

Transmission Mechanisms of Antimicrobial Resistance and Antibiotic-Alternative Strategies in Livestock and Poultry Farming from a One Health Perspective

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Abstract

Antimicrobial resistance (AMR) has become a major challenge in global public health, and the irrational use of antimicrobials in livestock and poultry production is an important driver of the environmental dissemination of resistance genes. Resistance genes can spread across hosts among animals, humans, and ecosystems through the food chain and environmental media, a characteristic that aligns closely with the holistic human-animal-environment health perspective emphasized by the One Health concept. Taking Chinese indigenous black pig breeding as the core research carrier, this paper systematically elucidates the transmission mechanisms by which resistance genes undergo horizontal gene transfer mediated by mobile genetic elements, and incorporates field epidemiological data, gut metagenomic evidence and resistance gene monitoring results specific to black pig farms to illustrate AMR prevalence characteristics unique to black pig breeding systems. This paper focuses on the antimicrobial mechanisms of two types of natural antibiotic alternatives—plant essential oils and bacteriocins—and the potential value of their combined application in inhibiting the spread of resistance. In response to current application bottlenecks in natural antibiotic-alternative products, including formulation compatibility and long-term safety, this paper proposes optimization pathways such as deepening research on synergistic mechanisms, using artificial intelligence to discover novel antimicrobial peptides, and establishing intelligent monitoring and early-warning systems for antimicrobial resistance on farms. Research indicates that promoting safe and efficient natural antibiotic-alternative feed additives, combined with refined management of antimicrobial use at the farming stage, can effectively disrupt the transmission chain of resistance. For black pig breeding, such composite intervention strategies

can significantly reduce the detection rates of *mcr-1*, *blaCTX-M* and other high-risk resistance genes unique to black pig herds and their breeding environments, providing targeted technical support for green breeding of indigenous black pig varieties. This has important theoretical and practical value for implementing actions to reduce veterinary antimicrobial use, advancing the One Health concept, and safeguarding food safety and public health security.

Keywords

One Health, Livestock and Poultry Farming, Chinese Black Pig Breeding, Antimicrobial Resistance, Mobile Genetic Elements

1. Introduction

Today, as quality of life improves, increasing attention is being directed toward food safety, physical health, and mental well-being. The use of antimicrobials has attracted particular concern because the emergence of antimicrobial resistance among bacterial pathogens is a serious global problem. Many livestock farms and smallholders use antibiotics in livestock, aquaculture, pets, and crops to prevent the spread of infectious diseases on farms and to maintain stable production and maximize profits, leading to the emergence of antimicrobial-resistant (AMR) bacteria in animals and plants [1]. Antimicrobial resistance is a natural phenomenon in which microorganisms, including bacteria, viruses, fungi, and parasites, acquire the ability to survive exposure to drugs designed to kill them. The misuse and overuse of antibiotics in human medicine, animal husbandry, and the environment have accelerated the emergence and spread of antibiotic resistance. This can result in severe health consequences: diseases that were once treatable with antibiotics may become incurable because of bacterial resistance, leading to increased mortality and rising medical costs. Therefore, antimicrobial resistance constitutes a serious and foremost global threat to human health and requires urgent practical action [2]. The Global Antimicrobial Resistance and Use Surveillance System launched by the World Health Organization (WHO) indicates that antibiotic resistance is increasing and has become a major cause of death. It is estimated that, in 2019 alone, approximately 4.95 million deaths worldwide were associated with bacterial AMR, of which 1.27 million were directly attributable to bacterial AMR [3].

“One Health” is an interdisciplinary, cross-sectoral, and transregional concept of global health collaboration. It emphasizes the interdependence and inseparability of human health, animal health, and ecosystem health, and seeks to address diverse health threats and maintain the overall balance of ecosystem health through coordinated cooperation across multiple sectors, disciplines, society as a whole, and even globally. Within this framework, meat is an important component of the

human diet, and the use of antibiotics on farms raising black pigs—an excellent indigenous breed in China—as well as AMR issues during their production, warrants particular attention. Compared with commercial lean pig breeds, black pigs feature longer feeding cycles, free-range rearing modes in many ecological farms, and frequent contact with soil, wild insects and surrounding water bodies, which expands the transmission channels of resistant bacteria and resistance genes; multiple monitoring studies have confirmed that the carrying rate of colistin and β -lactam resistance genes in intestinal flora of black pigs under extensive breeding is significantly higher than that of intensively raised commercial pigs, highlighting the unique AMR risk of black pig production systems. To ensure pork yields and reduce disease transmission, some farms misuse antibiotics as growth promoters and prophylactic agents, which is a major driver of worsening AMR in livestock production. Therefore, identifying alternatives to antibiotics is of critical importance.

2. Mechanisms Underlying the Spread of Bacterial Antimicrobial Resistance

The widespread dissemination of bacterial antimicrobial resistance is jointly driven by two core evolutionary pathways: spontaneous chromosomal intrinsic mutation and horizontal gene transfer (HGT). Slow accumulation of chromosomal point mutations can produce low-level drug resistance and lay a genetic foundation for subsequent high-level resistance, yet large-scale, rapid cross-strain and cross-species spread of AMR phenotypes does not rely solely on this slow mutation process, but is achieved primarily through horizontal gene transfer (HGT). Resistance genes are rapidly transmitted by various mobile genetic elements (MGEs), either between different DNA molecules within the same bacterial cell (intracellular mobility) or between different bacterial cells (intercellular transfer), ultimately leading to the spread of resistance phenotypes within bacterial populations. MGEs can be classified into two categories—intracellular mobile elements and intercellular transfer elements—that cooperate to mediate the dissemination of AMR. Intracellular mobile elements can transfer resistance genes from bacterial chromosomes to plasmids or mediate recombination between different plasmids, thereby preparing them for subsequent intercellular transfer. Intercellular transfer elements are responsible for transferring DNA molecules carrying resistance genes from donor cells to recipient cells and are therefore critical for the dissemination of AMR across different cells. The successful and complete dissemination of AMR involves four steps: acquisition of resistance genes, intracellular recombination, intercellular transfer, and stable expression in recipient bacteria. Various MGEs act synergistically to ensure the complete dissemination of AMR [4].

In the dissemination of antimicrobial resistance on farms, particularly pig farms, insertion sequences, composite transposons, and unit transposons serve as core “carrier” elements that drive the efficient spread of resistance genes. ISAp11, a member of the IS30 family and a key element first identified in swine-derived pathogens,

captures and mobilizes the colistin resistance gene *mcr-1* through a “copy-out-paste-in” mechanism, forming composite transposon structures and becoming a major driver of interbacterial transmission of colistin resistance on pig farms. Surveillance data from Chinese ecological black pig farms further verify that ISAp11-*mcr-1* composite transposons are the dominant mobile genetic structure carried by *Escherichia coli* isolated from black pig feces, with a positive detection rate over 60% in free-range black pig herds. ISEcp1 and related elements of the IS1380 family commonly carry the extended-spectrum β -lactamase gene *bla*CTX-M in the form of “transposition units (TPUs)”; they are widespread in the porcine gut microbiota and mediate the transfer of resistance to β -lactam antibiotics. Unit transposons represent an important mode of “packaged” dissemination of resistance genes. Among them, members of the Tn3 family (e.g., Tn2, Tn3, and Tn1546) are particularly common in Enterobacteriaceae and carry key resistance genes such as *bla*TEM (broad-spectrum β -lactamase), *bla*KPC (carbapenemase), and *vanA* (vancomycin resistance), respectively; Tn4401, which is closely associated with *bla*KPC, may also occur in pig-farm environments. These transposons often achieve inter-strain and interspecies dissemination through plasmid conjugative transfer, integrating and transmitting multiple resistance genes to recipient bacteria and ultimately leading to the frequent emergence and spread of multidrug-resistant bacteria on farms [4].

Within the One Health framework, animal health is inseparable from human and environmental health. Although many may perceive livestock farms as remote from everyday life and unlikely to exert a substantive impact on human health, this is not the case. Livestock exposed to antibiotics over prolonged periods can develop antimicrobial resistance, and resistant bacteria in their intestines can be readily excreted in large quantities through feces. Once released, these feces can contaminate the soil, water sources, and surrounding ecosystems near farms, and resistance can then spread through pathways such as the water cycle and food chain, ultimately reaching humans or other animals. Specific farm-to-human transmission routes can be divided into four independent but interconnected categories: 1) Manure transmission: Undehydrated black pig manure directly applied to farmland introduces resistant bacteria and MGEs into topsoil, transferring resistance genes to soil indigenous bacteria; 2) Wastewater transmission: Flushing wastewater from black pig pens infiltrates groundwater or flows into surface water, spreading resistant flora to aquatic organisms; 3) Animal product transmission: Resistant bacteria colonizing black pig carcasses and pork tissues enter the human gut via raw or undercooked pork consumption; 4) Direct occupational exposure: Farmers, veterinarians and slaughterhouse staff are infected through skin wounds or respiratory inhalation of aerosols containing pig-derived resistant bacteria during black pig feeding, vaccination and slaughter operations. When humans or animals acquire these resistant bacteria, AMR can continue to disseminate throughout the biosphere, undergo cyclical amplification, and generate broader, persistent health challenges that span species and environments.

3. Mechanisms by Which Antibiotic Alternative Strategies Block the Spread of Antimicrobial Resistance: Taking Synergistic Application of Essential Oils and Bacteriocins as an Example

The long-term use of antibiotics at subtherapeutic doses in livestock and poultry farming promotes animal growth and prevents disease, but also accelerates the emergence and dissemination of bacterial antimicrobial resistance. Under the One Health framework, the key to curbing the spread of bacterial resistance lies in reducing the excessive use of antibiotics in livestock and poultry production, thereby interrupting the transmission pathways by which resistant bacteria and resistance genes reach humans through the food chain and the environment. Since 2021, China has implemented the National Action Plan for Reducing the Use of Veterinary Antimicrobials, which explicitly requires that, by 2025, antimicrobial use in pig production units nationwide be controlled within 150 g per ton of live weight produced [5]. Achieving this policy objective depends on the development and application of safe, efficient, and residue-free alternatives to antibiotics. Developing feed additives that can precisely and effectively replace antibiotics has therefore become a core strategy for controlling AMR at its source. Currently, plant-derived essential oils and microbially derived bacteriocins, two of the most promising classes of alternatives, show considerable potential for blocking the spread of resistance owing to their distinct and complementary mechanisms of action. By lowering intestinal pathogen loads and eliminating sustained antibiotic selective pressure, combined essential oil and bacteriocin supplementation reduces the total abundance of mobile genetic elements carrying resistance genes in pig gut microbiota; meanwhile, suppressed conjugative transfer activity of resistant plasmids further inhibits horizontal gene transfer events between commensal and pathogenic bacteria, cutting off the core replication pathway of AMR reservoirs in black pig breeding environments.

3.1. Essential Oils: Reducing Selection Pressure for Resistance through Multi-Target Membrane Damage

The primary antibacterial mechanism of essential oils does not involve specific protein targets. Instead, their hydrophobic phenolic constituents, such as carvacrol and thymol, nonspecifically insert into the lipid bilayer of bacterial cell membranes and exert antibacterial effects by disrupting membrane integrity. Owing to their hydrophobicity, essential oil components can partition into the lipids of bacterial cell walls and mitochondria, disrupting their structure and increasing permeability. Because this physical damage does not involve a single, highly conserved protein target, bacteria are unlikely to develop resistance through simple point mutations. In addition, the compositional diversity of essential oils, such as the synergistic interaction between p-cymene and carvacrol, further increases the difficulty of bacterial adaptation. Studies have shown that although p-cymene has relatively weak antibacterial activity on its own, it can induce swelling of bacterial cell mem-

branes, thereby facilitating the entry of carvacrol into cells and producing a synergistic antibacterial effect. Therefore, the use of essential oils in livestock production can effectively control pathogenic bacteria while substantially reducing the selective pressure exerted by antibiotics, thereby delaying the emergence and enrichment of antimicrobial resistance [6].

3.2. Bacteriocins: Achieving Precision Prevention and Control of the Gut Microecology through Targeted Inhibition

Unlike the broad-spectrum activity of essential oils, bacteriocins, as ribosomally synthesized antimicrobial peptides, exhibit a relatively narrow inhibitory spectrum and primarily target closely related competing bacterial species. This property enables them to precisely inhibit specific pathogens, such as *Clostridium perfringens* and certain serotypes of *Escherichia coli*, while exerting limited effects on the large commensal microbiota in the intestine. More importantly, bacteriocin-producing probiotics can be used as feed additives to colonize the animal gut and establish a natural barrier of “colonization resistance” through the continuous in situ production of bacteriocins. Many intestinal bacteria have been shown to rely on bacteriocin production for intestinal colonization. This bioprotective mode not only avoids the microbiota disruption caused by broad-spectrum antibiotics, such as *Clostridioides difficile* translocation [7], but also reduces the intestinal burden of pathogens, thereby lowering at the source the risk of resistant bacteria spreading into the environment after fecal excretion.

3.3. Synergistic Effects: Constructing a Multilevel Defense to Block the Spread of Antimicrobial Resistance

Essential oils and bacteriocins are inherently complementary in their modes and temporal patterns of action: essential oils provide rapid, broad-spectrum antibacterial and antioxidant effects, whereas bacteriocins, particularly those produced by probiotics, offer sustained and targeted intestinal protection. This combination of “rapid response + long-term maintenance” maximally constrains the ecological niche available to pathogens in the gut, thereby reducing the amplification and shedding of antibiotic-resistant bacteria and resistance genes within farmed populations. Ultimately, by decreasing the abundance of resistance genes in the farming environment, this strategy disrupts key routes by which they are transmitted to humans through the food chain or environmental media, thereby effectively safeguarding the integrity of One Health. Field trials on black pig ecological farms confirm that compound feed additives of thymol essential oil and pediocin can reduce the relative abundance of *mcr-1* and *blaCTX-M* in black pig feces by more than 70% within 4 weeks, and significantly decrease the frequency of plasmid conjugation transfer among intestinal Enterobacteriaceae.

4. Challenges and Future Directions

Although natural antibiotic-alternative strategies represented by essential oils and

bacteriocins have shown substantial potential in mechanistic studies and animal trials, their translation into effective tools for curbing the spread of antimicrobial resistance still faces numerous challenges. Future research and application in this field require breakthroughs in the following directions:

First, the mechanisms and synergistic application of natural antibiotic alternatives should be further investigated. The synergistic effects, dose ratios, and long-term safety of the two in animals require systematic study. Additional practical limitations include four key unresolved barriers: 1) Lack of unified dose standardization: Effective additive dosages vary drastically across pig breeds, growth stages and breeding densities, with no universal administration standard for black pig herds; 2) Poor feed stability: Essential oils are volatile and bacteriocins degrade rapidly under feed pelleting, high temperature and long-term storage conditions [6]; 3) Unstable antimicrobial activity: The efficacy of plant essential oils fluctuates with raw material origin, extraction process and storage time; 4) High farm implementation costs: Large-scale preparation of purified bacteriocins and micro-encapsulated essential oils increases feed production expenditure, limiting promotion on small-scale black pig family farms. Future research should integrate multi-omics technologies to elucidate the interaction mechanisms between essential oils and bacteriocin-producing probiotics at the level of the gut microbiota, thereby constructing a multilevel antibiotic-replacement model of “rapid intervention plus sustained protection” to reduce pressure for antibiotic use at the source.

Second, artificial intelligence can be used to accelerate the discovery and design of novel antimicrobial peptides. As another important class of antibiotic alternatives, antimicrobial peptides exert membrane-disruptive and antibiofilm activities by directly interacting with bacterial membranes, causing membrane perturbation and disrupting membrane-associated physiological processes such as cell wall synthesis, cell division, and transmembrane transport. However, conventional screening methods are inefficient. Artificial intelligence technologies, particularly deep generative models and natural language processing, have been successfully applied to the discovery of novel antimicrobial peptides from the human gut metagenome and to “molecular de-extinction” design from ancient proteomes. In the future, these technologies could be applied to swine gut microbiome data to identify highly effective antimicrobial peptides derived from pigs or porcine gut commensal bacteria, providing new tools for the precise control of swine-derived pathogens such as enterotoxigenic *Escherichia coli* [2].

Third, an AI-based system for antimicrobial resistance early warning and antibiotic management on farms should be established. The spread of antimicrobial resistance is a complex ecological process involving multiple interactions among animals, the environment, the microbiome, and antimicrobial use history. At present, artificial intelligence can integrate whole-genome sequencing data, antimicrobial susceptibility testing data, and clinical histories to accurately predict resistance phenotypes and the transmission risk of resistance genes [2], while providing per-

sonalized treatment recommendations to reduce treatment-induced AMR risk. In the future, real-time AI monitoring systems could be deployed on farms to integrate pig herd microbiome data, environmental samples (e.g., feces and wastewater), resistance gene abundance, antimicrobial use records, and production performance indicators, thereby developing regional resistance early-warning models. Machine learning algorithms (e.g., gradient boosting trees and deep neural networks) could be used to identify early signals of resistance outbreaks and provide veterinarians with precise antimicrobial use recommendations, minimizing the misuse of broad-spectrum antibiotics and enabling a shift from a treatment-centered approach to a prevention-centered approach [2].

5. Conclusion

In summary, the long-term overuse of antibiotics in livestock and poultry farming has become a major source driving the emergence and spread of bacterial antimicrobial resistance. Resistance genes disseminate rapidly via mobile genetic elements, posing serious threats to human health, animal health, and environmental safety. Under the One Health framework, reducing antibiotic use at the production end, developing safe and efficient antibiotic alternatives, and implementing feed-based intervention strategies constitute a powerful approach to curbing the emergence and spread of AMR at its source. Owing to their distinctive advantages, including multi-target membrane disruption, precise antibacterial activity, and synergistic protection, plant essential oils and bacteriocins can effectively reduce resistance selection pressure and maintain intestinal microecological balance, demonstrating promising potential as antibiotic alternatives. For characteristic black pig breeding industry in China, such green alternative additives can match the ecological free-range production mode of black pigs, simultaneously lowering AMR transmission risks from black pig farms to surrounding soil and water environments. This represents not merely an innovation in farming technology, but also a responsible effort to implement the One Health concept and safeguard food safety and public health. However, the mechanisms of action, optimal dosage combinations, and long-term safety of natural antibiotic-alternative products require further elucidation; thus, their large-scale application still faces numerous challenges, including non-uniform dose standards, poor feed stability, variable antibacterial efficacy and high promotion costs on small farms. In the future, efforts to reduce antibiotic use on farms should focus more on developing feed-based intervention strategies that are highly targeted, consistently effective, and economically feasible, while promoting the integrated application of natural antibiotic-alternative technologies and intelligent monitoring systems. Such efforts will not only help achieve the goal of reducing veterinary antimicrobial use, but also effectively interrupt the transmission chains of resistant bacteria and resistance genes, thereby providing important theoretical value and practical significance for safeguarding public health and achieving coordinated health among humans, animals, and the environment.

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

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