the gut and urinary tract. This make their specific outer membrane machinery ideal therapeutic targets for the "Trojan Horse"mediated drug delivery.[8]

Bacteriocins — naturally produced ribosomally synthesized antimicrobial peptides — have emerged as scientifically compelling biological alternatives to chemical antibiotics. Their defining narrow-spectrum antimicrobial activity simultaneously constitutes their most distinctive clinical advantage: rather than broadly disrupting the human microbiome as broad-spectrum antibiotics do, bacteriocins target specific bacterial species or strains with high biochemical precision.[9]

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Despite the growing body of evidence on bacteriocins, a comprehensive synthesis that explicitly links their narrow-spectrum mechanistic advantages — particularly the siderophore receptor hijacking strategy — to precision therapeutic applications against UPEC in the framework of post-antibiotic era clinical strategy remains absent from the current literature. The present review addresses this knowledge gap by providing an evidence-based, mechanistically grounded, and clinically contextualized synthesis of bacteriocins as narrow-spectrum biological alternatives, with direct relevance to the UTI and AMR challenge in both global and Iraqi clinical contexts.

Literature Search Strategy

A structured search of PubMed/MEDLINE, Scopus and Web of Science databases was carried out to gather relevant literature from January 2019 to May 2026. The search terms used included "bacteriocins", "microcins", "colicins", "narrow-spectrum antimicrobials", "uropathogenic Escherichia coli", "UPEC virulence factors", "inhibition of siderophore production", "antimicrobial resistance" and "biological alternatives to antibiotics". Since 2022 is the most current year, it will offer the most clinical recent publications and therefore, will also take precedence; all other foundational pieces of literature have been retained where they were deemed substantively relevant either from a mechanistic or conceptual standpoint toward this current review.

Classification of Bacteriocins

Bacteriocins constitute a structurally and functionally heterogeneous family of antimicrobial peptides produced by a diverse range of Gram-positive and Gram-negative bacteria. Contemporary taxonomic systems are based on a combination of molecular weight, post-translational modifications (PTMs), biosynthetic gene cluster organization, mechanism of action, and producer organism phylogeny. The comprehensive classification of bacteriocins into four major classes, their representative members, and key biochemical characteristics are presented in Table (1).[10]

Table (1): Classification of Bacteriocins and Key Biochemical Characteristics

Class	Mol. Weight	PTM Status	Key Examples	Primary Mechanism	Heat Stability
Class I (Lantibiotics)	<5 kDa	Extensive (lanthionine)	Nisin, Mersacidin	Lipid II binding + pore formation	High
Class II (Non-modified)	<10 kDa	Minimal or none	Pediocin PA-1, Lacticin F	Membrane disruption	High
Class III (Large)	>30 kDa	None	Lysostaphin, Helveticin J	Cell wall lysis / enzymatic	Low
Class IV (Colicins)	25–80 kDa	None	Colicin E1, K, M, E7	Pore / DNase / RNase / Wall inhibit.	Moderate
Class IV (Microcins)	<10 kDa	Siderophore conjugation	MccH47, MccM, MccV	Trojan Horse / siderophore receptor	High

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Class IV encompasses two structurally and functionally distinct subgroups produced by Escherichia coli and related Enterobacteriaceae: (a) Colicins (25–80 kDa), large plasmid-encoded bacteriocins acting via pore formation, nuclease activity, or cell wall inhibition; and (b) Microcins (<10 kDa), small chromosomally or plasmid-encoded peptides modified with siderophore moieties enabling receptor-mediated entry. While some classification frameworks (Heilbronner et al., 2021; Reuben & Torres, 2024) treat these as entirely separate categories, the unified Class IV designation follows Darbandi et al. (2022) and Soltani et al. (2021), with the subgroup distinction clearly delineated herein.

Class I: Lantibiotics

Class I Type I bacteriocins, known as lantibiotics, possess lanthionine and methyl-lanthionine residues that are added to precursors through extensive post-translational modifications following ribosome synthesis of a peptide. These residues lead to the extraordinary conformational rigidity and thermal stability of the mature lantibiotic structure. Lantibiotics belong to two different types based upon their mechanism of action: the Type A lantibiotics (e.g., Mersacidin) are elongated and act via two mechanisms; binding to lipid II resulting in the formation of transmembrane pores. In contrast, the Type B lantibiotics (Mersacidin) exhibit a more compact structure and inhibit cell wall biosynthesis without the requirement for transmembrane pore formation. Nisin is produced by Lactococcus lactis, is the most studied and commercially utilized lantibiotic, is used as a food preservative (E234), and remains under pharmaceutical investigation.[11]

Class II: Non-Modified Antimicrobial Peptides

Class II Bacteriocins are a type of antimicrobial peptide that are linear and heat-stable and have not undergone any chemical modification. Class IIa (pediocin-like) bacteriocins have a highly conserved N-terminal sequence (YGNGVXC), and they can kill Listeria bacterium.12 Class IIb microcins can be modified by addition of catecholate siderophores during their biosynthesis, and they have exceptional therapeutic elegance because they utilize the siderophore receptors of UPEC to enter UPEC cells as described in more detail in later sections.[8]

Class III: Large Heat-Labile Bacteriocins

Class III Bacteriocins have a high molecular weight (>30 kDa) and are sensitive to heat. They have an antimicrobial effect through an enzyme mechanism. Class IIIa bacteriocins (bacteriolysins) act as murein hydrolases by degrading the peptidoglycan cell wall of target bacteria with enzymes. Class IIIb bacteriocins (non-lytic) disrupt membrane integrity but the details of these mechanisms are not fully known (e.g., Helveticin J).[10]

Class IV: Colicins and Microcins

Although unified under Class IV in this review, colicins and microcins represent two structurally and mechanistically distinct subgroups — differing fundamentally in molecular weight, biosynthetic pathway, and mode of antimicrobial action Colicins (25 - 80 kDa) and microcins (< 10 kDa) represent the standard narrow spectrum bacteriocins that are produced by Escherichia coli and Enterobacteriaceae that are closely related to E. coli and that are of directly clinical importance due to UPEC-associated UTIs. Colicins are encoded on plasmids and can act through a number of mechanisms: Colicin E1 and K cause

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the formation of inner membrane pores.[13] Colicin E7 & E9 cause the degradation of DNA; Colicin E3 causes hydrolysis of rRNA; and Colicin M inhibits peptidoglycan synthesis. Microcins use siderophore receptors to be taken into the affected cells, which accounts for their incredible specificity towards their target organism, which in this case is UPEC.[8]

Mechanisms of Action

Bacteriocins have many ways of acting on microbes and these have little in common with how traditional antibiotics work. However, this difference is important for clinical use in that bacteriocins target different receptors than traditional antibiotics do, thereby greatly reducing the opportunity for developing resistance to both types of drugs in the same organism..[14] The mechanisms of action of these antibiotics are: (i) disruption of the cell membrane; (ii) inhibition of cell wall biosynthesis; (iii) enzymatic degradation of nucleic acid; (iv) inhibition of protein synthesis (i.e. ribosomes); (v) interference with iron acquisition (e.g., by seizing iron-acquiring receptors) and (vi) destruction of biofilm formation. For an extensive summary of these mechanisms, refer to Table (2).

Table (2): Mechanisms of Action of Bacteriocins — Summary of Six Principal Antimicrobial Pathways (Adapted from Soltani et al., 2021; Telhig et al., 2020; Rutter et al., 2024; Massip & Oswald, 2020)

Mechanism	Bacteriocin Class	Primary Target	Cellular Outcome	Representative Examples
Membrane pore formation	Class I, II, IV (Colicins)	Cell membrane / Lipid II	Dissipation of PMF; ATP depletion; rapid cell death	Nisin, Colicin E1, K, Pediocin PA-1
Lipid II sequestration	Class I (Type B)	Cell wall precursor (Lipid II)	Inhibition of peptidoglycan biosynthesis	Mersacidin, Actagardine
DNA degradation (DNase activity)	Class IV (Colicins)	Chromosomal / plasmid DNA	Double-strand cleavage; irreversible cell death	Colicin E7, E8, E9
rRNA hydrolysis (RNase activity)	Class IV (Colicins)	16S ribosomal RNA	Translation inhibition; protein synthesis arrest	Colicin E3, E6
"Trojan Horse" siderophore entry	Class IV (Microcins)	FepA / Cir / FiU / IroN receptors	F_1F_o-ATP synthase inhibition; energy depletion	MccH47, MccM, MccV
Enzymatic cell wall lysis	Class III (Bacteriolysins)	Peptidoglycan / murein layer	Bacteriolysis; osmotic cell rupture	Lysostaphin, Zoocin A
Anti-biofilm disruption	Class I, II, IV	Biofilm matrix / Type I fimbriae	Prevention of UPEC adhesion and colonization	Nisin, MccM, Pediocin

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PMF = Proton Motive Force; F_1F_0 = mitochondria-homologous bacterial ATP synthase. Data synthesized from Soltani et al. (2021), Telhig et al. (2020), Rutter et al. (2024), and Massip & Oswald (2020).

Membrane Pore Formation and Disruption

The most prevalent mechanism among bacteriocins is targeted membrane disruption (Table 2, row 1). Pore-forming bacteriocins interact with specific membrane receptors or lipids to form ion-conducting channels that dissipate the proton motive force (PMF), leading to ATP depletion and rapid bactericidal death.[15] Critically, the pore-forming activity of many bacteriocins requires the initial interaction with lipid II — a highly conserved cell wall intermediate — providing an additional layer of target specificity and substantially reducing the frequency of spontaneous resistance emergence.[11]

Cell Wall Biosynthesis Inhibition

Several lantibiotics, such as Nisin and Mersacidin, are examples of bactericidal agents that act by high-affinity binding to lipid II and sequestering lipid II from transglycolases (table 2, row 2). The mechanism of action of these agents involves both the sequestering of lipid II and the formation of a pore in the bacterial cell membrane and may thus be analogous to that of vancomycin; however, since the structure of vancomycin is different, vancomycin-resistant VRE strains remain susceptible to Nisin, which is a significant clinical benefit.[11]

Enzymatic Nucleic Acid Degradation

Colicins E2, E7, E8, and E9 are enzymatic bacteriocins that translocate through the outer membrane via specific TonB-dependent receptor-translocator systems before degrading chromosomal DNA through DNase activity (Table 2, row 3). Colicins E3 and E6 target 16S ribosomal RNA, blocking protein translation (Table 2, row 4). Combinations of mechanistically distinct colicins demonstrably preclude the emergence of single-target resistance.[13]

The Trojan Horse Strategy: Siderophore-Mediated Entry

The most therapeutically innovative mechanism is the siderophore receptor hijacking strategy employed by Class IIb microcins (Table 2, row 5). In the iron-depleted urinary tract, UPEC dramatically upregulates siderophore receptors (FepA, Cir, FiU, IroN) to acquire iron for growth. Siderophore-microcins (MccH47, MccM) exploit this physiological dependency by mimicking natural siderophore-iron complexes via their post-translationally conjugated catecholate moieties.[8] Upon TonB-dependent receptor binding and subsequent translocation across the periplasm , the microcin payload disrupts inner membrane targets or directly inhibits bacterial the F^1F^0-ATP synthase complex, critically arresting cellular energy production. The elegance of this mechanism — using the pathogen's own iron-starvation response as the entry portal — confers inherent target specificity that no synthetic antibiotic has yet replicated.[8]

Iraqi journal of Bioscience and Biomedical
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Bacteriocins as Inhibitors of UPEC Virulence: Siderophore and Biofilm Targeting

UPEC-caused urinary tract infections (UTIs) showcase how narrow spectrum bacteriocins may be used as therapeutics. UPEC has many virulence factors like : adhesins (Type I fimbriae, P-fimbriae, curli), toxins (α-hemolysin, SPATE), biofilm-forming machinery, and iron-acquisition siderophores enabling UPEC to colonize, persist, and invade tissues in the severe environment of the urinary tract.[6]

Iron is an indispensable cofactor for bacterial replication, yet free iron concentrations in human urine and tissue are maintained far below the 10^{-6} M required for normal bacterial growth. To circumvent this iron scarcity, UPEC produces four structurally distinct siderophores — enterobactin, salmochelin, aerobactin, and yersiniabactin — each chelating iron with extraordinary affinity and transporting it back via specific outer membrane receptors.[7] Yersiniabactin, recently characterized as both a siderophore and a quorum-sensing autoinducer in UPEC, coordinates iron acquisition with population-level virulence behavior, representing a therapeutically significant emerging target.[16]

UPEC strains of phylogroup B2 harbor siderophore-microcin genomic islands encoding both siderophore biosynthetic genes and siderophore-modified microcin (MccH47, MccM) biosynthesis genes.[8] The iron-scarcity that drives UPEC siderophore receptor overexpression simultaneously increases microcin uptake efficacy — a mechanistic paradox with profound therapeutic implications: the pathogen's dominant virulence strategy becomes its primary vulnerability to microcin attack.

Apart from targeting the siderophore systems, bacteriocins also possess strong anti-biofilm action that is intimately tied to pathogenesis of chronic and recurrent urinary tract infections, as referenced in Table 3, row 7. Uropathogenic E. coli (UPEC) biofilms formed on uroepithelial surfaces produce intracellular bacterial communities that are resistant to traditional antibiotic treatment methods.[17] Bacteriocins have been shown in a number of research projects to alter the structure of biofilms, lessen their activity, and block the first step in the UPEC infection process, which is their adhesion and subsequent invasion into a host cell.[18]

The Narrow-Spectrum Paradigm: Bacteriocins versus Traditional Antibiotics

Because they are treated with clinical antibiotics, the difference between bacteriocins and the traditional antibiotic class carry profound clinical and microbiological implications that extend across three principal domains: spectrum management, microbiome preservation, and resistance mitigation. Broad-spectrum antibiotics target infections caused by both pathogenic (harmful to humans) and commensal (harmless) bacteria and cause well- documented health problems, such as Clostridioides difficile- associated diarrhea, fungal overgrowth and spread of resistance genes resulting from disruption of the microbiome.[19] In comparison, the narrow spectrum of activity exhibited by bacteriocins acts as a precision-based framework for antimicrobial activity that is in accordance with the evolving philosophy surrounding microbiome stewardship within the field of infection-related medicine. A detailed regulatory discussion regarding ten pragmatically germane clinical characteristics can be found in (Table 3) at the conclusion of this paper.

Iraqi journal of Bioscience and Biomedical
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Table (3): Comparative Analysis of Bacteriocins versus Traditional Chemical Antibiotics (Adapted from Soltani et al., 2021; Reuben & Torres, 2024; Vieco-Saiz et al., 2019)

Parameter	Bacteriocins	Traditional Antibiotics
Origin	Biological — ribosomally synthesized	Chemical or semi-synthetic
Spectrum of Activity	Narrow — species/strain specific	Broad — multiple genera affected
Microbiome Impact	Minimal — commensals preserved	Significant dysbiosis documented
Resistance Risk	Lower but not absent — multi-target mechanisms reduce spontaneous resistance frequency; receptor loss (e.g., FepA, BtuB) documented but rare	High — widespread global resistance
Host Cell Toxicity	Low — generally non-toxic to eukaryotes	Nephro-/hepatotoxicity reported
Mechanism Diversity	Pore, wall inhibit., DNase, Trojan Horse	Limited classes, shared targets
Biofilm Inhibition	Strong evidence across multiple studies	Limited biofilm penetration
Cross-resistance Risk	Rare — novel target sites	Frequent intra-class cross-resistance
Regulatory Status	Nisin approved (GRAS); others in pipeline	Established and well-regulated
Production Scalability	Currently challenging — improving rapidly	Standardized industrial processes

Production Pipeline and Clinical Translation

The process of taking bacteriocins discovered in laboratories and translating them into clinical use is done through a defined multi-step development pipeline. Each step has specific and unique technical issues that can be overcome as a result of recent technological developments related to biotechnology. The five step pipeline (from isolation of bacteria to the delivery of products to patients) is outlined in Table (4) and gives a clear direction or “roadmap” of how to take something from a research lab to clinical practice.

Table (4): Five-Stage Bacteriocin Development Pipeline: From Bacterial Isolation to Clinical Translation (Authors’ synthesis based on Darbandi et al., 2022; Rutter et al., 2024; Soltani et al., 2021)

Stage	Key Procedures	Primary Outcome / Goal
Stage 1 Isolation & Screening	Commensal and probiotic strain isolation; zone-of-inhibition screening; ABU isolate collection; bacteriocin gene cluster identification	Identification of high-yield, clinically relevant bacteriocin-producing candidates
Stage 2 Production & Extraction	Fermentation optimization; cell-free supernatant preparation; ammonium sulfate precipitation; initial concentration	High-yield, crude bacteriocin-containing fractions suitable for downstream purification

Iraqi journal of Bioscience and Biomedical
Published Online First: 30 / June /2026.
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Stage	Key Procedures	Primary Outcome / Goal
Stage 3 Purification & Characterization	Ion-exchange chromatography; gel filtration (Sephadex G-100); reversed-phase HPLC; LC-MS/MS structural analysis	Purified bacteriocin with confirmed molecular identity, purity, and structural integrity
Stage 4 In vitro & In vivo Testing	MIC/MBC determination; biofilm inhibition assays; siderophore suppression testing; cytotoxicity evaluation; animal model infection studies	Validated antimicrobial efficacy, safety profile, and mechanism confirmation
Stage 5 Clinical Translation	Engineered live biotherapeutic products (eLBPs); nanoencapsulation formulation; Phase I–III clinical trials; regulatory submission (FDA/EMA)	Clinically approved, scalable bacteriocin-based therapeutic for human use

ABU = Asymptomatic Bacteriuria; HPLC = High-Performance Liquid Chromatography; LC-MS/MS = Liquid Chromatography–Tandem Mass Spectrometry; eLBPs = Engineered Live Biotherapeutic Products; MIC = Minimum Inhibitory Concentration; MBC = Minimum Bactericidal Concentration

Engineered Live Biotherapeutic Products (eLBPs)

Among the most transformative developments in bacteriocin translation is the engineering of live biotherapeutic products — non-pathogenic bacterial chassis, typically probiotic strains, genetically programmed to produce and secrete bacteriocins in situ at the site of infection[9]. A platform was developed for the modular bacteriocin secretion using non-pathogenic Escherichia coli as the delivery vehicle. This enabled targeted delivery of antimicrobial agents against Enterococcus faecalis and E. faecium, and was validated as proof of concept through the demonstration of the efficacy of this approach using a controlled experimental system.[9] This platform is very important for use in the urinary tract due to its potential for direct transvaginal delivery of UPEC-inhibiting strains of microcins that would inhibit the growth of UPEC and their iron-chelating compound (siderophore) production within the urinary tract microenvironment.

Nanoencapsulation and Formulation Strategies

Bacteriocins that are not formulated have a key limitation of being degraded by proteases in biological settings. There are several nanostructured delivery systems (liposomes, nanoparticles made from chitosan, and polymeric nanocarriers) that can significantly improve the stability of bacteriocins, extend their biological half-lives, and provide control over their release.[21] Bacteriocin-nanoconjugate formulations have been shown to enhance the antimicrobial effectiveness against MDR pathogens and reduce the effective dose required for treatment; therefore, this is an exciting emerging area of development with great potential for the clinic.[22]

Challenges and Future Perspectives

While bacteriocins have an ideal biological characteristic, there are significant barriers to their use as a therapeutical tool in the clinic. The production of bacteriocins still presents a major challenge: the

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production of therapeutically active amounts of purified bacteriocin through the multi-step pathway (as illustrated in Table (4)) is both technically difficult and too expensive for pharmaceutical production.[23]

Bacteriocin resistance, while occurring rarely compared to antibiotic resistance, is still a major factor to consider. Resistance in Gram-positive bacteria may occur by changing the anionic charge of the surface, or by utilizing ABC transporters as efflux pumps. In E. coli, colicin resistance usually arises from the loss or mutation of outer membrane receptor proteins (i.e., BtuB, OmpF, and FepA). Because bacteriocins interact with multiple cellular targets at once, the probability of spontaneous resistance development is greatly diminished when compared with single target antibiotics; use of combination bacteriocin strategies can better decrease the ability of bacteria to develop resistance to this class of antimicrobial agents.[24]

In most countries, there is no defined regulatory framework for bacteriocin-based treatments, creating barriers to translation. An exception to this is nisin, which has GRAS status from the U.S. FDA as a food additive, but has yet to receive marketing authorization as a treatment for human infections. Moreover, developing standard analytical methods to measure bacteriocins' identity, purity, potency, and stability, which would be comparable to existing pharmacopoeial monographs for conventional antibiotics, is a critical regulatory need for the field.[11]

In the future, the coming together of synthetic biology, structural genomics and peptide design through artificial intelligence means that we will now have ways to develop next generation bacteriocins, with ideal characteristics such as: better spectra control; resistant to proteases; enhanced ability to penetrate (tissue) sites; and specific receptors. The use of machine learning to predict structure activity relationships enables the rational development of bacteriocin analog(s) for use in applications that would not be possible if only using natural materials.[9] Combining discovery through metagenomics of new biosynthetic gene clusters for bacteriocins from less well-studied ecological niches will represent perhaps the most promising area of growth in terms of expanding our current therapeutic capabilities based on the use of bacteriocins.

Conclusions

In this narrative review, three main points are drawn from the collection of evidence. Firstly, bacteriocins are scientifically established (research or experiments have been performed that back their claims) and have a very sophisticated biological mechanism of action. Their many mechanisms of action produce narrow-spectrum antibacterial activity (described further in Table 2); the narrow spectrum of bacteriocins provides a distinct clinical advantage when compared to conventional broad-spectrum antibiotics regarding their microbomic stewardship potential. Secondly, the Trojan Horse mechanism of siderophore receptor-mediated targeting used by Class IIb microcins against UPEC is an elegant way to target antimicrobial activity (mechanism) for the treatment of recurrent UTI in patients; therefore, Class IIb microcins would be both a scientifically valid use of microcin as a potential therapeutic for this common clinical issue in Iraq and a clinically reasonable option for treating recurrent UTI in patients suffering from recurrent UTI globally. Thirdly, the convergence of bioengineering, nano-encapsulation and emerging

liquid bandages has drastically changed the path to the final validation of bacteriocins, from scientific inquiries to an imminent, viable therapeutic in practice (please see Table 4).

The mechanistic diversity of bacteriocins provides a multi-target profile that intrinsically suppresses resistance emergence and offers mechanistic novelty unavailable in the existing antibiotic arsenal. Resistance to bacteriocins, while documented, develops at substantially lower frequencies than resistance to conventional antibiotics, as evidenced by the comparative analysis in Table (2), and combination bacteriocin strategies reduce this risk further.

It must be explicitly acknowledged that, to date, no bacteriocin-based therapeutic has received regulatory approval for the treatment of human urinary tract infections. The clinical directions outlined below therefore represent evidence-based future priorities rather than ongoing or imminent programs. Future research should prioritize four strategic directions:: (i) development of scalable, cost-effective fermentation and purification processes to overcome the production yield bottleneck; (ii) establishment of international regulatory frameworks and pharmacopoeial standards for bacteriocin-based pharmaceuticals; (iii) rigorous pre-clinical and, where safety data permits, Phase I clinical trial programs to evaluate the safety and tolerability of intravesical microcin delivery for recurrent UPEC-mediated UTIs — recognizing that this remains a translational aspiration pending regulatory pathway development (iv) integration of artificial intelligence and genomics-driven discovery platforms to expand the known bacteriocin repertoire from underexplored environmental and clinical microbial ecosystems.

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Author's Declaration

The authors declare no conflict of interest. This review paper was conducted in accordance with established academic and ethical research standards. No primary patient data or biological specimens were involved in the preparation of this review.

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