



Safeguarding Health and Sustainability: The Vital Role of Livestock Waste Management in Combating Antibiotic Resistance

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Abstract

Antibiotic resistance is a pressing global health concern, and livestock waste has emerged as a significant source of antibiotic resistance genes (ARGs) that can be transmitted to humans and the environment. To address this critical issue, efficient and sustainable livestock waste management strategies are essential to mitigate the spread of antibiotic resistance. Various studies have highlighted the importance of optimizing waste treatment processes to enhance ARG removal efficiency. Implementing anaerobic digestion, composting, and constructed wetlands has shown promise in reducing ARGs in livestock waste. Furthermore, research on additives such as biochar, clay, and surfactants, as well as optimization of operating conditions, have the potential to further improve ARG removal. A crucial aspect of livestock waste management is balancing animal welfare and profitability while ensuring the reduction of ARG dissemination. Responsible antibiotic use in animal husbandry, coupled with disease prevention strategies and alternative growth promoters, can minimize the need for antibiotics and, consequently, reduce the selection pressure for antibiotic resistance in livestock. Educating farmers, veterinarians, and consumers about the risks of antibiotic use in animals is vital in promoting behavioral changes towards responsible antibiotic usage. Nation-wide surveillance of veterinary antibiotic use, resistance, and residues is critical in monitoring the impact of interventions and identifying emerging resistance patterns. Strengthening regulations and policies related to manure storage and disposal practices can ensure proper waste management and minimize ARG discharge.

Key words: Anaerobic digestion, ARG's, Composting, Livestock waste

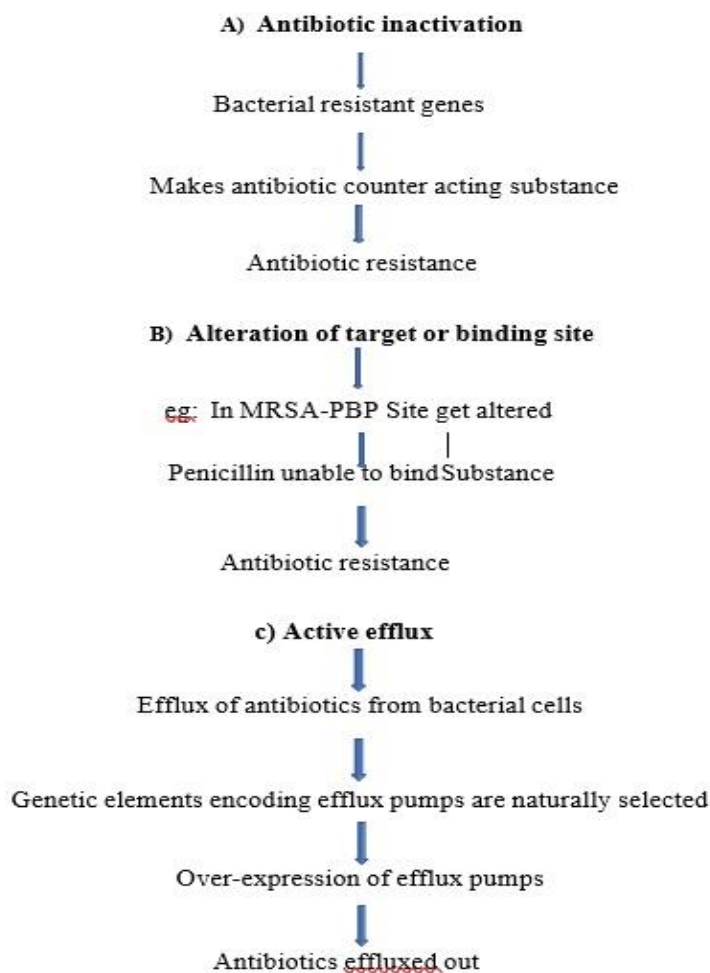
Introduction

Antibiotics are crucial medicines used to combat bacterial infections in both humans and animals. However, the misuse and overuse of antibiotics have led to the emergence of antibiotic-resistant bacteria, where bacteria adapt and become immune to the effects of these drugs. Alarmingly, antibiotic resistance is rapidly spreading worldwide, posing a severe threat to public health if we do not take immediate and concerted action. In 2014, approximately 700,000 deaths were attributed to antibiotic-resistant infections, and this number is projected to escalate dramatically, reaching a staggering 10 million deaths annually by 2050 if left unchecked. Animal husbandry is a significant contributor to the global consumption of antibiotics, accounting for more than half of their use. In 2013, the estimated antibiotic use in animal husbandry was 131,109 tons, and this figure is predicted to exceed 200,000 tons by 2030. It is essential to recognize that the excessive use of antibiotics in this sector has the potential to contribute significantly to the rise of antibiotic resistance. Regrettably, the seriousness of this issue is not adequately reflected in the scientific community. Only a mere 10% of publications on antibiotic resistance consider the potential impact of animal husbandry in fueling this crisis. However, it is crucial to acknowledge that livestock waste often contains various types of antibiotic resistance genes (ARGs), which are regularly detected in the environment. Conventional waste treatment processes used in livestock farming do not completely eliminate these ARGs, leading to their release into soil and water, where they can pose risks to human health. Combating antibiotic resistance requires urgent and coordinated efforts globally. We must take immediate steps to curb the misuse of antibiotics in both human healthcare and animal husbandry. Promoting responsible antibiotic use, investing in research and development of new antibiotics, and improving waste treatment processes in livestock farming are vital to preserving the effectiveness of these life-saving drugs and safeguarding public health for generations to come.

Mechanisms underlying the occurrence of antibiotic resistance

Antibiotic resistance occurs due to changes, or mutations, in the DNA of the bacteria, or the acquisition of antibiotic resistance genes from other bacterial species through horizontal gene transfer. These changes enable the bacteria to survive the effects of antibiotics designed to kill them. This means that when an antibiotic is used, all the bacteria that have not undergone a mutation are killed, while the antibiotic resistant bacteria remain unaffected. The antibiotic resistant bacteria are able to continue to divide and grow producing even more bacteria that are not affected by the antibiotic. The existence of resistant strains of bacteria means that antibiotics or drugs designed to kill them no longer work, allowing them to spread rapidly, posing a risk to public health. When, this happens it is necessary for scientists to develop new antibiotics that the bacteria do not have resistance to.

Through three fundamental resistance mechanisms viz. (A) Antibiotic deactivation, (B) Protection of targets by specific proteins (C) Extrusion through efflux pumps, ARGs can confer resistance to nine major classes of antibiotics: Tetracyclines (*tet*), Sulfonamides (*sul*), β -lactams (*bla*), Macrolide-lincosamid-streptogramin B (MLSB) (*erm*), Aminoglycosides (*aac*), FCA (fluoroquinolone, quinolone, florfenicol, chloramphenicol, and amphenicol) (*fca*), Colistin (*mcr*), Vancomycin (*van*) and multidrug (*mdr*). The mostly frequently detected ARG classes in livestock waste include *tet*, *sul*, *erm*, *fca*, and *bla* which match the major classes of antibiotics used in animal husbandry. Of these five ARG classes, *tet* and *sul* are generally the most abundant ARGs appearing in nearly all surveyed livestock waste.



Prevalence of Antibiotic Resistance Genes (ARGs) in Livestock Waste

The abundance and diversity of antibiotic resistance genes (ARGs) found in livestock waste vary significantly depending on factors such as the species, age, dosing patterns, geographical features, and the type of treatment process used. Studies have shown that pig waste tends to

contain higher levels of ARGs compared to other types of livestock waste, such as cow and fish waste. Similarly, chicken waste also exhibits higher ARG abundance compared to cow manure. When livestock waste is applied to the soil, it significantly increases the abundance of ARGs in the soil. Manured soil has been found to contain ARG levels that are up to 28,000 times higher than un-manured soil. Furthermore, ARGs can persist in the soil for more than 120 days after a single application of manure and may take approximately 3-6 months to attenuate to levels similar to the background.

Studies have identified various types of antibiotics in livestock waste, with fluoroquinolones, sulphonamides, and tetracyclines being the most commonly detected. These antibiotics are also of concern because they include compounds labeled as "critically important" for human medicine. As efforts are made to reduce the use of these antibiotics in animal feeding operations, it becomes crucial to detect residues from other antibiotic classes like beta-lactams, lincosamides, macrolides, and polypeptides. To gain a better understanding of the overall antimicrobial burden in manure streams, it is essential to identify the metabolic products of these antibiotics. Therefore, increased efforts should be directed towards developing novel analytical methods that can measure large suites of antibiotics in complex matrices like manure.

Impact of common Livestock Waste Treatment Processes on Antibiotic Resistance Occurrence

1. Composting

Composting is a beneficial method for managing manure, as it utilizes microbial processes to break down organic material in an aerobic environment. This process stabilizes the waste, reduces odors, and helps eliminate pathogens. In some composting practices, the manure is mixed with organic materials like sawdust or dried leaves, which not only balance nutrient levels but also enhance aeration. Turning the compost pile during the process increases oxygen availability, aiding in the microbial breakdown. The composting process elevates the temperature of the manure pile, which has been found to be unaffected by the presence of certain antibiotics like chlortetracycline, oxytetracycline, and tetracycline. Several studies have confirmed this by monitoring various composting parameters such as temperature, carbon dioxide production, volatile solids content, pH changes, moisture content, and carbon to nitrogen ratio.

Composting proves to be an effective approach for mitigating the dispersion of antibiotic resistance genes (ARGs) associated with the land application of organic wastes, with an efficiency of at least 90%. The highest efficiency is typically observed during the early, high-temperature thermophilic phase of composting. This process significantly reduces the diversity and abundance of ARGs. Comparatively, manure-treated soils contain a higher level of ARGs than compost-treated soils. The use of certain additives can further enhance ARG removal during composting by reducing the bio-availability of heavy metals and available carbon. Employing subsurface flow rather than surface flow, proper fillings like bricks and vegetation, decreasing the hydraulic loading rate, optimizing contact time, and maintaining appropriate dissolved oxygen levels can all contribute to improved composting efficiency.

The addition of bulking agents to compost, without affecting temperature, has been found to enhance the removal of antibiotics and ARGs. Among these agents, sawdust has been identified as the most efficient enhancer for antibiotic removal in manures. For many antibiotics, the level of management intensity in compost piles (such as turning and aeration) does not significantly impact antimicrobial degradation. Regardless of the management intensity, high treatment efficiencies have been observed. However, it's worth noting that the observed removal of antibiotics is believed to be attributed to sorption, and thus, antibiotics in manure may not be fully transformed into benign products during composting.

Thus composting is a valuable method for managing manure and reducing the spread of antibiotic resistance. By understanding the factors that influence the composting process and optimizing the use of additives and bulking agents, we can further improve the efficiency of ARG removal and contribute to the sustainable management of organic wastes. However, the potential long-term environmental impact of residual antibiotics in compost needs to be further explored to ensure safe and responsible waste management practices.

2. Anaerobic digestion

Anaerobic digestion is a two-step process involving acidogenic and methanogenic bacteria. During the first step, acidogenic bacteria hydrolyze a fraction of the organic content in manure, converting it into volatile fatty acids (VFAs). In the second step, methanogenic bacteria then convert these VFAs into methane. Although anaerobic digestion requires precise operational control compared to composting or long-term manure storage, it offers several advantages, including the production of methane, which can offset energy costs, reduce greenhouse gas emissions, and enhance the economic sustainability of farm operations.

Anaerobic digestion has shown some potential in removing antibiotic resistance genes (ARGs) from sewage sludge. Higher concentrations of total volatile solids (up to 15%) have been found to enhance the efficiency of ARB removal during anaerobic digestion. Other factors such as applying more lime to stabilize manure before land application, vegetating soil with suitable plants, employing specific land application methods like injection or incorporation, and using adsorbents can also help decrease residual antibiotic concentrations and improve the efficiency of anaerobic digestion.

Compared to anaerobic digestion and lagoons, composting generally exhibits more consistent and higher antibiotic treatment efficiencies. However, it's important to note that in composting, antibiotics are not transformed, and residues remain in the composted manure due to sorption. The bioavailability of antibiotics after land application depends on the reversibility of the sorption reaction. On the other hand, anaerobic digestion involves more prominent biodegradation, and both sorption and biodegradation play a role in lagoons. Both processes lead to lower antibiotic concentrations in treated manure and process effluent. However, the presence of biologically active metabolites in treated manure requires further investigation, particularly regarding antibiotics beyond fluoroquinolones and tetracyclines, where research gaps exist.

While surveillance programs for antibiotic-resistant bacteria in animals, food, and humans are in place in several countries, measuring antibiotic residues in manure is equally important. Land application of manure is a significant pathway for introducing antibiotics into the environment and water supplies.

Anaerobic digestion has demonstrated relatively high treatment efficiencies for most antimicrobials, except for lincosamides, selective sulfonamides, and danofloxacin. Research efforts have primarily focused on the impacts of antimicrobials on biogas production, but optimizing digesters for antibiotic degradation could lead to improved removal of antimicrobials from agricultural waste. Anaerobic digestion holds promise as a method for mitigating antibiotic resistance in agricultural waste. Further research on the degradation of various antibiotics, optimization of anaerobic digesters for antibiotic removal, and concerted efforts to measure antibiotic residues in manure are essential steps to address this pressing environmental and public health concern.

Addressing Antibiotic Resistance in Livestock Waste Management: Multifaceted Mitigation Strategies

Indeed, the global prevalence of antibiotic resistance genes (ARGs) in livestock waste is a significant concern, as these genes can potentially spread to the environment and eventually transfer to humans, posing a serious public health risk. To address this issue, there is an urgent need to improve our understanding and implement measures to reduce ARG proliferation on farms, mitigate ARG discharge, and attenuate their dissemination and fate in the environment.

1. **Reducing In-Farm ARG Proliferation:** To tackle ARG proliferation at its source, responsible antibiotic use in livestock farming is crucial. This involves implementing prudent antibiotic stewardship practices, including using antibiotics only when necessary and under veterinary supervision. The promotion of alternative disease prevention strategies, such as vaccination and improved farm management practices, can also help reduce the need for antibiotics. Management changes in animal husbandry can play a vital role in mitigating the spread of antibiotic resistance. Some of these changes include:
 - A. **Optimizing Animal Diets:** Providing animals with balanced and nutritious diets can enhance their immune system and reduce the occurrence of diseases, thereby decreasing the need for antibiotics.
 - B. **Minimizing Human-to-Animal Contact:** Limiting direct contact between humans and animals can reduce the risk of disease transmission and the need for antibiotic treatment.
 - C. **Waste Collection Methods:** Employing efficient waste collection methods, such as scrape versus flush systems, can help maintain clean and hygienic living conditions for animals, reducing the risk of infections.
 - D. **Frequent Waste Collection:** Increasing the frequency of waste collection can prevent the buildup of pathogens and reduce the likelihood of disease transmission.
 - E. **Containment Areas for Sick Livestock:** Creating separate containment areas for sick animals can prevent the spread of diseases to healthy ones, minimizing the need for widespread antibiotic use.
 - F. **Antibiotic Alternatives:** Exploring and implementing alternative approaches to combat infections, such as antimicrobial peptides, probiotics, and prebiotics, can reduce reliance on antibiotics.
 - G. **Improved Drug Delivery Systems:** Developing more effective and targeted drug delivery systems, like nanomaterials and gel vaccine delivery, can enhance treatment efficiency and minimize the need for broad-spectrum antibiotics.
2. **Mitigating ARG Discharge:** Proper manure management plays a pivotal role in mitigating ARG discharge from livestock operations. Implementing technologies like anaerobic

digestion, composting, and other advanced treatment processes can help reduce ARGs in manure before it is released into the environment. Additionally, optimizing land application practices and adhering to appropriate waiting periods before using manure as fertilizer can minimize the spread of ARGs to receiving environments.

3. **Attenuating Dissemination and Fate of ARGs:** Understanding the fate and transport of ARGs in the environment is essential to develop targeted mitigation strategies. Research on how ARGs move through soil, water, and air can guide the development of measures to attenuate their dissemination. This may involve adopting best management practices for land application, using vegetative buffers to filter runoff, and implementing wastewater treatment technologies to remove ARGs before discharge.
4. **Surveillance and Monitoring:** Regular surveillance and monitoring of ARGs in livestock waste, environmental samples, and human populations are critical to assess the effectiveness of mitigation efforts and identify emerging risks. This data can help inform policies and interventions to curb the spread of antibiotic resistance.
5. **Education and Awareness:** Raising awareness among farmers, veterinarians, and the general public about the importance of responsible antibiotic use, proper manure management, and the potential risks of antibiotic resistance is essential for promoting behavioral changes and collective action.
6. **Regulatory Measures:** Governments and regulatory bodies should play a crucial role in enforcing policies and regulations related to antibiotic use in livestock farming and manure management. Implementing strict guidelines for antibiotic use, manure handling, and treatment can significantly impact ARG dissemination.

To combat the issue of antibiotic resistance in livestock waste requires a multidisciplinary approach involving researchers, policymakers, veterinarians, farmers, and the public. By focusing on reducing in-farm ARG proliferation, mitigating ARG discharge, and attenuating dissemination and fate, we can work towards safeguarding public health and preserving the effectiveness of antibiotics for future generations.

Conclusion

Addressing the issue of antibiotic resistance in animal husbandry and livestock waste requires a comprehensive and collaborative approach. Some key steps that can be taken to mitigate the impact of ARGs from livestock wastes includes enhancing source control and removal efficiency, balancing livestock welfare and profitability with ARG mitigation, promoting collaborative and cross-disciplinary research, optimizing anaerobic digesters for antibiotic degradation, educating farmers, veterinarians, and consumers, promoting alternative growth promoters and surveillance of veterinary antibiotic use, resistance, and residues. By combining these strategies and involving all stakeholders, including researchers, policymakers, farmers, veterinarians, and consumers, we can work towards sustainable and responsible animal husbandry practices that protect human and animal health, and the environment from the threat of antibiotic resistance.

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