FUDMA Journal of Sciences (FJS)
ISSN online: 2616-1370
ISSN print: 2645 - 2944
Vol. 10 No. 13, July, 2026, pp 298 – 302
DOI: https://doi.org/10.33003/fjs-2026-1013-5918

Alternative Approaches to Antibiotics: Phage Therapy, Antimicrobial Peptides, and Phytotherapeutics

***[1,2]Abdullahi Haruna, [3]Kabiru Haliru Ahmad, [3]Paul Habila Mamman, [3]James Satvil Dalis, [3]Muibat Taiye Salawudeen and [1]Ndidi Uche Samuel**

[1]Department of Biochemistry, Faculty of Life Sciences, Ahmadu Bello University, Zaria-Nigeria
[2]Department of Human Nutrition and dietetics, Faculty of Food Science and Technology, Federal University of Agriculture, Mubi, Nigeria
[3]Department of Veterinary Microbiology, Faculty of Veterinary Medicine, Ahmadu Bello University, Zaria-Nigeria

*Corresponding authors' email: get2haruna@gmail.com Phone: +2348132150519

Received: 03 July 2026
Accepted: 22 Aug. 2026
Published: 09 Sept. 2026

ABSTRACT

Antibiotic resistance has emerged as a critical threat to global health, food security, and economic stability due to the overuse of antibiotics in human medicine and livestock production. This review examines the mechanisms of antibiotic action and resistance, clinical and environmental consequences of resistance, and evaluates current alternative strategies to conventional antibiotics. Bacteria develop resistance through enzymatic degradation, target modification, reduced membrane permeability, alternative metabolic pathways, and horizontal gene transfer. The misuse of antibiotics in animal breeding as growth promoters has further accelerated the spread of resistant and multidrug-resistant pathogens such as *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, and *Escherichia coli*. To address this crisis, the review discusses three major alternatives: phage therapy, antimicrobial peptides (AMPs), and phytochemicals/plant extracts. Phage therapy offers highly specific bacterial lysis with minimal impact on microbiota, though challenges include narrow host range and phage resistance. AMPs exhibit broad-spectrum antimicrobial, antibiofilm, and immunomodulatory activities, with several FDA approved peptides already in clinical use, but limitations include high minimum inhibitory concentrations and potential toxicity. Plant-derived phytochemicals demonstrate antibacterial and efflux pump inhibitory effects and show synergistic potential when combined with antibiotics. The findings suggest that a multifaceted approach combining prudent antibiotic stewardship with investment in phage therapy, AMPs, and plant-based compounds is essential to mitigate resistance and ensure sustainable treatment options. Further *in vivo* studies and clinical trials are needed to optimize efficacy, safety, and large-scale application of these alternatives.

Keywords: Antibiotic resistance, Phage therapy, Antimicrobial peptides, Phytochemicals, Multidrug resistance, Alternative therapies

INTRODUCTION

An antibiotic is any natural or synthetic compound that either kills bacteria or stops their growth (Lewis, 2020). These drugs work by targeting specific bacterial structures such as the cell wall (Kobras *et al*., 2020), cytoplasmic membrane (Heesterbeek *et al*., 2021), protein synthesis pathways (Stokes *et al*., 2019), or nucleic acids like RNA and DNA, while some affect multiple targets at once (Grandclaudon *et al*., 2020). Since antibiotics were discovered, many new compounds have been developed and their importance in treating bacterial infections in humans and animals is well established. In the U.S., about 80% of antibiotics are used in livestock production as feed additives and growth promoters to improve yield and quality (Ventola, 2015). Unfortunately, a large portion of these drugs are excreted in animal waste and eventually reaches groundwater or is applied to soil as fertilizer (Ventola, 2015). This practice has led to environmental contamination and the rise of resistant and multidrug-resistant bacteria (Ventola, 2015). Bacterial resistance develops mainly through enzyme-mediated antibiotic breakdown (Reis *et al*., 2020), alteration of antibiotic targets (Schaenzer & Wright, 2020), reduced membrane permeability (Xu *et al*., 2020), and alternative metabolic pathways (Pollock *et al*., 2020). Resistance also spreads rapidly between bacteria through horizontal gene transfer by conjugation, transduction, and transformation, making it a global health threat (Lima *et al*., 2020).

Antibiotic resistance is defined as the ability of bacteria to survive the inhibitory or lethal effects of an antimicrobial agent to which they were previously susceptible (Palma *et al*., 2020). The problem affects both human and veterinary medicine, and studies continue to report increasing resistance in bacterial strains (Mbarga *et al*., 2020; Rabello *et al*., 2020). In hospital settings, the most resistant pathogens include *Staphylococcus aureus*, coagulase-negative staphylococci, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Escherichia coli*, *Enterobacter* spp., *Enterococcus* spp., and *Acinetobacter* spp. (Cleven *et al*., 2006; Antoinette & Dieudonne, 2020). Many of these organisms cause common infections and are frequently involved in nosocomial infections (Cleven *et al*., 2006). Researchers agree that controlling resistance requires judicious antibiotic use, prescriptions limited to professionals, routine antibiograms before treatment, and development of new compounds effective against resistant strains (Cleven *et al*., 2006; Lima *et al*., 2020; Palma *et al*., 2020).

Bacterial Antimicrobial Resistance was directly responsible for 1.27 million deaths in 2019 and contributed to nearly 5

million deaths globally (WHO, 2023). WHO reports resistance rose in more than 40% of bacteria-drug combinations tracked between 2018 and 2023. WHO notes the Research and Development pipeline for new antibiotics remains thin and access to new and existing treatments is still a challenge (WHO, 2018). The "silent pandemic" is driven by misuse and overuse of antibiotics in humans, animals and agriculture, plus poor infection control (WHO, 2018, WHO, 2023). Most papers review phage therapy OR AMPs OR phototherapeutics separately. There are very few integrative reviews comparing all 3 on resistance risk, manufacturing, and clinical readiness Modern phage practice emphasizes combination approaches, but literature rarely maps how phage, AMPs, or Photodynamic therapy (PDT) could be used with antibiotics to restore susceptibility or target biofilms (WHO, 2023) [*]. Clinical trials also struggle with recruitment because patients must carry strains covered by the product host range (Ghanavati. 2024). Bring phage therapy, AMPs, and phototherapeutics under one framework for direct comparison. Map common barriers including resistance evolution, immune interactions, manufacturing/standardization, and regulatory hurdles. Highlight combination strategies and the need for standardized protocols and regulatory harmonization to support stewardship (Di Pierro. 2025). Address AMR burden with 1.27M direct AMR deaths in 2019 and a thin antibiotic pipeline, alternatives must be evaluated for deployability, not just lab activity.

Resistance to Antibiotics and Current Issues

Antibiotic resistance is now one of the greatest threats to global health, food security, and economic development (World Health Organization [WHO], 2019). Infections such as pneumonia, tuberculosis, gonorrhea, and salmonellosis are becoming harder to treat as drugs lose effectiveness (WHO, 2019). This affects all age groups and populations worldwide, leading to longer hospital stays, higher healthcare costs, and increased mortality (WHO, 2019; Jit *et al*., 2020). Current estimates attribute 700,000 deaths per year to antibiotic resistance, including 230,000 from multidrug-resistant tuberculosis (WHO, 2019). If no action is taken, drug-resistant infections could cause 10 million deaths annually by 2050 and economic damage comparable to the 2008–2009 financial crisis. Resistance could also push up to 24 million people into extreme poverty by 2030 (WHO, 2019). To slow this trend, researchers recommend more careful use of antibiotics in both agriculture and human medicine, limiting their use to necessary cases under prescription and after antibiogram testing (Doidge *et al*., 2020; Mbarga *et al*., 2020; Morel *et al*., 2020; WHO, 2020). A major part of the solution also lies in new therapeutic strategies using bioactive compounds such as antimicrobial peptides, nanoparticles, antibodies, cytokines, phytochemicals, bacteriophages, and probiotics (Morel *et al*., 2020).

Phage Therapy

Phage therapy began in 1919 when Félix d'Hérelle used bacteriophages at the Pasteur Institute in Paris (Dublanchet & Schwartz, 2017). The approach gained attention and by 1925 mass treatments in Brazil at the Oswaldo Cruz Institute showed promising results, with 9,999 out of 10,000 patients recovering (Biacchesi *et al*., 2017). Despite early success, phage therapy was largely abandoned in favor of antibiotics due to easier production and administration (Mireille *et al*., 2020). Today, rising multidrug resistance has renewed interest in phages, though their use remains limited to specialized centers.

Mechanism of Action of Phages and Application in Medicine

Unlike antibiotics that target bacterial structures or metabolism, phages act through a highly specific virus-bacteria interaction and cannot replicate without a host (Koskella & Meaden, 2013). As shown in Figure 1, phages attach to bacteria, inject their DNA, hijack the host machinery to produce viral genomes and proteins, assemble new virions, and lyse the cell to release progeny phages (Jun, 2017). The time between attachment and lysis depends on factors such as adsorption rate, burst size, latency period, bacterial density, and phage-to-bacteria ratio (Van Belleghem *et al*., 2018). Modeling phage pharmacokinetics is complex because it must account for bacterial growth, resistance development, and *in vivo* variables, which may explain past failures of phage therapy (Payne & Jansen, 2001; Skurnik & Strauch, 2006). Despite these challenges, recent studies confirm phage efficacy. A 2018 UK study showed three phages *Escherichia* phage ECP311, *Klebsiella* phage KPP235, and *Enterobacter* phage ELP140were effective against *E. coli*, *K. pneumoniae*, and *Enterobacter cloacae* (Prasanth *et al*., 2018). An FDA-approved Phase I trial with 42 patients having skin ulcers also demonstrated safety and efficacy of eight phage combinations targeting *S. aureus*, *P. aeruginosa*, and *E. coli* (Criscuolo *et al*., 2017; http://clinicaltrials.gov NCT00663091). Another Spanish trial (NCT00937274) found oral phage T4 safe and effective for *E. coli* diarrhea in children, without disrupting gut microbiota (Criscuolo *et al*., 2017). A Polish study of 157 patients with multidrug-resistant infections treated with phages for weeks showed therapeutic benefit and no significant changes in blood, liver, kidney, or inflammatory markers, confirming safety (Międzybrodzki *et al*., 2012). Oral administration of phage T4 to 15 volunteers also showed no adverse effects or antibody development (Bruttin & Brüssow, 2005). However, some bacteria have developed resistance mechanisms against phages (Jorge & Eduardo, 2019; Sadhana *et al*., 2018).

Advantages and Disadvantages of Phage Therapy

Phage therapy has both strengths and limitations. A major drawback is the need for rapid bacterial identification because most phages are highly specific (Mireille *et al*., 2020). This can be addressed using phage cocktails or pre-selected lytic phages for empirical therapy (Nobrega *et al*., 2015). Other concerns include neutralizing antibody production, variable stability under different pH, temperature, UV conditions, and the potential for generalized transduction that could transfer virulence or resistance genes (Jun, 2017). Endotoxin release during bacterial lysis is another issue shared with antibiotics (Jun, 2017). On the positive side, phages spare beneficial microbiota, have low potential for resistance development, can be easily isolated, replicate at infection sites, penetrate tissues, and show antibiofilm activity and bactericidal action independent of antibiotic resistance (Bruttin & Brüssow, 2005; Sadhana *et al*., 2018).

Use of Antimicrobial Peptides (AMP) as Alternatives to Antibiotics

Antimicrobial peptides, also called host defense peptides, are key components of innate immunity in multicellular organisms (Andersson *et al*., 2016). These cationic, amphiphilic peptides, usually 12:50 amino acids long, have diverse structures and broad antimicrobial, antibiofilm, anti-inflammatory, and immunomodulatory activities, making them promising against resistant bacteria (Vasilchenko & Rogozhin, 2019).

Antibacterial Properties of Known AMPs

The Antimicrobial Peptide Database lists 3,201 AMPs, 2,680 of which are antibacterial. Many AMPs are active against both Gram-positive and Gram-negative bacteria (Baltzer & Brown, 2011). Synthetic analogs porcine myeloid antimicrobial peptide (PMAP-36PW and PMAP-36PK) showed strong *in vivo* activity in mice infected with *Salmonella choleraesuis* and *Listeria monocytogenes* by reducing bacterial load and inflammation in liver and lungs, lowering mortality (Zhou *et al*., 2019). Unlike conventional antibiotics, peptides such as melittin, LL:37, and alamethicin increase membrane permeability in *E. coli* spheroplasts (Faust *et al*., 2017). Others inhibit intracellular processes like DNA/RNA synthesis (buforin II, pleurocidin, dermaseptin), protein synthesis (indolicidin, PR-39), or enzymatic activity (Jenssen *et al*., 2006). Several AMPs approved by the FDA, including telavancin, teicoplanin, and daptomycin, are used for resistant infections such as *C. difficile colitis*, MRSA skin and blood infections, and endocarditis (Lei *et al*., 2019).

Combinations of AMP–AMP and AMP–Antibiotics

AMPs are also effective against biofilms. For example, gH625, its analog gH625-GCGKK, and cyclic polymyxin B/gramicidin S combinations inhibit *P. aeruginosa* biofilms (Rončević *et al*., 2019). Combining AMPs with antibiotics also improves outcomes. LL:37 and cecropin (1:7), melittin (2:9) with colistin or imipenem were effective against sensitive and resistant *S. aureus and P. aeruginosa*, reducing MICs and toxicity of the antibiotics (Geitani *et al*., 2019).

AMP and Brain Infections

A key advantage for treating brain infections is the ability of some AMPs to cross the blood-brain barrier. Peptides like oncocin, apidaecin (1:37), and drosocin (Pro5Hyp) can selectively target brain cells, suggesting potential for CNS infections (Li *et al*., 2014). Overall, AMPs are a strong alternative to antibiotics, but high minimum inhibitory concentrations (MICs) and potential toxicity limit use (Raheem & Straus, 2019). They are best applied against resistant bacteria, in infections where MICs are low, or in combination with antibiotics to reduce resistance and antibiotic use.

Phytochemicals and Plant Extracts as Alternatives to Antibiotics

Herbal medicine uses whole plants or parts such as roots, leaves, and fruits, often extracted by infusion, maceration, decoction, or solvents like ethanol and methanol. Plants with strong antibacterial activity can diversify treatment options and combat resistance alone or in synergy with antibiotics (Arsène *et al*., 2021; Mbarga *et al*., 2021; Nascimento *et al*., 2000).

Antibacterial Properties of Plant Extracts and Phytochemicals

Between 2015 and 2019, about 11,000 studies on plant antibacterial activity were published (PubMed). Many plants, including spices and edible species, show activity against *E. coli*, *Salmonella infantis*, *L. monocytogenes*, *S. aureus*, and *Bacillus cereus* (Alzoreky & Nakahara, 2002). In Cameroon, 15 of 20 culinary spices inhibited *Mycobacterium tuberculosis* H37Rv and H37Ra, with *Echinops giganteus* showing the lowest MIC of 16:32 µg/mL (Fankam *et al*., 2011). Most studies remain *in vitro*, so *in vivo* validation is needed before clinical use. Still, traditional use of plant extracts for urinary and diarrheal infections suggests they can reduce antibiotic dependence (Ibrahim *et al*., 2015; Ullah *et al*., 2016).

Synergy between Common Antibiotics and Phytochemical Compounds to Counteract Antibiotic Resistance

Plant compounds often enhance antibiotic activity. Nascimento *et al*. (2000) reported synergy between clove, jambolan, pomegranate, and thyme extracts and antibiotics against multidrug-resistant *P. aeruginosa* and *K. pneumoniae*. Anacardic acid and totarol combined with methicillin inhibited MRSA (Nascimento *et al*., 2000). This synergy likely involves inhibition of multidrug efflux pumps on bacterial membranes (Shriram *et al*., 2018). Flavonoids and carvotacetones from *Sphaeranthus africanus* also act as efflux pump inhibitors and antimicrobials against mycobacteria (Solnier *et al*., 2020; Tran *et al*., 2020). Thus, plant extracts and phytochemicals are promising, but more *in vivo* studies are needed to confirm safety and optimal use alone or with antibiotics.

CONCLUSION

Antibiotic resistance represents a growing threat to human health, animal production, and global economies. While antibiotics remain essential, their overuse in medicine and agriculture has accelerated the emergence of multidrug-resistant pathogens. This review highlights that alternatives such as phage therapy, antimicrobial peptides, and plant-derived compounds offer promising, more sustainable strategies to combat resistant infections. Phages provide targeted bacterial killing with minimal impact on microbiota, AMPs deliver broad-spectrum activity and immunomodulatory benefits, and phytochemicals can act both as antimicrobials and as enhancers of antibiotic efficacy through efflux pump inhibition. However, challenges including specificity, stability, toxicity, and limited *in vivo* data must be addressed through continued research and clinical trials. A multifaceted approach that combines prudent antibiotic stewardship with investment in alternative therapies will be critical to reducing resistance and ensuring effective treatment options for future generations.

REFERENCES

Alzoreky, N. S., & Nakahara, K. (2002). Antibacterial activity of extracts from some edible plants commonly consumed in Asia. *International Journal of Food Microbiology*, 80, 223–230.

Andersson, D. I., Hughes, D., & Kubicek-Sutherland, J. Z. (2016). Mechanisms and consequences of bacterial resistance to antimicrobial peptides. *Drug Resistance Updates*, 26, 43–57.

Antoinette, K. D., & Dieudonne, A. (2020). Etiologic profile and sensitivity pattern of germs responsible for urinary tract infection among under-five in Douala: A hospital-based study. *International Journal of Infectious Diseases*, 101: 358.

Arsène, M. M., Podoprigora, I. V., Davares, A. K., Razan, M., Das, M. S., & Senyagin, A. N. (2021). Antibacterial activity of grapefruit peel extracts and green-synthesized silver nanoparticles. *Veterinary World, 14:(5), 1330:1341.*

Baltzer, S. A., & Brown, M. H. (2011). Antimicrobial peptides: Promising alternatives to conventional antibiotics. *Journal of Molecular Microbiology and Biotechnology*, 20(4), 228:235.

Bruttin, A., & Brüssow, H. (2005). Human volunteers receiving *Escherichia coli* phage T4 orally: A safety test of phage therapy. Antimicrobial Agents and Chemotherapy, 49(7), 2874:2878.

Cairns, B. J., Timms, A. R., Jansen, V. A., Connerton, I. F., & Payne, R. J. (2009). Quantitative models of *in vitro* bacteriophage-host dynamics and their application to phage therapy. *PLoS Pathogens*, 5(1), e1000253.

Cleven, B. E., Palka-Santini, M., Gielen, J., Meembor, S., Krönke, M., & Krut, O. (2006). Identification and characterization of bacterial pathogens causing bloodstream infections by DNA microarray. *Journal of Clinical Microbiology*, 44(7), 2389.

Criscuolo, E., Spadini, S., Lamanna, J., Ferro, M., & Burioni, R. (2017). Bacteriophages and their immunological applications against infectious threats. *Journal of Immunology Research*, 2017:3780697.

Doidge, C., Ruston, A., Lovatt, F., Hudson, C., King, L., & Kaler, J. (2020). Farmers' perceptions of preventing antibiotic resistance on sheep and beef farms: Risk, responsibility and action. *Frontiers in Veterinary Science*, 7: 524.

Di Pierro, F. (2025). _Phage to ESKAPE: Personalizing Therapy for MDR Infections. Host-range gaps and combination approaches.

Dublanchet, A., & Schwartz, M. (2017). Autobiographie de Félix d'Hérelle 1873:1949. *Éditions Médicales Internationales.*

Fankam, A., Kuete, V., Voukeng, I., & Kuiate, J. (2011). Antibacterial activities of selected Cameroonian spices and their synergistic effects with antibiotics against multidrug-resistant phenotypes. *BMC Complementary and Alternative Medicine*, 11(1), 104.

Faust, J. E., Yang, P. Y., & Huang, H. W. (2017). Action of antimicrobial peptides on bacterial and lipid membranes: A direct comparison. *Biophysical Journal*, 112(8), 1663:1672.

Geitani, R., Moubareck, C. A., Touqui, L., & Sarkis, D. K. (2019). Cationic antimicrobial peptides: Alternatives and/or adjuvants to antibiotics active against methicillin-resistant *Staphylococcus aureus* and multidrug-resistant P*seudomonas aeruginosa*. *BMC Microbiology*, 19(1), 54.

Ghanavati, R. (2024). The Evolution of Phage Therapy: A Comprehensive Review. Table of challenges: host range, immune clearance, resistance, regulation.

Grandclaudon, C., Birudukota, N. S., Elgaher, W. A., Jumde, R. P., Yahiaoui, S., Arisetti, N., Hennessen, F., Huettel, S., Stadler, M., Herrmann, J., & Miethke, M. (2020). Semisynthesis and biological evaluation of amidochelocardin derivatives as broad-spectrum antibiotics. *European Journal of Medicinal Chemistry*, 188:112005.

Heesterbeek, D. A., Muts, R. M., van Hensbergen, V. P., de Saint Aulaire, P., Wennekes, T., Bardoel, B. W., van Sorge, N. M., & Rooijakkers, S. H. (2021). Outer membrane permeabilization by the membrane attack complex sensitizes Gram-negative bacteria to antimicrobial proteins in serum and phagocytes. *PLoS Pathogens*, 17(1), e1009227.

Ibrahim, O. M. S., Sarhan, S. R., & Hameed, A. A. (2015). In vivo and in vitro antibacterial activities of cranberry extract against *E. coli* O157:H7 in urinary tract infected rats. *Advances in Animal and Veterinary Sciences*, 3, 233:244.

Jenssen, H., Hamill, P., & Hancock, R. E. (2006). Peptide antimicrobial agents. *Clinical Microbiology Reviews*, 19(3), 491:511.

Jit, M., Ng, D. H., Luangasanatip, N., Sandmann, F., Atkins, K. E., Robotham, J. V., & Pouwels, K. B. (2020). Quantifying the economic cost of antibiotic resistance and the impact of related interventions: Rapid methodological review, conceptual framework and recommendations for future studies. *BMC Medicine*, 18(1), 1:14.

Jorge, A. M. S., & Eduardo, R. (2019). Environmental structure drives resistance to phages and antibiotics during phage therapy and to invading lysogens during colonisation. *Scientific Reports*, 9(1), 3149.

Jun, K. (2017). Phage as a therapeutic agent. Medium. https://thryve.medium.com/phage-as-a-therapeutic-agent-ed4c466302e5

Kobras, C. M., Piepenbreier, H., Emenegger, J., Sim, A., Fritz, G., & Gebhard, S. (2020). BceAB-type antibiotic resistance transporters appear to act by target protection of cell wall synthesis, 64(3), e02241:19.

Koskella, B., & Meaden, S. (2013). Understanding bacteriophage specificity in natural microbial communities. *Viruses*, 5, 806:823.

Lei, J., Sun, L., Huang, S., Zhu, C., Li, P., He, J., Mackey, V., Coy, D. H., & He, Q. (2019). The antimicrobial peptides and their potential clinical applications. *American Journal of Translational Research,* 11(7), 3919:3931.

Li, W., Tailhades, J., O'Brien-Simpson, N. M., Separovic, F., Otvos, L., Hossain, M. A., & Wade, J. D. (2014). Proline-rich antimicrobial peptides: Potential therapeutics against antibiotic resistant bacteria. *Amino Acids*, 46(10), 2287:2294.

Lima, T., Domingues, S., & Da Silva, G. J. (2020). Manure as a potential hotspot for antibiotic resistance dissemination by horizontal gene transfer events. *Veterinary Sciences*, 7(3), 110.

Mahlapuu, M., Håkansson, J., Ringstad, L., & Björn, C. (2016). Antimicrobial peptides: An emerging category of therapeutic agents. *Frontiers in Cellular and Infection Microbiology*, 6, 194.

Mbarga, M. J. A., Andreevna, S. L., & Viktorovna, P. I. (2020). Evaluation of apparent microflora and study of antibiotic resistance of coliforms isolated from the shells of poultry eggs in Moscow Russia. *Journal of Advances in Microbiology*, 20(4), 70:77.

Mbarga, M. J. A., Podoprigora, I. V., Anyutoulou, K. L. D., Ngah, E., & Senyagin, A. N. (2021). Urinary tract infections (UTIs): Virulence factors, resistance to antibiotics and management of uropathogenic bacteria with medicinal plants. A review. *Journal of Applied Pharmaceutical Science*, 11(7), 001:012.

Mireille, A., Pascale, B., Charlotte, B., Laurent, D., Nicolas, D., Rémy, F., Sylvain, G., Claire, L. H., Marie-Agnès, P., Eduardo, R., & Clara, T. B. (2020). Les applications antibactériennes des bactériophages. *Virologie*, 24(1), 23:36.

Morel, C. M., Lindahl, O., Harbarth, S., de Kraker, M. E., Edwards, S., & Hollis, A. (2020). Industry incentives and antibiotic resistance: An introduction to the antibiotic susceptibility bonus. *Journal of Antibiotics*, 73(7), 421:428.

Międzybrodzki, R., Borysowski, J., Weber-Dąbrowska, B., Fortuna, W., Letkiewicz, S., Szufnarowski, K., Pawełczyk, Z., Rogóż, P., Kłak, M., Wojtasik, E., & Górski, A. (2012). Clinical aspects of phage therapy. *Advances in Virus Research*, 83, 73:121.

Nascimento, G. G. F., Locatelli, J., Freitas, P. C., & Silva, G. L. (2000). Antibacterial activity of plant extracts and phytochemicals on antibiotic-resistant bacteria. *Brazilian Journal of Microbiology*, 31, 247:256.

Nobrega, F. L., Costa, A. R., Kluskens, L. D., & Azeredo, J. (2015). Revisiting phage therapy: New applications for old resources. *Trends in Microbiology*, 23, 185:191.

Palma, E., Tilocca, B., & Roncada, P. (2020). Antimicrobial resistance in veterinary medicine: An overview. *International Journal of Molecular Sciences*, 21(6), 1914.

Payne, R. J., & Jansen, V. A. (2001). Understanding bacteriophage therapy as a density-dependent kinetic process. *Journal of Theoretical Biology*, 208(1), 37:48.

Pollock, J., Low, A. S., McHugh, R. E., Muwonge, A., Stevens, M. P., Corbishley, A., & Gally, D. L. (2020). Alternatives to antibiotics in a one health context and the role genomics can play in reducing antimicrobial use. *Clinical Microbiology and Infection*, 26(12), 1617:1621.

Prasanth, M., Ramesh, N., & Bruno, S. L. (2018). The therapeutic potential of bacteriophages targeting gram-negative bacteria using. *Galleria mellonella infection model*. BMC Microbiology, 18: 97.

Rabello, R. F., Bonelli, R. R., Penna, B. A., Albuquerque, J. P., Souza, R. M., & Cerqueira, A. M. (2020). Antimicrobial resistance in farm animals in Brazil: An updated overview. *Animals*, 10(4), 552.

Raheem, N., & Straus, S. K. (2019). Mechanisms of action for antimicrobial peptides with antibacterial and antibiofilm functions. *Frontiers in Microbiology*, 10, 2866.

Reis, A. C., Kolvenbach, B. A., Nunes, O. C., & Corvini, P. F. (2020). Biodegradation of antibiotics: The new resistance determinantsPart I. *New Biotechnology*, 54, 34:51.

Rončević, T., Puizina, J., & Tossi, A. (2019). Antimicrobial peptides as anti-infective agents in pre-post-antibiotic era? *International Journal of Molecular Sciences*, 20(22), 5713.

Sadhana, S. S., Ram, N. A., Rajesh, K., & Shilpa, D. K. (2018). Reversal of antibiotic resistance by phage resistant *Pseudomonas aeruginosa* PA01. *Journal of Biosciences and Bioengineering*, 6(1), 11:15.

Schaenzer, A. J., & Wright, G. D. (2020). Antibiotic resistance by enzymatic modification of antibiotic targets. *Trends in Molecular Medicine*, 26(8), 768:782.

Shriram, V., Khare, T., Bhagwat, R., Shukla, R., & Kumar, V. (2018). Inhibiting bacterial drug efflux pumps via phyto-therapeutics to combat threatening antimicrobial resistance. *Frontiers in Microbiology*, 9, 2990.

Skurnik, M., & Strauch, E. (2006). Phage therapy: Facts and fiction. *International Journal of Medical Microbiology*, 296(1), 5:14.

Solnier, J., Martin, L., Bhakta, S., & Bucar, F. (2020). Flavonoids as novel efflux pump inhibitors and antimicrobials against both environmental and pathogenic intracellular mycobacterial species. *Molecules*, 25, 734.

Stokes, J. M., Lopatkin, A. J., Lobritz, M. A., & Collins, J. J. (2019). Bacterial metabolism and antibiotic efficacy. *Cell Metabolism*, 30(2), 251:259.

Tran, H. T., Solnier, J., Pferschy-Wenzig, E. M., Kunert, O., Martin, L., Bhakta, S., Huynh, L., Le, T. M., Bauer, R., & Bucar, F. (2020). Antimicrobial and efflux pump inhibitory activity of carvotacetones from Sphaeranthus africanus against mycobacteria. *Antibiotics*, 9(7), 390.

Ullah, N., Parveen, A., Bano, R., Zulfiqar, I., Maryam, M., Jabeen, S., Liaqat, A., & Ahmad, S. (2016). In vitro and in vivo protocols of antimicrobial bioassay of medicinal herbal extracts: A review. *Asian Pacific Journal of Tropical Disease*, 6, 660:667.

Van Belleghem, J. D., Dabrowska, K., Vanee, M., Barr, J. J., & Bollyky, P. L. (2018). Interactions between bacteriophage, bacteria and the mammalian immune system. *Viruses*, 11(1), 10.

Vasilchenko, A. S., & Rogozhin, E. A. (2019). Sub-inhibitory effects of antimicrobial peptides. *Frontiers in Microbiology*, 10, 1160.

Ventola, C. L. (2015). The antibiotic resistance crisis: Part 1: Causes and threats. *Pharmacy and Therapeutics*, 40(4), 277:283.

World Health Organization. (2019, April 29). New report calls for urgent action to avert antimicrobial resistance crisis. https://www.who.int/news/item/29-04-2019-new-report-calls-for-urgent-action-to-avert-antimicrobial-resistance-crisis

World Health Organization. (2020). Antibiotic resistance. https://www.who.int/news-room/fact-sheets/detail/antibiotic-resistance

WHO. (2024). Antibiotic resistance surges globally, UN health agency warns. 2024. 1.27M deaths directly from AMR in 2019; 40% rise 2018-2023.

WHO. (2023). Antibiotic resistance surges globally, UN health agency warns. (1.27M deaths directly from AMR in 2019.

WHO. 2018). Antibiotic resistance surges globally, UN health agency warns. 1.27M deaths directly from AMR in 2019

WHO. (2023). Product & Delivery Research: AMR a significant global health threat. Pipeline and access challenges.

Xu, L., Zhou, Z., Zhu, L., Han, Y., Lin, Z., Feng, W., Liu, Y., Shuai, X., & Chen, H. (2020). Antibiotic resistance genes and microcystins in a drinking water treatment plant. *Environmental Pollution*, 258, 113718.

Zhou, J., Liu, Y., Shen, T., Chen, L., Zhang, C., Cai, K., Liao, C., & Wang, C. (2019). Antimicrobial activity of the antibacterial peptide PMAP-36 and its analogues. *Microbial Pathogenesis*, 136, 103712.