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Case Study

Strategies for Combating the Global Health Threat of Antibiotic Resistance: Novel Therapeutics and Combination Approaches

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ABSTRACT

Background: Antibiotic resistance represents one of the most pressing global public health crises of the 21st century. The increasing prevalence of multidrug-resistant (MDR) bacterial pathogens has significantly reduced the clinical efficacy of existing antimicrobial therapies, resulting in prolonged hospitalizations, increased healthcare costs, and higher morbidity and mortality rates.

Objective: This review critically examines the molecular mechanisms underlying antibiotic resistance and explores emerging therapeutic strategies designed to overcome resistance and restore antibiotic efficacy.

Methods: A comprehensive analysis of recent scientific literature was conducted to evaluate advances in antimicrobial discovery, resistance-modifying strategies, host-directed therapies, and combination approaches.

Results: Resistance mechanisms include enzymatic drug inactivation, target modification, efflux pump overexpression, permeability alterations, and horizontal gene transfer. Emerging interventions such as quorum-sensing inhibitors, bacteriophage therapy, antimicrobial peptides, nanobiotics, CRISPR-Cas systems, immunotherapeutic agents, and photodynamic therapy demonstrate promising potential in combating resistant pathogens.

Conclusion: Although innovative strategies offer hope, challenges including regulatory barriers, economic limitations, and potential resistance evolution persist. A multidisciplinary, globally coordinated approach integrating antimicrobial stewardship, novel therapeutics, and policy reforms is essential to mitigate the antibiotic resistance crisis.

Keywords: Antibiotic resistance, multidrug resistance, bacteriophage therapy, CRISPR-Cas systems, antimicrobial peptides, nanobiotics, quorum sensing.

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INTRODUCTION

Antibiotic resistance has emerged as one of the most pressing threats to global public health (1,11). According to the World Health Organization, antimicrobial resistance ranks among the top global health concerns (1).

The discovery of penicillin by Alexander Fleming in 1928 revolutionized infectious disease treatment (8). However, the subsequent emergence of multidrug-resistant (MDR) organisms such as *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, and *Acinetobacter baumannii* has significantly compromised therapeutic efficacy (9,38).

The global burden of antimicrobial resistance was estimated to be directly responsible for 1.27 million deaths in 2019 (2). The overuse and misuse of antibiotics in healthcare and agriculture are major drivers of resistance development (4,11).

A Brief Antibiotics History

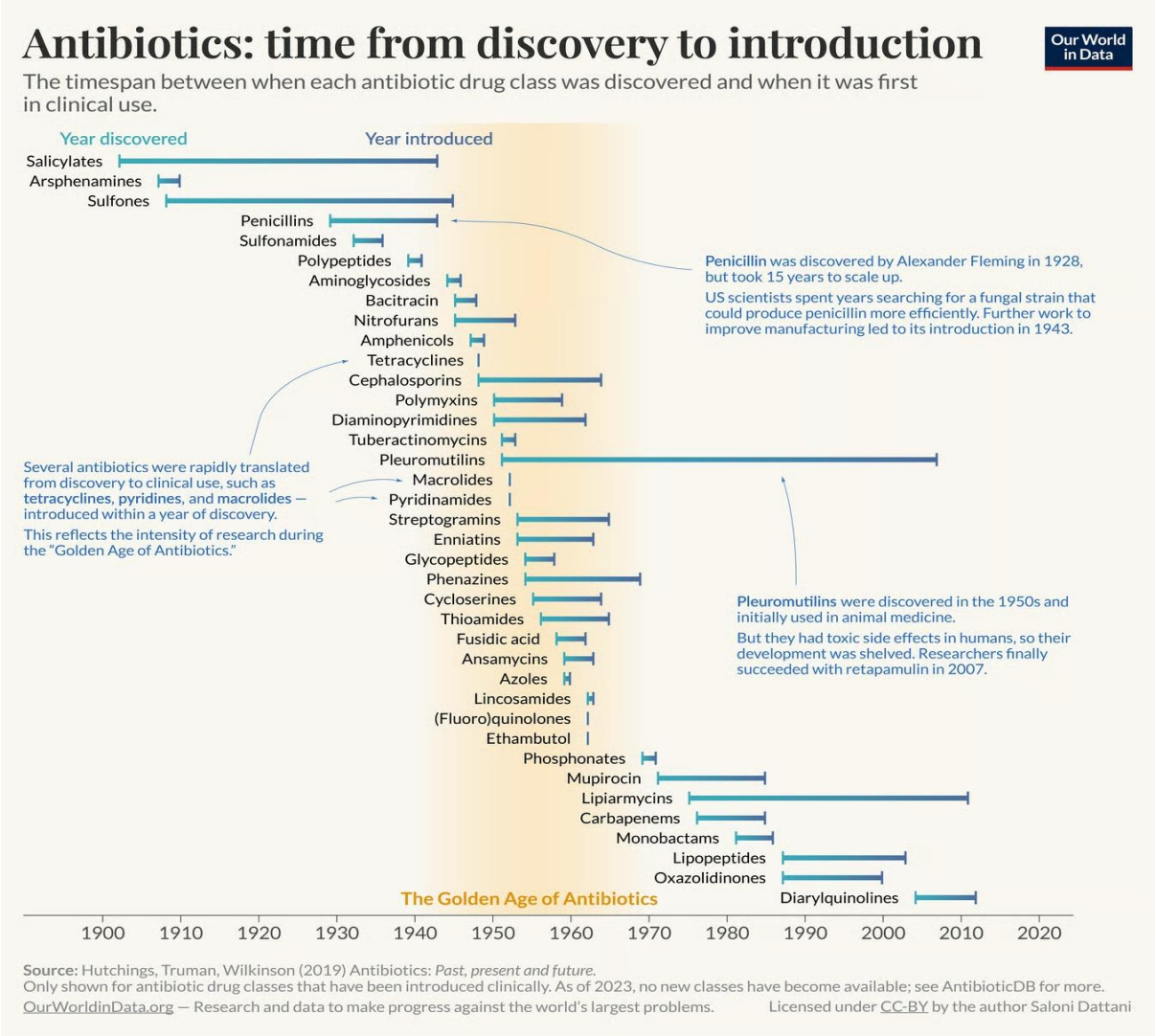

Figure: 1 A Brief Antibiotics History

Table 1: Historical Milestones in Antibiotic Discovery and Development

Year / Period	Milestone / Event	Description	Reference No.
Early 20th Century	Therapeutic role of antibiotics	Antibiotics inhibit bacterial growth by blocking or reducing bacterial activity and are essential in treating and preventing infectious diseases.	11
1928	Discovery of Penicillin	Alexander Fleming isolated penicillin from *Penicillium notatum*, marking the beginning of modern antibiotic therapy.	12
1941	First Clinical Use of Penicillin	Penicillin was first introduced into medical practice, revolutionizing infectious disease treatment.	12
1940s-1960s	Golden Age of Antibiotics	Majority of major antibiotic classes were discovered and developed during this period (often referred to as the "Golden Age" of antibiotic discovery).	13
Before 1987	Peak Antibiotic Development Era	Most antibiotics currently used in clinical practice were developed and launched prior to 1987.	13
Post-1987	Decline in Novel Classes	Very few new antimicrobial classes were introduced into the market after 1987, leading to stagnation in antibiotic innovation.	14
Present Era	Post-Antibiotic Era Concern	Slow rate of novel antibiotic discovery alongside rapid emergence of antibiotic-resistant (AR) bacteria.	15
2017	Delafloxacin (Baxdela)	Approval of delafloxacin for treatment of acute bacterial skin and skin structure infections.	16
2018	Ceftazidime/Avibactam	β-lactam/β-lactamase inhibitor combination approved for resistant Gram-negative infections.	17
2019	Lascufloxacin (La Svic)	Introduction of a novel fluoroquinolone antibiotic.	18
2020	Imipenem/Relebactam and Cefiderocol	Advanced antibiotics developed for carbapenem-resistant bacterial infections.	19

Mechanisms of Antibiotic Resistance

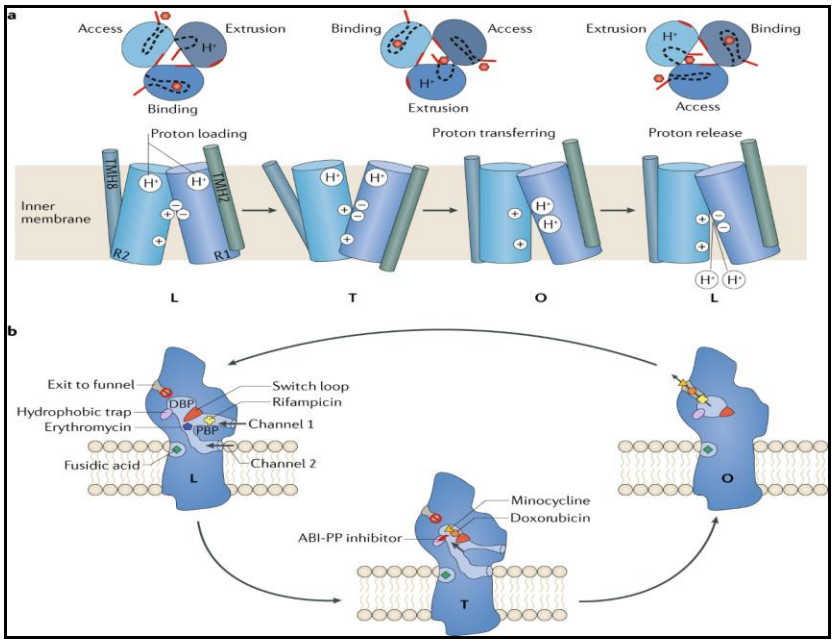

Figure: 2 Mechanisms of Antibiotic Resistance

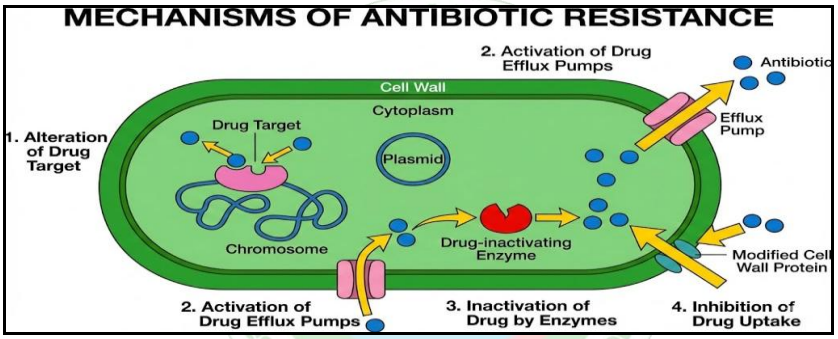

Figure: 3 Mechanisms of Antibiotic Resistance

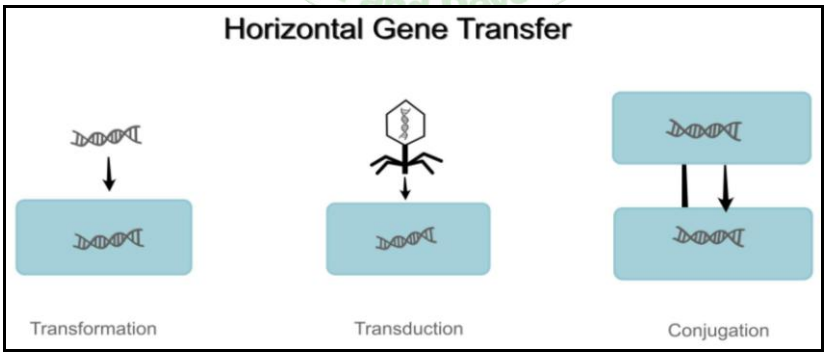

Figure: 4 Horizontal gene transfer

Bacteria employ multiple survival strategies:

Enzymatic Inactivation

Production of β-lactamases degrades β-lactam antibiotics (33,48).

Target Modification

Altered penicillin-binding proteins reduce antibiotic affinity (44).

Efflux Pumps

Efflux transporters actively expel antibiotics (34,35).

Reduced Permeability

Porin mutations decrease intracellular antibiotic concentration (6).

Horizontal Gene Transfer

Plasmid-mediated gene transfer accelerates resistance dissemination (47).

Table 2: Examples of Antibiotic Resistance Mechanisms in Clinically Significant Pathogens

Pathogen	Type of Resistance	Mechanism	Antibiotic Class Affected	Molecular Basis	Clinical Implication
Staphylococcus aureus (MRSA)	Acquired	Target modification	β-lactams	mecA gene encoding altered PBP2a	Reduced efficacy of penicillins and cephalosporins
Enterococcus faecium (VRE)	Acquired	Target site alteration	Glycopeptides	vanA / vanB gene clusters	Vancomycin treatment failure
Klebsiella pneumoniae	Acquired	Enzymatic degradation	Carbapenems	KPC, NDM carbapenemases	Limited therapeutic options
Pseudomonas aeruginosa	Intrinsic & Acquired	Efflux pump overexpression	Fluoroquinolones, β-lactams	MexAB-OprM efflux system	Multidrug resistance
Acinetobacter baumannii	Adaptive	Biofilm formation	Multiple classes	Biofilm matrix protection	Persistent hospital infections
Escherichia coli (ESBL-producing)	Acquired	β-lactamase production	Third-generation cephalosporins	CTX-M enzymes	Extended-spectrum resistance
Mycobacterium tuberculosis (MDR-TB)	Acquired	Gene mutation	Isoniazid, Rifampicin	katG, rpoB mutations	Prolonged multidrug therapy required
Salmonella enterica	Acquired	Efflux and plasmid-mediated resistance	Fluoroquinolones	qnr genes	Reduced susceptibility

Emerging Strategies to Combat Resistance

Bacteriophage Therapy

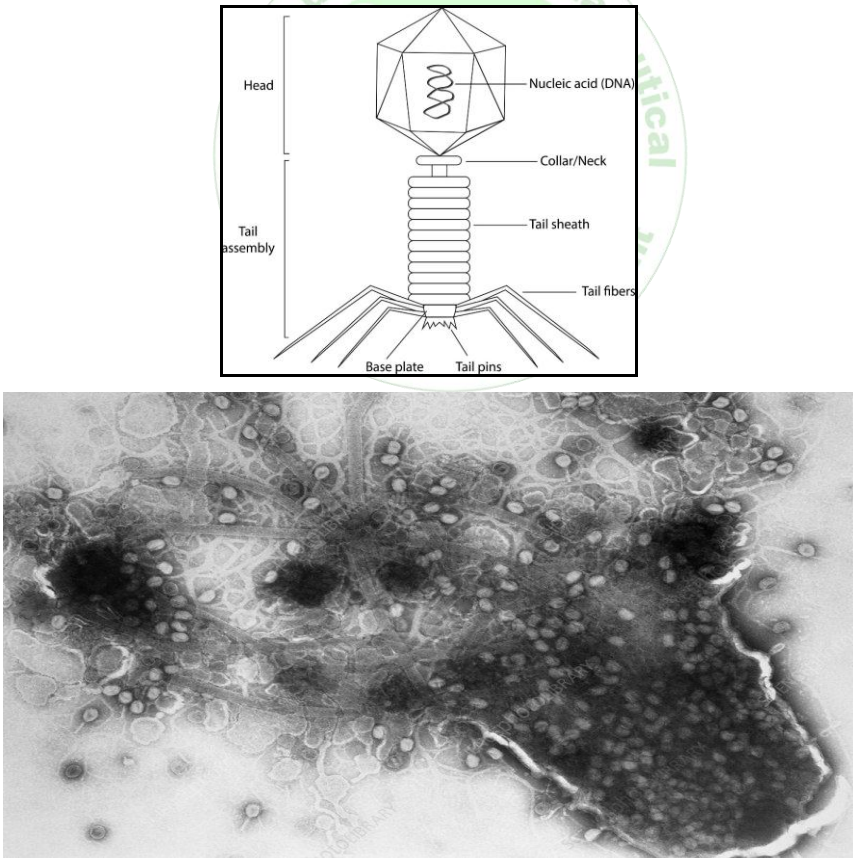

Figure: 5 Bacteriophage Therapy

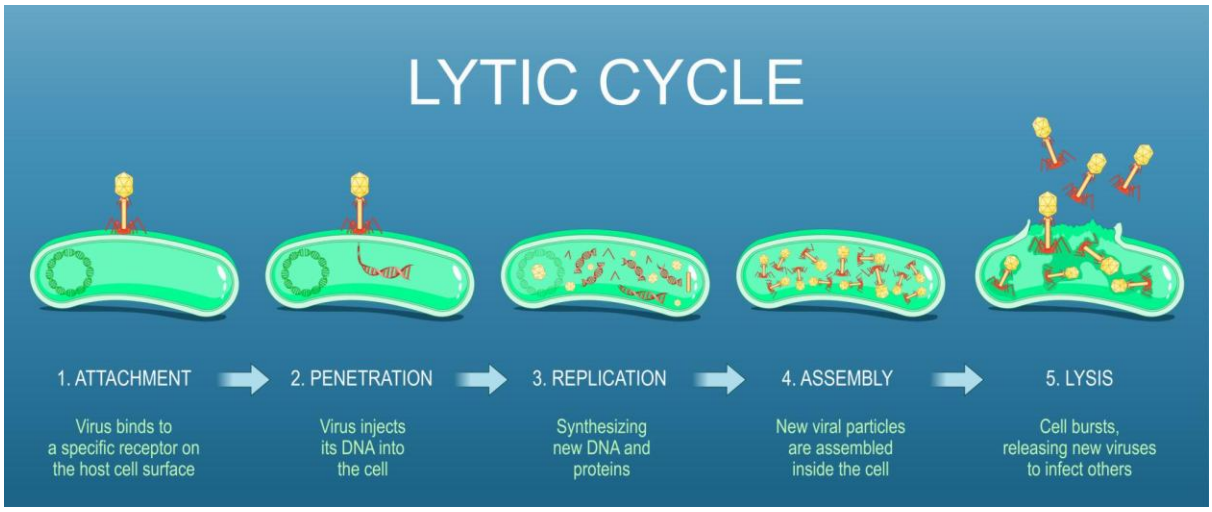

Figure: 6 Bacteriophages selectively infect bacteria and offer promising alternatives to antibiotics (21,22,55).

Antimicrobial Peptides

AMPs disrupt bacterial membranes and enhance host immunity, Antimicrobial peptides (AMPs) are small, naturally occurring bioactive molecules that constitute a critical component of innate immunity across diverse organisms, including humans, animals, plants, and microorganisms. Typically composed of 10–50 amino acids, AMPs are cationic and amphipathic in nature, enabling selective interaction with negatively charged bacterial membranes(23,24).

CRISPR-Cas Systems

CRISPR-based antimicrobials target resistance genes directly, Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) and CRISPR-associated (Cas) proteins constitute an adaptive immune system in bacteria and archaea, providing protection against invading genetic elements such as bacteriophages and plasmids. In recent years, CRISPR-Cas systems have emerged as a promising precision tool to combat antibiotic resistance by specifically targeting and eliminating resistance genes. (18,19,59).

Nanobiotics

Nanoparticles enhance drug delivery and reduce resistance development, Nanobiotics refer to nanoparticle-based antimicrobial systems designed to enhance the efficacy of conventional antibiotics and combat multidrug-resistant (MDR) pathogens. Nanotechnology offers innovative strategies to improve drug delivery, overcome bacterial resistance mechanisms, and reduce systemic toxicity. Due to their small size (1–100 nm), nanoparticles possess unique physicochemical properties, including high surface area-to-volume ratio and enhanced cellular penetration. (26,50,57).

Quorum-Sensing Inhibitors

Interfering with bacterial communication reduces virulence and biofilm formation, Quorum sensing (QS) is a bacterial cell-to-cell communication mechanism that regulates gene expression in response to population density through the production and detection of signaling molecules known as autoinducers. This system controls various pathogenic behaviors, including biofilm formation, toxin production, virulence factor expression, and antibiotic resistance. (28,29).

Combination Therapies

Combination approaches reduce selective pressure and improve therapeutic outcomes (32). β-lactam/β-lactamase inhibitor combinations are successful examples (33).

Table 3: Comparative Overview of Emerging Strategies to Combat Antibiotic Resistance

Strategy	Primary Target	Mechanism of Action	Spectrum of Activity	Key Advantages	Major Limitations	Clinical Status
Bacteriophage Therapy	Specific bacterial strains	Phage infects bacteria, replicates, and causes cell lysis	Highly strain-specific	Precision targeting; minimal microbiome disruption; effective against MDR pathogens	Regulatory challenges; phage resistance; narrow host range	Clinical trials and compassionate use
Antimicrobial Peptides (AMPs)	Bacterial cell membrane & intracellular targets	Membrane disruption, pore formation, immunomodulation	Broad-spectrum (Gram+ / Gram− / fungi)	Rapid bactericidal action; low resistance probability; anti-biofilm	Stability issues; toxicity at high doses; high cost	Preclinical and limited clinical evaluation
CRISPR-Cas Systems	Resistance genes & plasmids	Sequence-specific DNA cleavage of resistance determinants	Highly gene-specific	Precision gene editing; eliminates resistance genes; preserves	Delivery challenges; regulatory concerns; off-	Experimental / early translational research

				microbiota	target risk	
Nanobiotics	Bacterial membranes, biofilms, efflux systems	ROS generation, membrane damage, enhanced drug delivery	Broad-spectrum	Improved bioavailability; biofilm penetration; synergistic with antibiotics	Cytotoxicity concerns; production cost; long-term safety unknown	Some formulations approved; many in development
Quorum-Sensing Inhibitors (QSIs)	Bacterial communication pathways	Inhibits signal synthesis, signal degradation, receptor blockade	Anti-virulence (indirect antimicrobial effect)	Reduces virulence; lowers resistance pressure; disrupts biofilms	Limited clinical validation; may require combination therapy	Mostly preclinical research

Table 4: Types and Resistance Mechanisms of Bacteria to Antibiotics

Type of Resistance	Bacterial Species	Specific Mechanism	Antibiotic Class	Resistance Strategy	Clinical Implications	References
Intrinsic	Pseudomonas aeruginosa	Efflux Pump Overexpression	Carbapenems	Reduced Antibiotic Accumulation	High Treatment Failure Rates	25
Acquired	Staphylococcus aureus	mecA Gene Horizontal	β-Lactam Antibiotics	Transfer PenicillinBinding Protein Modification	MRSA Infections	26
Adaptive	Acinetobacter baumannii	Biofilm Formation	Multiple Antibiotics	Phenotypic Heterogeneity	Persistent Infections	27
Intrinsic	Klebsiella pneumoniae	β-Lactamase Production	Cephalosporins	Enzymatic Antibiotic Degradation	ExtendedSpectrum Resistance	28
Acquired	Enterococcus faecium	Vancomycin Resistance	Gene (vanA) Glycopeptide	Antibiotics Target Site Modification	VRE Nosocomial Infections	29
Adaptive	Multiple Bacterial Species	Metabolic Dormancy	BroadSpectrum	Reduced Metabolic Activity	Antibiotic Tolerance	30
Intrinsic	Multiple Bacterial Species	ABC Transporter Regulation	BroadSpectrum Antibiotics	Complex Efflux Mechanism Therapeutic	Targeting Challenges	31,32

Limitations and Challenges

Despite promising advances, challenges remain:

- Regulatory barriers
- High development costs
- Potential evolution of resistance against novel agents
- Limited accessibility in developing countries (3,37)

Table 5: Major Mechanisms of Antibiotic Resistance in Bacteria

S. No.	Resistance Mechanism	Description	Molecular Basis	Clinical Impact	References
1	Enzymatic Inactivation	Bacteria produce enzymes that chemically modify or degrade antibiotics, rendering them ineffective.	β-lactamases, carbapenemases, aminoglycoside-modifying enzymes	Treatment failure, resistance to β-lactams and other classes	[33]
2	Target Site Modification	Structural alteration of antibiotic-binding sites reduces drug affinity.	Mutations in penicillin-binding proteins (PBPs), ribosomal subunits, DNA gyrase	Reduced antibiotic efficacy; multidrug resistance	[33]
3	Reduced Permeability	Alterations in membrane porins decrease antibiotic entry into bacterial cells.	Porin mutations or downregulation in Gram-negative bacteria	Decreased intracellular drug concentration	[33]

4	Efflux Pump Overexpression	Active transport systems expel antibiotics from the bacterial cell before they reach their target.	Overexpression of multidrug efflux transporters (e.g., ABC transporters, RND family pumps)	Multidrug resistance across diverse antibiotic classes	[33,34]
5	Horizontal Gene Transfer (HGT)	Transfer of resistance genes between bacteria via mobile genetic elements.	Plasmids, transposons, integrons carrying MDR-associated genes	Rapid dissemination of resistance across species	[33]
6	Genetic Variations in Regulatory Genes	Mutations or insertions in genes encoding transcriptional regulators alter resistance expression.	DNA polymorphisms, regulatory gene insertions	Enhanced adaptability and resistance evolution	[33]

MDR: Multidrug Resistance
ABC: ATP-binding cassette
RND: Resistance-nodulation-division family

Strategies to Combat Antibiotic Resistance

antibiotic resistance remains a critical challenge in global healthcare, threatening the effectiveness of treatments and increasing the burden of resistant infections. While no single approach can completely eliminate this problem, various strategies can help mitigate its spread and impact. Antibiotic overuse is a major driver of resistance evolution, as epidemiological studies have shown a direct link between consumption and the emergence of resistant strains [4]. Resistance genes can transfer between bacterial species via horizontal gene transfer or arise naturally through mutations, which are processes exacerbated by inappropriate prescribing practices and suboptimal dosing [7]. These factors not only enhance pathogen virulence, but also accelerate the dissemination of resistance determinants.

Addressing these challenges requires a multifaceted approach that includes improving antibiotic stewardship, enhancing infection prevention measures, and advancing alternative treatments such as phage therapy and immunotherapies. Public awareness campaigns and education on the prudent use of antibiotics also play a vital role in mitigating resistance. The declining efficacy of conventional antibiotics has necessitated the investigation of alternative antimicrobial approaches. This section examines emerging interventions for combating antibiotic resistance, including quorum quenching mechanisms that disrupt bacterial communication networks, microbial-based therapies, stem cell applications, immunotherapeutic modalities, photodynamic antimicrobial techniques, and CRISPRCas systems and their relationship to resistance mechanisms, bacteriophage therapy, and bioactive compounds derived from animal venoms.

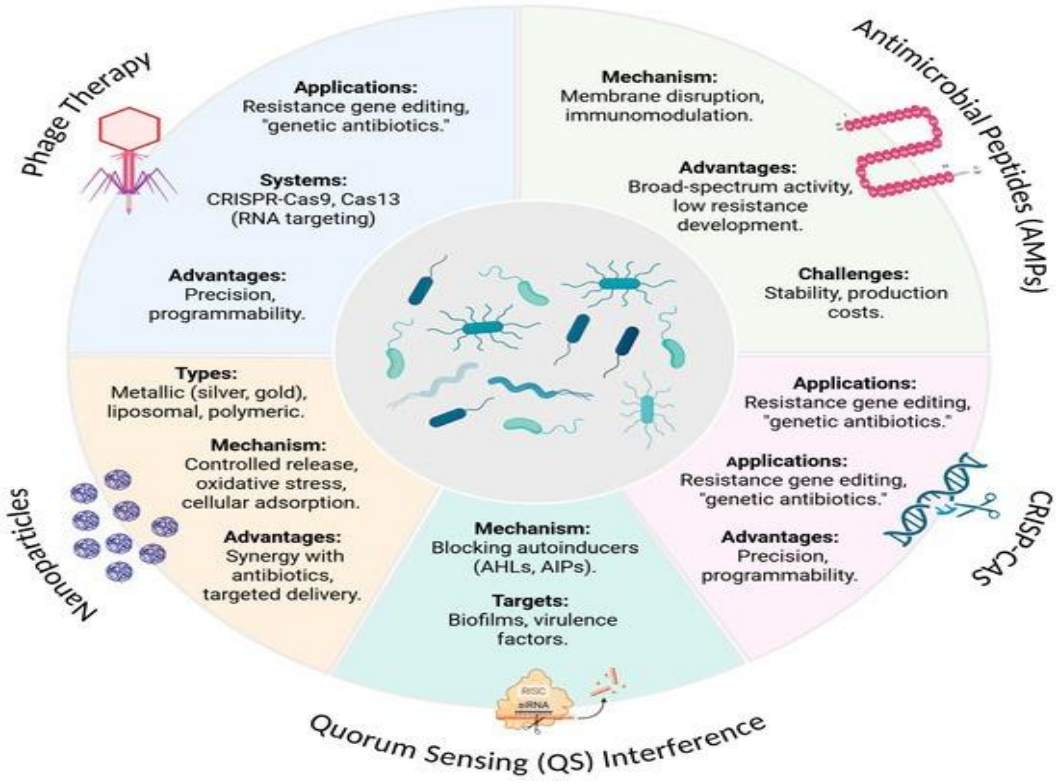

Table 6: Strategies to Combat Antibiotic Resistance

S. No.	Strategy	Mechanism / Approach	Examples	Advantages	Limitations
1	Antimicrobial Stewardship	Rational prescribing, dose optimization, and restricted antibiotic use	Hospital stewardship programs	Reduces emergence of resistance; cost-effective	Requires compliance and monitoring
2	Infection Prevention & Control	Hygiene measures, vaccination, surveillance programs	Hand hygiene, sterilization, vaccination	Prevents spread of resistant pathogens	Implementation challenges in low-resource settings
3	Combination Therapy	Use of two or more antimicrobial agents to enhance efficacy	β-lactam + β-lactamase inhibitors	Synergistic action; delays resistance	Increased cost; potential toxicity
4	Bacteriophage Therapy	Use of viruses that selectively infect and lyse bacteria	Phage cocktails for MDR pathogens	High specificity; minimal microbiome disruption	Regulatory and standardization issues
5	Antimicrobial Peptides (AMPs)	Disrupt bacterial membranes and modulate immune responses	Defensins, synthetic peptides	Broad-spectrum activity; low resistance development	Stability and toxicity concerns
6	Nanobiotics	Nanoparticle-based drug delivery systems	Silver nanoparticles, liposomal antibiotics	Improved drug penetration and bioavailability	Safety and long-term toxicity evaluation required
7	CRISPR-Cas Systems	Targeted gene editing to eliminate resistance genes	CRISPR-based antimicrobials	High specificity; gene-level targeting	Delivery challenges; ethical concerns
8	Quorum-Sensing Inhibitors	Disrupt bacterial communication and biofilm formation	AHL inhibitors	Reduces virulence without strong selective pressure	Limited clinical validation
9	Immunotherapy / Host-Directed Therapy	Enhances host immune response to infections	Monoclonal antibodies, immuno-antibiotics	Reduces reliance on antibiotics	High cost; limited availability
10	Photodynamic Therapy	Light-activated compounds generate reactive oxygen species	Photosensitizers + light exposure	Effective against biofilms; low resistance risk	Limited systemic application

MDR: Multidrug Resistant
AHL: Acyl-homoserine lactone
CRISPR: Clustered Regularly Interspaced Short Palindromic Repeats

Potential Limitations of Combatting Antibiotic Resistance Strategies

Despite the promising potential of the strategies outlined in Sections 4.1-4.9, several critical limitations impede their clinical implementation and widespread adoption. Many of these approaches remain predominantly in preclinical or early clinical investigation phases, with insufficient validation through randomized controlled trials and longitudinal studies [48]. The evolutionary adaptability of bacterial pathogens presents another significant concern, as selective pressures may drive the development of resistance mechanisms even against these novel therapies. For instance, bacteria could potentially evolve modified quorum-sensing receptors, bacteriophage resistance, or mechanisms to neutralize antimicrobial peptides from animal venoms [49]. Economic considerations further constrain practical applications, as the high costs associated with the production, purification, and quality control of biologics-based therapies (e.g., bacteriophages, stem cells, and venomderived peptides) make them potentially inaccessible in resource-limited settings [50]. Additionally, regulatory frameworks remain underdeveloped for many of these novel approaches, creating uncertainty regarding safety assessment, standardization protocols, and approval pathways [51]. These multifaceted challenges necessitate concurrent advances in regulatory science, cost-effective manufacturing processes, and innovative clinical trial designs to facilitate the translation of promising laboratory findings into clinically viable alternatives to conventional antibiotics.

CONCLUSIONS

The antibiotic resistance crisis, fueled by the overuse of antibiotics and stagnation in new drug development, remains a critical global health challenge. This review delved into the complex resistance mechanisms of multidrug-resistant pathogens and highlighted alternative strategies, including quorum-sensing inhibitors, probiotics, antimicrobial peptides, venoms, nanobiotics, bacteriophages, CRISPR-Cas systems, immunotherapy, and photodynamic therapy. The significance of the environment as both a reservoir for resistance genes and a source of novel antimicrobials was also underscored. Despite these promising alternatives, significant challenges remain. The high costs associated with developing and commercializing new therapies, the need for rigorous regulatory approvals, and the potential for resistance evolution against novel treatments pose major hurdles. Moreover, the complexity of microbial ecosystems necessitates further research to understand the long-term efficacy and ecological impact of these interventions. Future efforts should focus on enhancing the scalability and affordability of novel antimicrobials, optimizing combination therapies to prevent resistance, and fostering global collaborations to implement sustainable antibiotic stewardship programs. Addressing this crisis demands a unified interdisciplinary effort.

REFERENCES

1. World Health Organization. Global action plan on antimicrobial resistance. Geneva: WHO; 2015.
2. Murray CJL, Ikuta KS, Sharara F, et al. Global burden of bacterial antimicrobial resistance in 2019: A systematic analysis. Lancet. 2022;399(10325):629–655.
3. O'Neill J. Tackling drug-resistant infections globally: Final report and recommendations. London: Review on Antimicrobial Resistance; 2016.
4. Ventola CL. The antibiotic resistance crisis: Part 1: Causes and threats. P T. 2015;40(4):277–283.
5. Davies J, Davies D. Origins and evolution of antibiotic resistance. Microbiol Mol Biol Rev. 2010;74(3):417–433.
6. Blair JMA, Webber MA, Baylay AJ, Ogbolu DO, Piddock LJV. Molecular mechanisms of antibiotic resistance. Nat Rev Microbiol. 2015;13(1):42–51.

7. Munita JM, Arias CA. Mechanisms of antibiotic resistance. Microbiol Spectr. 2016;4(2):1–37.
8. Fleming A. On the antibacterial action of cultures of Penicillium. Br J Exp Pathol. 1929;10(3):226–236.
9. Boucher HW, Talbot GH, Bradley JS, et al. Bad bugs, no drugs: No ESKAPE! Clin Infect Dis. 2009;48(1):1–12.
10. Tacconelli E, Carrara E, Savoldi A, et al. Discovery, research and development of new antibiotics: WHO priority list. Lancet Infect Dis. 2018;18(3):318–327.
11. Laxminarayan R, Duse A, Wattal C, et al. Antibiotic resistance—the need for global solutions. Lancet Infect Dis. 2013;13(12):1057–1098.
12. Wright GD. Something old, something new: Revisiting natural products in antibiotic drug discovery. Can J Microbiol. 2014;60(3):147–154.
13. Fischbach MA, Walsh CT. Antibiotics for emerging pathogens. Science. 2009;325(5944):1089–1093.
14. Payne DJ, Gwynn MN, Holmes DJ, Pompliano DL. Drugs for bad bugs: Confronting antibiotic resistance. Nat Rev Drug Discov. 2007;6(1):29–40.
15. Lewis K. Platforms for antibiotic discovery. Nat Rev Drug Discov. 2013;12(5):371–387.
16. Brown ED, Wright GD. Antibacterial drug discovery in the resistance era. Nature. 2016;529(7586):336–343.
17. Wright GD. The antibiotic resistome: The nexus of chemical and genetic diversity. Nat Rev Microbiol. 2007;5(3):175–186.
18. Koonin EV, Makarova KS. CRISPR-Cas: Evolution of adaptive immunity. Nat Rev Microbiol. 2019;17(6):331–345.
19. Bikard D, Barrangou R. Using CRISPR-Cas systems as antimicrobials. Nat Biotechnol. 2017;35(3):225–233.
20. Czaplewski L, Bax R, Clokie M, et al. Alternatives to antibiotics. Lancet Infect Dis. 2016;16(2):239–251.
21. Abedon ST, García P, Mullany P, Aminov R. Phage therapy: Past, present and future. Front Microbiol. 2017;8:981.
22. Chan BK, Abedon ST, Loc-Carrillo C. Phage cocktails and resistance development. Future Microbiol. 2013;8(6):769–783.
23. Hancock REW, Sahl HG. Antimicrobial peptides and host-defense peptides. Nat Biotechnol. 2006;24(12):1551–1557.
24. Mahlapuu M, Håkansson J, Ringstad L, Björn C. Antimicrobial peptides: An emerging category of therapeutic agents. Front Cell Infect Microbiol. 2016;6:194.
25. Rai M, Deshmukh SD, Ingle AP, Gade AK. Silver nanoparticles as new antimicrobials. Biotechnol Adv. 2012;30(1):46–56.
26. Pelgrift RY, Friedman AJ. Nanotechnology as a therapeutic tool to combat microbial resistance. Adv Drug Deliv Rev. 2013;65(13-14):1803–1815.
27. Ventola CL. The antibiotic resistance crisis: Part 2: Management strategies. P T. 2015;40(5):344–352.
28. Rutherford ST, Bassler BL. Bacterial quorum sensing. Cold Spring Harb Perspect Med. 2012;2(11):a012427.
29. Kalia VC. Quorum sensing inhibitors: An overview. Biotechnol Adv. 2013;31(2):224–245.
30. Davies D. Understanding biofilm resistance. Nat Rev Drug Discov. 2003;2(2):114–122.
31. Hoiby N, Bjarnsholt T, Givskov M, Molin S, Ciofu O. Antibiotic resistance of bacterial biofilms. Int J Antimicrob Agents. 2010;35(4):322–332.
32. Wright GD. Antibiotic adjuvants: Rescuing antibiotics from resistance. Trends Microbiol. 2016;24(11):862–871.
33. Bush K, Bradford PA. β-Lactams and β-lactamase inhibitors. Cold Spring Harb Perspect Med. 2016;6(8):a025247.
34. Li XZ, Plesiat P, Nikaido H. Efflux-mediated antimicrobial resistance. Drugs. 2015;75(14):1555–1623.
35. Poole K. Efflux pumps as antimicrobial resistance mechanisms. J Antimicrob Chemother. 2005;56(1):20–51.
36. WHO. 2023 antibacterial agents in clinical and preclinical development: An overview and analysis. Geneva: WHO; 2023.
37. Spellberg B, Bartlett JG, Gilbert DN. The future of antibiotics and resistance. N Engl J Med. 2013;368(4):299–302.
38. Rossolini GM, Arena F, Pecile P, Pollini S. Update on antibiotic resistance crisis. Lancet Infect Dis. 2014;14(12):125–133.
39. Fair RJ, Tor Y. Antibiotics and bacterial resistance. Perspect Medicin Chem. 2014;6:25–64.
40. Clatworthy AE, Pierson E, Hung DT. Targeting virulence. Nat Chem Biol. 2007;3(9):541–548.
41. Andersson DI, Hughes D. Microbiological effects of sublethal antibiotic levels. Nat Rev Microbiol. 2014;12(7):465–478.
42. Aminov RI. A brief history of the antibiotic era. Front Microbiol. 2010;1:134.
43. Brown SP, Cornforth DM, Mideo N. Evolution of virulence. Philos Trans R Soc Lond B Biol Sci. 2012;367(1590):1865–1878.
44. Tang SS, Apisarnthanarak A, Hsu LY. Mechanisms of β-lactam resistance. Ann Acad Med Singapore. 2014;43(11):514–523.
45. Davies J. Where have all the antibiotics gone? Can J Infect Dis Med Microbiol. 2006;17(5):287–290.
46. Wright GD. Q&A: Antibiotic resistance. J Biol. 2010;9(3):1–5.
47. Lerminiaux NA, Cameron ADS. Horizontal gene transfer in bacteria. FEMS Microbiol Rev. 2019;43(5):490–518.
48. Bush K. Past and present perspectives on β-lactamases. Antimicrob Agents Chemother. 2018;62(10):e01076-18.
49. Tacconelli E, Sifakis F, Harbarth S, et al. Surveillance for control of antimicrobial resistance. Lancet Infect Dis. 2018;18(3):e99–e106.
50. Singh R, Smitha MS, Singh SP. The role of nanotechnology in combating multidrug resistance. J Nanosci Nanotechnol. 2014;14(7):4745–4756.
51. Hwang AY, Gums JG. The emergence and evolution of antimicrobial resistance. Clin Ther. 2016;38(6):1234–1247.
52. Bush K, Courvalin P, Dantas G, et al. Tackling antibiotic resistance. Nat Rev Microbiol. 2011;9(12):894–896.
53. World Health Organization. Antimicrobial resistance: Global report on surveillance. Geneva: WHO; 2014.
54. Piddock LJV. The crisis of antibiotic resistance. Clin Microbiol Infect. 2012;18(9):846–853.
55. Kaur T, Rishi P. Bacteriophage therapy: An alternative approach. Crit Rev Microbiol. 2018;44(1):1–16.
56. Shankar PR. Book review: The antibiotic era. J Pharmacol Pharmacother. 2016;7(1):46–48.
57. Makvandi P, Wang CY, Zare EN, Borzacchiello A, Niu L, Tay FR. Metal-based nanomaterials in antimicrobial therapy. Adv Funct Mater. 2020;30(17):1910021.
58. Ventola CL. The antibiotic resistance crisis: Overview and updates. P T. 2015;40(4):277–283.
59. Koonin EV, Zhang F. Coupling immunity and genome engineering. Cell. 2017;168(3):377–389.
60. Laxminarayan R. Antibiotic resistance and stewardship. Clin Infect Dis. 2014;59(Suppl 3):S88–S94.