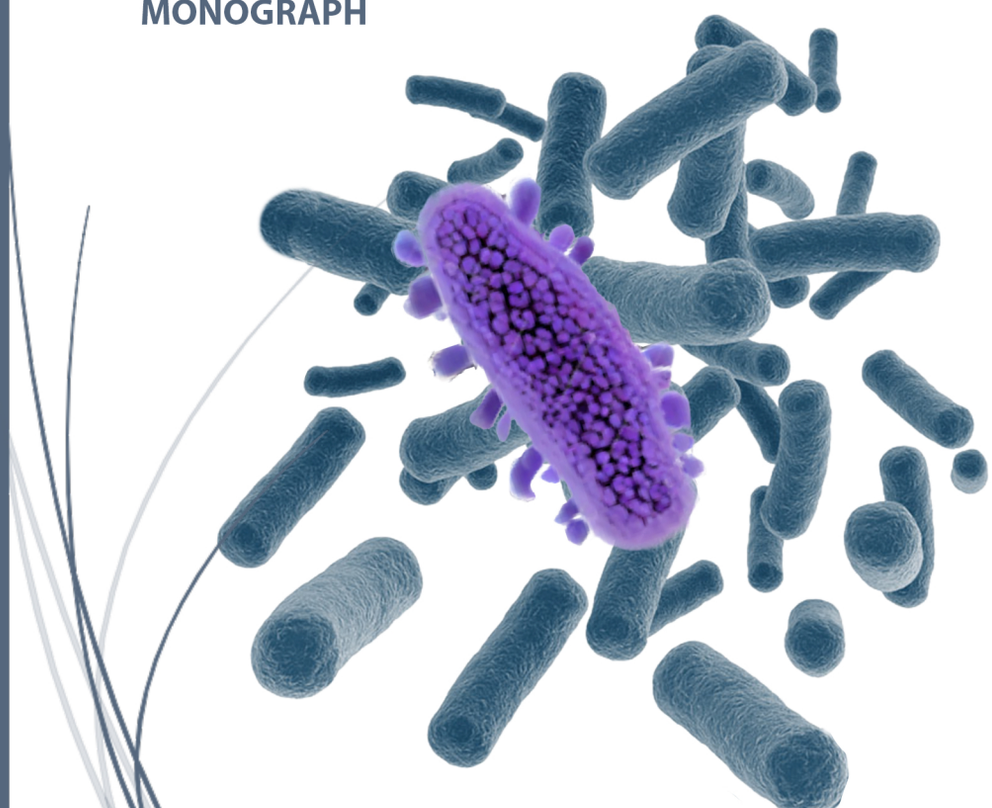
Yuliia HORIUK

ANTIBIOTIC RESISTANCE: PERSPECTIVES ON NEW THERAPEUTIC STRATEGIES

MONOGRAPH



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Reviewers:
Mykola KUKHTYN, Doctor of Veterinary Science, Professor, Head of the Department of Food Biotechnology and Chemistry, Ternopil Ivan Pului National Technical University;

Yevhen KRYVOKHYZHA, Doctor of Agricultural Science, Senior Researcher, Professor of the Department of Ecology and Healthcare, West Ukrainian National University;

Maria KUCHERUK, Doctor of Veterinary Science, Associate professor, associate professor of the Department of Animal Hygiene and Veterinary Support of the Cynological Service of the National Police of Ukraine, Higher educational institution «Podillia State University».

Y. Horiuk
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The monograph discusses the global problem of antibiotic resistance, which has emerged since the discovery of penicillin by Alexander Fleming in 1928. Efforts to combat resistance include antibiotic stewardship programs and strategies to minimize unnecessary antibiotic use, but problems such as overprescription and cost remain. The monograph also explores alternative treatments, including nanomaterials, herbal medicines, and bacteriophage therapy, which offer promising solutions for combating multidrug-resistant bacteria.

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ABSTRACT

Since the discovery of penicillin, the first antibiotic, by Alexander Fleming in 1928, bacterial infectious diseases have ceased to be the leading cause of death worldwide, and the average life expectancy of humans has nearly doubled. However, antibiotic resistance quickly emerged in many clinical bacteria, threatening the initial effectiveness of antibiotics. Furthermore, the overuse and misuse of antibiotics have exacerbated this resistance problem. In 2017, the World Health Organization published a list of twelve bacteria of concern, all of which were resistant to a significant number of currently available antibiotics. These bacteria included: *Acinetobacter baumannii* (carbapenem-resistant), *Pseudomonas aeruginosa* (carbapenem-resistant), *Enterobacteriaceae* (carbapenem-resistant, extended-spectrum beta-lactamase-producing), *Enterococcus faecium* (vancomycin-resistant), *Staphylococcus aureus* (methicillin-resistant), *Helicobacter pylori* (clarithromycin-resistant), *Campylobacter* spp. (fluoroquinolone-resistant), *Salmonella* spp. (fluoroquinolone-resistant), and *Neisseria gonorrhoeae* (cephalosporin-resistant, fluoroquinolone-resistant), *Streptococcus pneumoniae* (penicillin-insensitive), *Haemophilus influenzae* (ampicillin-resistant), and *Shigella* spp. (fluoroquinolone-resistant). Six of these bacteria are common nosocomial pathogens (E. faecium, S. aureus, Klebsiella pneumoniae, A. baumannii, P. aeruginosa, and *Enterobacter* spp.), collectively known as ESKAPE, which frequently evade the lethal effects of antibiotics. The Infectious Diseases Society of America (IDSA) highlights them as representative paradigms of pathogenesis, transmission, and resistance.

Antibiotic and antimicrobial stewardship is essential in combating antibiotic resistance. The Netherlands and Sweden, where antibiotic strategies are applied in outpatient settings, are countries with the lowest levels of antibiotic resistance in Europe. In England, a reduction in antibiotic prescriptions has significantly mitigated the already increasing rates of antimicrobial resistance in subsequently identified bloodstream infections caused by *E. coli*. A systematic review reports that antibiotic stewardship programs (ASPs) can reduce antibiotic use, antibiotic costs, treatment duration, and local resistance levels without negatively impacting mortality in patients requiring intensive care. However, there are still certain limitations that hinder the accurate implementation of antibiotic therapy. Fearing insufficient coverage of the pathogen, doctors often empirically prescribe broad-spectrum antibiotics. As a result, such treatments are typically prolonged or excessively broad. Additionally, the high cost of treatment and patients' unwillingness to bear the expenses of hospitalization limit the applicability of antibiotic therapy in low- and middle-income countries.

Currently, many researchers worldwide are focused on developing solutions to combat antibiotic-resistant bacteria (ARB) to prevent effective antibiotics from becoming clinically unavailable in the future. This review discusses recent advances in strategies to combat ARB emergence based on literature reporting effective chemical, microbiological, and immunological methods.

Nanomaterials are capable of circumventing existing bacterial resistance mechanisms and have a lower potential for developing resistance compared to traditional antibiotics. Furthermore, nanoparticles can effectively destroy bacteria in biofilms, indicating the potential use of nanotechnology as a tool for developing new treatments for infections caused by multidrug-resistant bacteria. In this review, we analyze the potential of nanomaterials in the fight against multidrug-resistant bacterial infections, investigate their characteristics and design components that contribute to their therapeutic effectiveness, and discuss how these materials can be adapted to combat both biofilms and planktonic bacteria. Finally, we discuss the current status of clinical developments of antibacterial nanomaterials.

Traditional healing systems used herbs containing compounds such as alkaloids, terpenoids, tannins, steroids, coumarins, and flavonoids, which typically do not induce resistance. The essential oils (EOs) of parsley, lovage, basil, and thyme can disrupt the physiological state of bacterial cells by increasing the permeability of cell membranes, causing leakage of cellular components, changes in bacterial cell walls and membranes, ATP loss, inhibiting protein synthesis,

altering the pH of the environment, causing intracellular damage, damaging DNA, and inhibiting quorum sensing among bacteria such as *Bacillus cereus*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli*, and the serovar *Salmonella enterica Typhimurium*.

Bacteriophages (or phages) are viruses that specifically target bacteria. Phage therapy was researched over a century ago, but its use decreased after the discovery of broad-spectrum antibiotics, such as penicillin. However, in recent decades, phage therapy has regained attention due to the rise of antibiotic resistance, and it is actively being studied both in vitro and in vivo.

Key words: antibiotics, antibiotic resistance, bacterial infections, World Health Organization (WHO), treatment strategies, ESKAPE pathogens, nanomaterials, plant extracts, bacteriophages.

CONTENT

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