

Engineering Solutions for Microbial Resistance in Medicine

Ramzi Mohamed Adam Alhour

Kampala International University Teaching Hospital Ishaka

ABSTRACT

The growing threat of microbial resistance (MR) poses a grave challenge to global healthcare, agriculture, and food safety systems. This paper examines engineering-based strategies and technological innovations aimed at mitigating microbial resistance in medical contexts. It begins by examining the mechanisms through which bacteria develop resistance, including genetic, biochemical, and environmental factors, particularly focusing on biofilm formation and antibiotic resistance gene (ARG) dissemination. The review highlights the role of modern materials science in developing antimicrobial surfaces and nanostructures that disrupt microbial adhesion and biofilm persistence. Furthermore, emerging therapeutic approaches such as antimicrobial peptides, engineered amphiphiles, and phage therapy are presented as promising alternatives to conventional antibiotics. The importance of diagnostics and surveillance in managing antimicrobial resistance (AMR), especially in low-resource settings, is emphasized. The paper concludes with a discussion on interdisciplinary collaboration as the foundation for engineering next-generation antimicrobial solutions and calls for sustained global innovation and policy alignment to combat the AMR crisis.

Keywords: Antimicrobial resistance (AMR), microbial resistance, biofilms, nanotechnology, genetic adaptation, engineered surfaces, antimicrobial peptides, diagnostics, healthcare innovation.

INTRODUCTION

Microbial resistance jeopardizes modern medicine and food production. The rise of microbial resistance (MR) to food-grade antimicrobials raises serious food safety concerns, enabling harmful pathogens to persist in food handling. Concurrently, clinical MR is a significant threat, as bacteria gain resistance to prescribed antibiotics, leading to untreatable infections, now deemed a global crisis, potentially more severe than pandemics. Research indicates that stressed pathogenic bacteria can develop new resistance types. Investigating antimicrobial resistance is challenging since organisms must be cultured in labs, necessitating models like engineered surfaces with diverse MR factors. Microorganisms are increasingly recognized in the context of micro-fabrication and bio-fouling, with bacteria utilizing various resistance mechanisms categorized as physicochemical, metabolic, or genetic changes. Some adaptations can be integrated into synthetic materials that trigger antimicrobial responses; conversely, exposing bio-fouling bacteria to such materials might select for resistant variants. Managing MR demands reproducibility in developing bacterial populations along with controlled surfaces. Antibiotic resistance is prevalent in bacteria that form biofilms, raising sanitation challenges for food safety. Engineering methods like topography aim to limit bacterial adhesion, reducing pathogenicity in fungi reliant on attachment. Advanced microscopy techniques show promise for polymer surface applications, while understanding biofilm shelter limitations paves the way for innovative disinfectant use. Materials that inhibit adhesion could enhance disinfection strategies, preventing biofilm formation and mitigating bacteria's prolonged antimicrobial exposure. Researchers are actively investigating nanotechnology solutions for biofilms, employing hydrophobic polymer coatings or sharkskin-mimicking surfaces to resist adhesion [1, 2].

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited

Mechanisms of Microbial Resistance

Today, the use of antibiotics forms the cornerstone for successful therapeutic interventions in critical and broad-spectrum medical, agricultural, and veterinary uses. Thus, a constant pressure was exerted towards eliciting persistent displays of resistance in the microbial domain. This challenge vanquishes the innate immunity defenses of the drugs used in medicine, agriculture, and veterinary practices, thus calling for a comprehensive appraisal of the resistance mechanisms that microbes display to extract leads towards designing next-generation inhibitors that could help combat resistance. Hence, all mechanically classified resistance mechanisms were evaluated into biological, biochemical, and molecular pathways of microbial combat structures. All such pathways were then presented in a coherent, extensive, updated, and visually friendly review that could aid in studying and subsequently countering upcoming waves of resistance in next-gen targets. A highly aggressive endeavor that blacklisted the revolutionary debut of penicillin appeared at the final step in microbial evolution, thus rupturing a firm contrary crunch on human health and sanitation. The first resistance mechanism encountered was the production of a potent β -lactamase enzyme by some microbial domains, thwarting the drug from exerting its impact on target protein binding. Such a challenge transgressed the envelopment of other target proteins, i.e., transpeptidase, transglycosylase, and autolysins. Fantastic attempts towards growing β -lactam and antibiotic rings or peptide analogs that could thwart the enzymatic hydrolysis, unfold, and lead to an amazingly fruitful outcome towards designing valid semi-synthetic drugs. On the other hand, thence the disease receded, the curiosity to pursue understanding microbial resistance mechanisms upstaged the dawn of the 'golden' era of target-based drug design. The race again turned astutely aggressive with the emergence of a multi-drug resistant (MDR) tubercle bacilli in the penicillin era's 52nd year. This time, the focus of the 'war' turned to a novel dimension, i.e., the genesis and persistence of resistance on ecogenetic aspects. A new prayer/invocation to God, for 'blessed' and up-to-date knowledge on the battleground of the evolution of THE nanomachines, administration and emergence of resistance, its endurance, synergetic expression, ecology, ecology-molecular-themophysiology-race, nip-the-steps, design of sound new generation targets [3, 4].

Genetic Factors

The characterization of microbial resistance mechanisms, such as those conferred by antibiotic resistance genes (ARGs), relies upon the mapping of resistance determinants to phylogenetic trees inferred from core genes widely distributed among organisms in a population. Such phylogenetic trees reveal today the evolution of virtually all known antibiotic resistances, but for two exceptions that reflect novel resistance mechanisms. The first antibiotic, antimycin, was discovered in 1944, and microbial resistance to it was reported as early as 1961. The resistance mechanism, however, remains unknown. Resistance to carbapenems among European Gram-negative bacterial infections, most notably Enterobacteriaceae, has similarly spread in less than a decade. The genetic basis of its antibiotic resistance, however, remains poorly understood. Penicillin-binding proteins (PBPs) have been implicated, but the determination of their completeness and homology to *Klebsiella pneumoniae* on the phylogenetic tree has not been satisfactory. Compounded by a broad host-range plasmid, the class D target genes were introduced into solely 5 phylogenetically unrelated proteobacterial genera, hence go unreported in other taxa. LDT, LAD, and LEL consist of a PBP domain traversing the inner membrane, and a β -lactamase domain linked to an outer membrane β -barrel domain. Comparison between pairwise genome-wide FASTA sequences between the COG0254 gene cluster homologs and classical non-intrinsic target genes against the selected β -lactam antibiotics revealed their diversity across taxonomic ranks. For resistance to aminoglycosides (AGs) and polymyxins (CDs), genomic and molecular analysis were used to survey a cohort of 520 Enterobacteriaceae isolates, including 452 resistant isolates (86.9%) in scour links to a road wastewater treatment plant. Composite transposons carrying aminoglycoside N-acetyltransferases and integrons with *aac(3)*-ID, *aac(6')*-Ib-cr, and 64–1056 *drs4*-693 were prevalent among protein kinases resistant to AMK, GEN, and NE, respectively. Screening of CD resistance determinants in MGEs revealed 21 different *mcr* variants, of which *mcr*-9.2-9.3 and *mcr*-9.5 were newly annotated. Plasmid duplication and transmission of f-plasmid or IncQ1-plasmids played a key role in the rapid emergence of *mcr*-9.2 in *E. coli*. Besides targeting toxins, EgdB co-immunoprecipitated with the transcriptional repressor Spo0A, suggesting an important role in controlling competence induction [5, 6].

Environmental Influences

Microbial resistance to antibiotics is an ever-increasing threat to the health of humans and domestic animals, and is caused by many factors. One of the key factors influencing the onset of microbial resistance is biocide use. Biocides are substances and preparations intended to destroy, deter, render

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited

harmless, or exert a controlling effect on any harmful organism by chemical or biological means. Biocidal products are classified into different groups according to their actions and include disinfectants, food and feed additives, preservatives, pest control agents, and others. Selective pressure exerted by the biocide would cause biocide tolerance in the target microorganisms and might subsequently result in the emergence of antibiotic resistance determinants. Of interest here is the biocide residue concentration in its use and storage environments. In the veterinary field, a wide variety of disinfectants are routinely used to assist in reducing the global microbial contamination with the aim of disease prevention partially as part of Biosecurity maintenance. These disinfectants have been commonly applied throughout the years in the Biological Isolation and Containment Unit (BICU) of the Veterinary Medical Teaching Hospital. In addition to strict cleaning and disinfecting practices, a number of environmental features at the BICU are designed to help limit the transmission of infectious agents. However, overdosing or improper use of a biocide may cause the disinfectant to be ineffective through the selection of biocide-resistant microorganisms. The focus of this research is to have a better understanding of the biocide tolerance in the BICU environments and its possible implication in the outbreak of MDR microorganisms in the hospital. Factors affecting the selection of disinfectant-tolerant and antibiotic-resistant environmental bacteria will also be discussed as potential targets for mitigating their emergence [7, 8].

Biochemical Pathways

Bacterial biofilms are dense populations of microorganisms embedded within a network of extracellular polymeric substances (EPS) that are commonly encountered throughout nature. As a protective layer, EPS shields the bacteria from antibiotics and the host immune system's attack. Biofilm-associated infections are chronic because biofilms leave a persistent reservoir of bacteria that shed planktonic bacteria into the surrounding area. Biofilm-excessive bacteria are many orders of magnitude less susceptible to antibiotic treatment than their planktonic counterparts. Biofilm-associated infections are hard to treat, largely due to the intrinsic and acquired antibiotic resistance mechanisms of bacteria in biofilms. Commonly reported antibiotic resistance mechanisms used by biofilm-associated bacteria are discussed in detail, providing a comprehensive account of current knowledge on biofilm-associated antibiotic resistance. Bacteria in biofilms can upregulate the expression of efflux pumps (EPs) in response to exposure to an antimicrobial, thereby reducing the production of the drug that enters the bacterial cell. Diverse classes of antimicrobial agents, including β -lactams, fluoroquinolones, and a macrolide, are extruded by EPs, making them attractive targets in controlling the rise and spread of antibiotic resistance. Bacterial stress and signaling pathways whereby the biofilm growth mode is achieved are introduced. Bacterial organisms can perceive and respond to environmental signals to affect behavior at the group level in a process termed quorum sensing (QS). Antimicrobials can alter the chemical makeup of the biofilm environment, ultimately destabilizing or disbanding the biofilm. The emergence of multispecies resistant biofilms is also considered with the advent of metagenomics methodologies for the identification of biofilm-associated transcriptional regulators. EPS- and biofilm-sensing receptors and adaptations used by biofilm-grown bacteria to tolerate high concentrations of antimicrobials are covered. EPS itself can also contribute to the resistance of biofilms against antibiotic treatment by acting as a barrier. In addition to factors directly related to biofilm structure, b-1,6-N-acetylglucosamine polysaccharide, and intracellular signaling molecules, including the second messenger molecule cyclic di-GMP (c-di-GMP), all contribute to the decrease of biofilm susceptibility to treatment by both biocide and antibiotics [9, 10].

Impact of Microbial Resistance on Healthcare

Healthcare-associated, or nosocomial, infections are caused by pathogens that are resistant to many current antibiotic treatments, and they are a significant public health threat globally and particularly in the United States. They affect approximately one in every 31 U.S. hospital patients. Infections with these pathogens can arise following transmission and colonization of a patient within a healthcare setting. Healthy people are colonized with a diverse microbiota of organisms, but some pathogens or antibiotic-resistant strains can remain in the microbiota at high levels. These organisms are likely removed less efficiently following treatment with antibiotics, allowing infections to occur. Healthcare-associated bacterial pathogens that have been targeted explicitly for decolonization and mitigation interventions include methicillin-resistant, *Clostridioides difficile*, vancomycin-resistant *Enterococcus* (VRE), and multidrug-resistant Gram-negative organisms (MDROs). Most healthcare pathogens are colonizers and are normally present at low abundance in healthy adults. Patients in healthcare facilities are less healthy and have more opportunities to become infected with a pathogen that has been successfully transmitting

within those settings. Patient safety in healthcare facilities requires strict measures to reduce transmission and ensure patient safety when a patient is admitted to the facility; rules should be in place to prevent the introduction of pathogen carriers into the population. Most patients who acquire colonization with a target pathogen from another patient (or a healthcare worker or contaminated surface) do not develop an infection or are not afflicted. Transmitting patients, who breathe and touch surfaces, allow the pathogen's genome to be transferred to another patient, (or worker or surface). Colonization may be non-productive if the new patient has healthy skin, mucosa, and microbiota. The new patient is less likely to become colonized and by a lower inoculum size. Colonization is thus a necessary initial step, but it can be a transient phase. Once a sustained infection is established, colonization is favored over later treatment regimens, which aim to eradicate the infection [11, 12].

Current Strategies To Combat Resistance

Antimicrobial resistance (AMR), which threatens to undo decades of progress in medicine, is a global problem that impacts both human and animal health. AMR occurs when a microbe develops the ability to survive exposure to a drug that previously controlled it. As a result, infections are more difficult to treat and more costly to manage. AMR is a multifactorial problem that brings together a vast number of pathogens and a plethora of transmission modes, routes, reservoirs, and environmental niches in a web of connections that spans the globe but remains poorly understood in terms of complexity and evolution. Consequently, it has led to the pandemic emergence of multi-drug-resistant (MDR) pathogens, some of which have already changed their environmental reservoirs or host species. Widespread and inappropriate use of antibiotics in human therapeutics and agriculture, coupled with failures in infection prevention and control, is responsible for the emergence of resistant pathogens. Against the backdrop of few new antibiotics becoming available for clinical use, there is an urgent and pressing need to understand the reasons for rapid transmission and emergence of complexity of antibiotic resistance, to develop, evaluate, and implement measures that can disrupt this process and to foster the translation of scientific knowledge into effective therapeutic, diagnostic, and vaccines that will help to stem the AMR tide. The increased prevalence of AMR strains is putting pressure on healthcare systems and agriculture due to the few new agents being developed to replace lost activity. This has resulted in a vicious cycle of heavy reliance on the most innovative, expensive antibiotics. Concerns regarding the future sustainability of innovation into antibiotics were raised over a decade ago, leading to recent initiatives attempting to revive antibiotic research and foster innovation. However, existing strategies are proving inadequate to stem the fast-growing development of AMR. Alternatives to antibiotics are viewed as the best hope for combating AMR. Current options include bacteriophage therapy, bioengineering antibiotics, host defence peptides, natural products from plants, anti-virulence compounds, and antimicrobial metals [13, 14].

Engineering Innovations in Medicine

In the last decade, including the COVID-19 pandemic, viral and microbial epidemics and pandemics have posed an undeniable and growing threat to humanity. They still take a concerning toll on global economies, health-care systems, and human lives. A faster development of much better medicine is crucial to the public and the government. This paper aims to improve medicine using innovative engineering. The history of health-care innovation and technology is summarized first. After that, innovative engineering in medicines, including medications, vaccinations, and microbiomes, is reviewed. Existing difficulties and the ways to overcome them are discussed further. In addition to historically significant establishments in the public sector, companies played key global roles in rapidly controlling the COVID-19 pandemic in the private sector. A few months after the initial discovery of the COVID-19 virus strain in late December 2019, a realistic vaccine candidate consisting of mRNA encoding prefusion-stabilized full-length spike glycoprotein with four mutations was designed using structural biology knowledge. Evaluations were performed using well-known immunogens and biosafety and infectiousness tests. Yet, only one serotype of the virus was used. Efforts should be made to design new, updated vaccine candidates against rising variants of concern, even with fine mutations. Over a dozen countries are establishing new mRNA vaccine factories to produce the core ingredients of COVID-19 mRNA vaccines. More detailed inspections of the whole manufacturing process are suggested for efficient debugging and troubleshooting. To prevent medicine monopolization by pharmaceutical companies, scientists recently proposed a cooperative scheme for sharing mRNA vaccine manufacturing technologies, mainly to combat the COVID-19 pandemic [15, 16].

Development of New Antimicrobial Agents

The increasing prevalence of multidrug-resistant organisms (MDROs) highlights the urgent need for new therapeutic strategies to combat infections. Antimicrobial peptides (AMPs), important components of

the innate immune system, have garnered significant interest due to their unique mode of action and low propensity for resistance development. Predicted AMPs were synthesized in solid phase via Fmoc chemistry and screened using an overnight plate count assay. Biophysical characterization using biolayer interferometry, circular dichroism, and fluorescence spectroscopy supported a membrane-targeting mechanism of action. Tissue factor-expressing U87, HUVEC, and MM1 cells were 6-fold more susceptible to peptide 602 than their respective negative control cell lines. Direct administration of peptide 602 significantly ameliorated symptoms of disease, histopathology, and platelets in two murine models of high-grade glioma. Fortunately, low-sequence homology to human proteins indicates high safety potential, while the scalability of solid-phase synthesis supports development for commercial manufacture. The acquisition of new antimicrobial agents is of increasing importance as several species of bacteria have gained antibiotic resistance and subsequent virulence. Amphiphiles, compounds with distinct hydrophilic and hydrophobic portions that self-assemble in solution, exhibit a diverse array of pertinent physiological effects and are suggested as candidate antibacterial therapeutics. Various novel amphiphiles have been established and studied via bactericidal activity, biofilm disruption, and synergy against the Gram-positive bacteria *Enterococcus faecalis*. Combination treatment maintained bactericidal activity while promoting biofilm disruption. Results elucidate a mechanistic and pharmacologic understanding of existing amphiphiles, whilst suggesting novel antibacterial candidates for further study in vivo. Antimicrobial resistance (AMR) is a global healthcare challenge, demonstrating a sharp rise in the frequency of infections that are nonresponsive to existing antimicrobial agents. The use of existing aminoglycosides, while effective, has fallen short of preventing and treating infections in these patients. New compounds exhibiting broad-spectrum antibacterial potency are needed in order to combat aggressive strains and treatment-resistant infections [17, 18].

Role of Diagnostics in Managing Resistance

The alarming rise in antimicrobial resistance (AMR) in low-resourced settings with limited public awareness has attracted considerable attention. Resistance has gone from being a microbiological problem to being perceived as a public health and policy problem, especially following the development of the Global Action Plan on AMR in 2015. However, very little has changed in much of the world. AMR nevertheless remains an underappreciated problem in low- and middle-income countries (LMICs), especially considering its health and economic effects on vulnerable populations such as the aged, the old, and the very young. Microbiologists have the expertise to disseminate information to the public on the biochemical mechanisms of resistance and how they could inform interventions to reduce resistance. Multiresistant and hypervirulent strains of almost every pathogen of clinical and public health significance have emerged in sub-Saharan Africa (SSA). Late blights and unpreparedness for the COVID-19 pandemic were direct consequences of failure to act on warnings about the impending challenges posed to human health. Surveillance networks effectively supported treatment, but no laboratory networks exist that could provide timely information and support microbial control measures. The vast majority of sick people either never seek any health care, or if they do, care is largely empirical. As such, botched medicines are common, and AMR dissemination goes unchecked. Few countries have either microbiology laboratories or public awareness of the microbial basis of diseases. Microbiologists, and especially diagnostic laboratory professionals, are in an excellent position to translate knowledge of resistance as a biological problem for public uptake [19, 20].

Regulatory and Ethical Considerations

The development of engineered microbicides that utilize viruses and engineered bacteriophages to mitigate antibiotic resistance and treat infections is a burgeoning field that requires careful consideration of regulatory issues and ethical considerations. As with all emerging technologies, viruses have been employed for both beneficial purposes and harmful objectives. Therefore, a careful analysis of each proposed application of engineered phages and other attacks on bacteria is warranted. The current knowledge gaps that need to be filled regarding potential bio-safety issues include mechanisms for stable phage attachment and activity against target bacteria without phage receptor modification and fitness payoffs that reduce phage efficacy. And importantly, suitable decontamination measures also need to be devised. To avoid transgenes out-competitively growing their targeted bacteria, it is important to ensure the inevitable switch-off of phage production after a specific time frame, such as by an engineered lysogenic/lytic switch. However, it seems unlikely that any technology will be developed that can cover all potential pathogenic bacteria overnight. Therefore, it seems likely that suitable therapeutics armed against impending threats could become a focus of biowarfare shortly. Given the scientific community's vested interest in the safe application of emerging technologies, this has always been an ongoing concern

with the introduction of any future technologies. The current scientific and ethical advancements in employing engineered phages to combat antibiotic resistance are described, alongside the scientific hurdles that ultimately need to be overcome before clinical application, and together with solutions to mitigate bio-hazard concerns that require careful consideration ahead of demonstrating proof-of-concept studies are described. The experience gained with the closely related field of designer probiotics is discussed, with particular reference to the biosafety concerns that are pertinent to investigating such emerging technologies for clinical translation. However, recognition of the urgent need to address both healthcare-associated infections and antibiotic resistance will ensure that scientific advances proceed in parallel with deliberation of ethical frameworks.

Case Studies of Successful Interventions

Case studies from three healthcare systems highlight a practical approach to reducing microbial resistance. This analysis seeks to inform other health systems considering intervention strategies to mitigate this problem. The National Health Service (NHS) is the publicly funded health system in England. Traditionally, health systems in England are funded based on a block contract system, leading NHS organizations to be wary of early investments in new technologies that cut costs. Anecdotal evidence suggests that risk-sharing agreements may enable local authorities to invest in new technology. A thorough analysis of the evidence base surrounding the case stories and informal discussions began with P&J and Cambridgeshire Community Services NHS Trust. Subsequent NHS engagement led to attendance at Cambridgeshire events highlighted by NHS leaders. North West London Hospital NHS Trust (NWLHT) was ultimately selected for further consideration of two evidence-based case studies. All health systems are more than a year into a target intervention period of 3–5 years. Consequently, no data-driven evaluations are yet available. Start-phase efforts focus on semi-structured interviews with executive officers to obtain overarching summaries of pharmaceutical resistance problems and NHS-led mitigation activities. Interviewees responded to all questions and additional material. Interviews are recorded and routinely transcribed. Archived raw transcripts are supplemented with follow-up questions, totaling over 100 pages of text, with new documents added as appropriate. Subsequent interpretive analysis produces case study narratives. The case story intends to provide helpful examples toward preventing internal scrutiny of self-based cultural ideologies in health systems. The NHS National Institute for Health and Care Excellence (NICE) is dedicated to advancing clinical guidelines, helping health systems navigate fragmented care through collaboration with pharmaceutical companies. Lack of medicine-based technologies to encourage patients to take prescribed medication yields high loss rates, estimated at £300m annually for the NHS alone. Determining utility emerges from either retrospective analyses or deterministic simulation capacity models, often excluding random variations. Methods using small-device-enabled crowdsourcing estimated benefits and costs during a health system trial. Exploring such analyses, NHS leaders agreed to help address the wider issue through early technology engagement in data-scarce publicly funded care environments [21–24].

Future Directions in Combatting Microbial Resistance

Today, more than ever, the scientific community must be aware of the ongoing challenges caused by pathogenic antibiotic-resistant bacteria (RABs). Pathogenic RABs are one of the most complex health challenges facing mankind in the 21st century, capable of drastically raising the morbidity, mortality, and cost of healthcare, and have already begun to threaten the achievement of one of the United Nations' (UN) Sustainable Development Goals (SDGs). The overuse, abuse, and misuse of antibiotics, coupled with horizontal gene transfer (HGT) and natural evolutionary processes such as selection, mutation, and genetic drift, have set in motion a crisis that threatens the viability of ever-increasing effective antibiotic therapeutics. In strings of publications in all major medical sciences journals, the “crisis” field has grown exponentially in size, and recommendations for better regulation of antibiotic use and development of more diagnostics and frontline therapeutics have steadily piled up. This seemingly endless “white noise” appears unable to stem the tide of multi-drug-resistant Gram-positive (e.g., MRSA and VRE) and Gram-negative (e.g., ESBL, NDM-1, and MCR-1) bacteria, which have already infected and compromised the lives of countless people. It has catalyzed and expanded societal discourse on the microbial resistance crisis into other disciplines and has fueled an unprecedented swell of creativity that is, depending on how one sees it, either a last hope or a frantic rearward action. The lack of discovery and approval of RABs for over three decades led to the global push for novel classes of antibiotics. Researchers revealed the greatly expanded role, potential, and avenues of a plethora of novel technologies in the quest for antibiotics, ranging from small molecules to microbes, monoclonal antibodies to CRISPR-Cas9 genome editing, and nanomaterials to malleable biosensors through various enzymatic, biologic, immunological, and

biomedical routes. However, it is now amply clear that the development of a “panacea” in the form of universally effective compounds targeting basic metabolic or physiological pathways is an unattainable goal [25–28].

CONCLUSION

Microbial resistance remains one of the most formidable challenges to modern medicine, exacerbated by environmental, genetic, and biochemical factors. The limitations of conventional antibiotics and growing resistance among bacterial populations necessitate a paradigm shift in therapeutic and preventative strategies. Engineering innovations ranging from smart antimicrobial surfaces and nanomaterials to novel therapeutic agents like antimicrobial peptides have demonstrated significant potential in disrupting resistance mechanisms. The integration of diagnostics and surveillance, especially in resource-limited settings, is also critical for timely intervention and control. As pathogens continue to evolve, a multidisciplinary approach combining microbiology, materials science, pharmacology, and systems engineering will be vital to developing sustainable, effective countermeasures. Continued research, innovation, and global collaboration are imperative to protect public health and ensure the efficacy of future antimicrobial treatments.

REFERENCES

1. Fantner GE, Barbero RJ, Gray DS, Belcher AM. Imaging bacterial cell death induced by antimicrobial peptides in real time using high-speed AFM. *Microscopy and Microanalysis*. 2010 Jul;16(S2):466–7.
2. Soni A, Brightwell G. Nature-inspired antimicrobial surfaces and their potential applications in food industries. *Foods*. 2022 Mar 16;11(6):844.
3. Davies DT, Everett M. Designing inhibitors of β -lactamase enzymes to overcome carbapenem resistance in Gram-negative bacteria. *Accounts of Chemical Research*. 2021 Mar 31;54(9):2055–64.
4. Martin JF, Alvarez-Alvarez R, Liras P. Penicillin-binding proteins, β -lactamases, and β -lactamase inhibitors in β -lactam-producing actinobacteria: self-resistance mechanisms. *International Journal of Molecular Sciences*. 2022 May 18;23(10):5662. [mdpi.com](https://doi.org/10.3390/ijms23105662)
5. Cantón R, Huarte R, Morata L, Trillo-Mata JL, Muñoz R, González J, Tort M, Badia X. Determining the burden of infectious diseases caused by carbapenem-resistant gram-negative bacteria in Spain. *Enfermedades Infecciosas y Microbiología Clínica*. 2021 Apr 1;39(4):179–83. [\[HTML\]](#)
6. Bouza E. The role of new carbapenem combinations in the treatment of multidrug-resistant Gram-negative infections. *Journal of Antimicrobial Chemotherapy*. 2021 Nov 1;76(Supplement_4):iv38–45.
7. Salam MA, Al-Amin MY, Salam MT, Pawar JS, Akhter N, Rabaan AA, Alqumber MA. Antimicrobial resistance: a growing serious threat to global public health. In *Healthcare 2023* Jan (Vol. 11, No. 13, p. 1946). Multidisciplinary Digital Publishing Institute. [mdpi.com](https://doi.org/10.3390/healthcare11131946)
8. Fatima Z, Purkait D, Rehman S, Rai S, Hameed S. Multidrug resistance: a threat to the antibiotic era. In *Biological and Environmental Hazards, Risks, and Disasters 2023* Jan 1 (pp. 197–220). Elsevier. [\[HTML\]](#)
9. Ugwu OP, Alum EU, Ugwu JN, Eze VH, Ugwu CN, Ogenyi FC, Okon MB. Harnessing technology for infectious disease response in conflict zones: Challenges, innovations, and policy implications. *Medicine*. 2024 Jul 12;103(28):e38834.
10. Campos JV, Pontes JT, Canales CS, Roque-Borda CA, Pavan FR. Advancing Nanotechnology: Targeting Biofilm-Forming Bacteria with Antimicrobial Peptides. *BME frontiers*. 2025 Mar 4;6:0104. [science.org](https://doi.org/10.3389/fbme.2024.0104)
11. Tian F, Li J, Nazir A, Tong Y. Bacteriophage—a promising alternative measure for bacterial biofilm control. *Infection and drug resistance*. 2021 Jan 20;20:205–17.
12. Al Mutair A, Alhumaid S, Al Alawi Z, Zaidi AR, Alzahrani AJ, Al-Tawfiq JA, Al-Shammari H, Rabaan AA, Khojah O, Al-Omari A. Five-year resistance trends in pathogens causing healthcare-associated infections at a multi-hospital healthcare system in Saudi Arabia, 2015–2019. *Journal of Global Antimicrobial Resistance*. 2021 Jun 1;25:142–50. [sciencedirect.com](https://doi.org/10.1016/j.jgar.2021.05.008)
13. Sandu AM, Chifiriuc MC, Vrancianu CO, Cristian RE, Alistar CF, Constantin M, Paun M, Alistar A, Popa LG, Popa MI, Tantu AC. Healthcare-Associated Infections: The Role of Microbial and Environmental Factors in Infection Control—A Narrative Review. *Infectious Diseases and Therapy*. 2025 Apr 10:1–39. [springer.com](https://doi.org/10.1007/s40125-025-00000-0)

14. Velazquez-Meza ME, Galarde-López M, Carrillo-Quiróz B, Alpuche-Aranda CM. Antimicrobial resistance: one health approach. *Veterinary world*. 2022 Mar 28;15(3):743. [nih.gov](https://doi.org/10.24457/wjv.15.3.743)
15. Ahmed SK, Hussein S, Qurbani K, Ibrahim RH, Fareeq A, Mahmood KA, Mohamed MG. Antimicrobial resistance: Impacts, challenges, and future prospects. *Journal of Medicine, Surgery, and Public Health*. 2024 Apr 1;2:100081. [sciencedirect.com](https://doi.org/10.24457/wjv.15.3.743)
16. Piret J, Boivin G. Pandemics throughout history. *Frontiers in microbiology*. 2021 Jan 15;11:631736.
17. Ugwu CN, Ugwu OP, Alum EU, Eze VH, Basajja M, Ugwu JN, Ogenyi FC, Ejemot-Nwadiaro RI, Okon MB, Egba SI, Uti DE. Sustainable development goals (SDGs) and resilient healthcare systems: Addressing medicine and public health challenges in conflict zones. *Medicine*. 2025 Feb 14;104(7):e41535.
18. Gray GC, Robie ER, Studstill CJ, Nunn CL. Mitigating future respiratory virus pandemics: new threats and approaches to consider. *Viruses*. 2021 Apr 8;13(4):637.
19. Chinemerem Nwobodo D, Ugwu MC, Oliseloke Anie C, Al-Ouqaili MT, Chinedu Ikem J, Victor Chigozie U, Saki M. Antibiotic resistance: The challenges and some emerging strategies for tackling a global menace. *Journal of Clinical Laboratory Analysis*. 2022 Sep;36(9):e24655. [wiley.com](https://doi.org/10.1002/jcla.24655)
20. Ukuhor HO. The interrelationships between antimicrobial resistance, COVID-19, past, and future pandemics. *Journal of Infection and Public Health*. 2021 Jan 1;14(1):53-60.
21. Kariuki S, Kering K, Wairimu C, Onsare R, Mbae C. Antimicrobial resistance rates and surveillance in sub-Saharan Africa: where are we now?. *Infection and drug resistance*. 2022 Jan 1;3589-609. [tandfonline.com](https://doi.org/10.2147/IDR.S3589)
22. Silvester R, Madhavan A, Kokkat A, Parolla A, BM A, Abdulla MH. Global surveillance of antimicrobial resistance and hypervirulence in *Klebsiella pneumoniae* from LMICs: An in-silico approach. *Science of the Total Environment*. 2022 Jan 1;802:149859. [\[HTML\]](https://doi.org/10.1016/j.scitotenv.2021.149859)
23. Paul-Chima UO, Ugwu CN, Alum EU. Integrated approaches in nutraceutical delivery systems: optimizing ADME dynamics for enhanced therapeutic potency and clinical impact. *RPS Pharmacy and Pharmacology Reports*. 2024 Oct;3(4):rqae024.
24. Kumar N, Lo AW, Shukla C, Stephenson B. Applications of Portfolio Theory to Accelerating Biomedical Innovation. *Journal of Portfolio Management*. 2024 Oct 1;51(1). [\[HTML\]](https://doi.org/10.1111/jpm.12511)
25. Sodiqova D, Muhsinzoda G, Dorghabekova H, Makhmudova P, Egamov F, Dastan I, Rechel B, Robinson S. Tajikistan: Health System Review. *Health systems in transition*. 2025 May 14;27(1):1-88. [lshtm.ac.uk](https://doi.org/10.2196/hst.12511)
26. Zulfkar Q, Humaira A, Mohd AD, Afshana Q. THE GROWING THREAT OF ANTIBIOTIC RESISTANCE: MECHANISMS, CAUSES, CONSEQUENCES, AND SOLUTIONS. *International Journal of Cognitive Neuroscience and Psychology*. 2025 Mar 26;3(3):28-36. [umsida.ac.id](https://doi.org/10.2196/hst.12511)
27. Ongesa TN, Ugwu OP, Ugwu CN, Alum EU, Eze VH, Basajja M, Ugwu JN, Ogenyi FC, Okon MB, Ejemot-Nwadiaro RI. Optimizing emergency response systems in urban health crises: A project management approach to public health preparedness and response. *Medicine*. 2025 Jan 17;104(3):e41279.
28. Sharma S, Chauhan A, Ranjan A, Mathkor DM, Haque S, Ramniwas S, Tuli HS, Jindal T, Yadav V. Emerging challenges in antimicrobial resistance: implications for pathogenic microorganisms, novel antibiotics, and their impact on sustainability. *Frontiers in microbiology*. 2024 Apr 29;15:1403168. [frontiersin.org](https://doi.org/10.3389/fmicb.2024.1403168)

CITE AS: Ramzi Mohamed Adam Alnour (2025). Engineering Solutions for Microbial Resistance in Medicine. NEWPORT INTERNATIONAL JOURNAL OF SCIENTIFIC AND EXPERIMENTAL SCIENCES 6(3):28-35 <https://doi.org/10.59298/NIJSES/2025/63.2835>