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Evaluating Alternative Therapies to Combat Antimicrobial Resistance in Comparison to Traditional Treatments

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ABSTRACT

Antimicrobial resistance (AMR) is when microorganisms, including bacteria, viruses, fungi, and parasites, stop responding to antimicrobial medicines, making infections and other illnesses rather difficult to treat. AMR poses a significant challenge to global health that threatens the very essence of the standard equitable treatment of microbes, hence causing extended durations of illnesses, more expenses in healthcare, and higher mortality rates. This research investigates how effective alternative therapies like phage therapy, antimicrobial peptides, and probiotics are in fighting AMR infections versus mainstream antibiotic treatments. Additionally, this research aims to conduct a comprehensive literature review using existing data and previous studies to point out weaknesses in current care methods. This can be used to assess the effectiveness of alternative therapies through the development of a theoretical framework. Prior findings suggest alternative therapies show a promising ability that can target resistant infections, overcoming the challenges associated with traditional treatments. Furthermore, this research also examines factors that contribute to the spread of AMR, including inadequate infection control and antibiotic misuse. The findings from this study will provide significant public health implications, giving policymakers and healthcare providers crucial insight into improving infection control practices as well as promoting effective antibiotic use. Through the findings of this study, there could be an expansion of possible, more efficient treatments that may contribute to the global effort to curb AMR and ensure antimicrobial resistance can stop posing a significant threat worldwide.

INTRODUCTION

The growing threat of antimicrobial resistance necessitates the exploration of alternative therapies, which may be found to be more effective and sustainable solutions in comparison to the traditional antibiotic treatments. Antibiotics have been the primary method for treating bacterial infections since they were discovered in 1928 by bacteriologist Alexander Fleming. The discovery of Penicillin started the golden age of antibiotic discovery between 1950-1960, which gave rise to some of the most commonly used antibiotics today. However, there has been a major decline in antibiotic discoveries and development since, due to the evolution of bacterial resistance in many human pathogens leading to the antimicrobial resistance crisis today (Gajdacs and Albericio, 2019).

Although the use of antibiotics has allowed numerous modern medical techniques and procedures to be possible, it has also become the cause of some untreatable infections due to the rise of AMR (Hutchings et al., 2019). Combination therapies and optimizing existing antibiotics have been attempted, but face limitations such as if microbes become resistant to one of the antibiotics, the synergistic impact of the combination would also be compromised leading to strategy failure (Fuente-Nunez et al., 2023).

Recent research has explored various alternative therapies such as phage therapy, antimicrobial peptides, and probiotics. These methods show promise in addressing AMR but face challenges such as funding, regulatory barriers, and public perception (Singha et al., 2024). Alternative therapies are expected to provide targeted and efficient solutions to combat AMR. These therapies may offer long-term benefits by reducing reliance on antibiotics and minimizing resistance development. Insights from this research could inform policymakers and healthcare providers to improve infection control practices and promote effective antibiotic use.

LITERATURE REVIEW

Antibiotic resistance can occur through natural or acquired forms. It can be expressed in the organisms as innate or mediated if they have the genes for resistance already present in the bacteria but would have resistance levels activated after antibiotic treatment (Reygaert, 2018). AMR development occurs through several mechanisms in bacterial structures such as the limitation of drug uptake, drug target modification or degradation, inactivation of certain drugs as well as efflux. All these mechanisms are especially utilized by gram negative bacteria than gram positive since the latter lacks an outer membrane- an essential barrier that limits the passage of antibiotics into the bacterial cell (Munita and Arias, 2016).

Antibiotics have been the primary treatment for bacterial infections since their discovery, however, their constant misuse has given rise to the increase of resistance, which is a major public health crisis worldwide making the treatment of bacterial infections challenging (Pabst, 2023). More than 4.95 million deaths occurred in association to antibiotic resistance in 2019 (Jangra et al, 2025). These deaths occur when patients stop taking their antibiotics prematurely, creating resistant bacteria, or when modern medical procedures become riskier due to infections that are harder to treat, leaving critically ill patients on their death beds. In some cases, the inaccessibility to healthcare can lead to death when infections aren't treated in time (Murray, 2019).

Since the development of new antibiotics has slowed over the years, there are fewer and fewer options left for combating resistant strains. Existing antibiotics can also be optimized through adjusting dosages and treatment durations, but due to the complex nature of resistance mechanisms, there is no lasting or reliable solution, leading to an increasingly urgent and vital need for the development of safe, efficient, and alternative novel antimicrobial agents in the medical and healthcare field (Zhu et al., 2025).

ALTERNATIVE THERAPIES

Alternative therapies can be therapeutic or preventative, meaning they can be used directly in antimicrobial resistance, or they can be used to prevent the need of antibiotics and therfore the effect of antimicrobial resistance. There are several existing alternative therapies which are not utilized as much as they should and some of them include:

Phage therapy, also known as bacteriophage therapy, involves the use of viruses called bacteriophages to target and destroy specific bacteria. It was discovered and used before the rise of antibiotics between the early 1920s to the late 1930s to treat infectious diseases (Aswani & Shukla, 2021)-before antibiotics became widely available. In recent years, due to its promising outcomes and safety, phage therapy has re-emerged as a potential alternative to antibiotics, particularly in addressing antimicrobial resistance. As bacteria become increasingly resistant to antibiotics, phage therapy provides a directed solution due to its ability to specifically target and kill strains of bacteria, including biofilm cells, without harming the host microbiome and exhibiting minimal toxicity (Zrelovs et al., 2021). Moreover, phages are naturally occurring and can evolve alongside bacteria, potentially overcoming the bacterial resistance. Recent studies suggest that phage therapy may be more effective when administered before antibiotic treatment (Suh et al., 2022). Bacteria that develop resistance to phages often become weaker, allowing antibiotics to work more effectively. Using phage therapy could, therefore, help improve the effectiveness of antibiotics and delay the development of resistance over time.

Phage therapy is considered relatively safe due to its highly specific nature, which leaves all untargeted cells unharmed. In comparison, broad-spectrum antibiotics kill both harmful (targeted) and normal flora (untargeted). This makes phage therapy a biologically innovative tool

for dealing with AMR. Additionally, while bacteria can develop resistance to phages, an advantage of phage therapy is that phages can evolve alongside bacteria, potentially regaining their effectiveness against resistant strains.

Despite these advantages, phage therapy is not yet widely utilized due to regulatory and practical struggles. One of the key challenges lies in its highly personalized nature- phage formulations often need to be tailored to individual infections. This makes large scale production and standardization difficult. Nevertheless, there are notable successes. A 2017 case reported by Schooley et al. (2017), involving a 69-year-old diabetic patient suffering from a life-threatening multi-drug--resistant *Acinetobacter baumanni* infection. After all antibiotic treatments failed and the patient's condition deteriorated, personalized phage therapy was given to the patient. The infection was successfully cleared, and the patient tolerated the treatment well. This case highlights the potential for phage therapy to serve as life-saving measure when traditional antibiotics no longer work.

However, not all clinical efforts have proven effective. For instance, a 2017 study conducted in Bangladesh tested the oral administration of a phage preparation in children with *E. coli*-related diarrheal disease (Sarker et al., 2017). While the treatment was safe and did not disrupt the gut microbiomes, the phages failed to replicate sufficiently in the gut, and no clinical benefits were observed compared to standard (rehydration) therapy. This case demonstrates a limitation: oral delivery may be ineffective in cases where bacterial load is low, or phage replication conditions are not optimum. Another concern about phage therapy is the endotoxins released by the bacteria when they die after being attacked by phages, which may trigger inflammatory responses. Additionally, repeated or high-dose exposure to phages could provoke

immune responses in humans, leading to the production of antibodies (immunogenicity). However, advances in genetic engineering offer promising solutions to these challenges. Phages can be modified to reduce immunogenicity and enhance effectiveness-broadening their potential uses (Gosh et al., 2019).

As research on phage therapy progresses, there is growing hope that it will become a more widely accessible and routine treatment option. Further clinical trials and approval will be essential to establish its broader applicability. Phage therapy holds the promise to complement or even replace antibiotics in specific cases. Increased investment in research and global collaboration will be crucial for advancing this field. By overcoming current challenges, the medical community can reap the full potential of phage therapy, offering new hope in the fight against drug-resistant infections.

Antimicrobial Peptides (AMPs), which are defense molecules found in complex organisms that show promise against antibiotic-resistant bacteria. They target a wide range of microbes, including bacteria, fungi, and viruses, by disrupting their membranes or interfering with vital functions like protein production and DNA replication. Since bacterial membranes carry a negative charge while AMPs are positively charged, they are naturally attracted to bacterial surfaces (Berger & Loewy, 2024), allowing them to destroy their membranes, interfere with critical functions like DNA replication, or enhance antibiotic effectiveness by increasing membrane permeability.

AMPs have key benefits over traditional antibiotics. Their ability to attack bacteria in multiple ways makes resistance development less likely. They also work against drug-resistant microbes and can boost the immune system's response.

Despite their potential, AMPs face challenges. The body's enzymes can quickly break them down, reducing effectiveness. Some AMPs can be toxic to human cells in high doses, and their production is costly compared to standard antibiotics. One of the biggest challenges with AMPs is that more research is needed to ensure they are safe, effective, and can be used in real medical treatments. Getting regulatory approval and finding affordable ways to manufacture them are also major struggles.

Compared to bacteriophages, which only target specific bacteria, AMPs offer broader effectiveness. However, phages self-replicate at infection sites, potentially requiring fewer doses, whereas AMPs must be continuously administered. The best choice depends on the infection type. AMPs also offer advantages over conventional antibiotics by targeting bacteria through multiple mechanisms, making resistance less likely. While AMPs alone are promising, studies suggest combining them with traditional antibiotics enhances their effectiveness. As antibiotic resistance rises, AMPs represent a valuable strategy for future treatments (Gani et al., 2025).

Probiotics, which are live microorganisms that when taken in adequate quantities, provide a health benefit to the host by maintaining healthy balance of microbes to prevent infections and reduce antibiotic resistant bacteria. Probiotics are typically microorganisms from the genera Lactobacillus, Bifidobacterium, and Saccharomyces as part of either dietary supplements or fermented foods, which are receiving increased emphasis as a complementary strategy to reduce AMR because they have the ability to manage and restore a balanced microbial population, particularly in the gastrointestinal tract. The ways in which probiotics are associated with AMR can be classified as multiple mechanisms involved. A key mechanism is competitive exclusion

where probiotics take the binding sites on mucosal surfaces, thus preventing the pathogenic microbe from colonizing (Bron et al., 2012).

Probiotics also produce antimicrobial substances, such as bacteriocins, organic acids, and hydrogen peroxide, which prevent pathogenic microbes from growing. Furthermore, probiotics can enhance the immune system, which promotes clearance of infection without the need for (high) antibiotic use. After contact with antibiotics, where gut microbes are often disrupted, probiotics may help restore balance and thus reduce the risk of opportunistic infection by microbes such as Clostridium difficile (Goldenberg et al., 2017). In addition, new research says that certain probiotics might inhibit the transfer of antibiotic resistance genes in bacterial populations in the gut, which is a new way to combat the spread of resistance (Zhao et al., 2020). Probiotics have been used in various medical contexts, most notably in the prevention of antibiotic-associated diarrhea, enhancing immune system function, and in the treatment of certain gastrointestinal diseases, such as irritable bowel syndrome and inflammatory bowel disease. Some strains have been used as adjunctive therapy for respiratory and urogenital infections.

Some advantages of probiotics include their natural origins, relatively low incidence of adverse events, easy administration, and confirmed benefit in some clinical situations. Lactobacillus rhamnosus GG, for example, has been shown to be effective in reducing diarrhea in children. However, they do have disadvantages. The benefits of probiotics are strain specific, and not all available products are effective. Further, there is a possibility of infection in immunocompromised patients, especially with systemic use and concern about the extent of non-standardized and unregulated commercial probiotic products (Sanders et al., 2018). Overall, probiotics help reduce AMR by acting as preventive and adjunctive therapies that will reduce the

frequency and severity of infection and thus reduce the overall use of antibiotics and reduce the selective pressure that fosters resistant bacterial populations. Furthermore, the ability of probiotics to reduce resistance gene prevalence in the greater microbial community adds an additional layer of support in tackling AMR (Zhao et al., 2020). While probiotics should not substitute antibiotics when they are required medically, they are an exciting adjunct strategy in the global fight against antimicrobial resistance.

CONCLUSION

The alternative methods mentioned above are only a few of the currently discovered methods that could be used with, or without antibiotics, to reduce AMR globally. There could be many other, more effective methods that have not even been discovered yet, due to the lack of urgency being given to AMR in general. The reason some of these aren't already primary methods of battling bacterial infections instead of antibiotics, despite proven to be less harmful, is because pharmaceutical and research companies do not have enough resources or funding for something that isn't deemed a global crisis, even when it has been declared to be one by the World Health Organization since 2014 whereby Dr. Keiji Fukuda, WHO's Assistant Director-General for Health Security mentioned that "without urgent, coordinated action by many stakeholders, the world is headed for a post-antibiotic era, in which common infections and minor injuries which have been treatable for decades can once again kill." This statement of urgency was made over a decade ago and yet the crisis continues with no definite solution in sight. Antimicrobial resistance was not a minor issue then, and it certainly isn't one now, therefore, we need to take a stand immediately and build on the existing solutions before more innocent lives are lost due to the lack in advancement of medicine despite having available resources and technology today.

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