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Review

Antibiotic Use in Aquaculture: Residues, Health Risks and Environmental Implications from a One Health Perspective

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Abstract: Aquaculture plays an increasingly important role in global food production, but intensive production systems may increase the risk of bacterial diseases and consequently the use of antibiotics. Although antimicrobial therapy remains necessary for the control of bacterial infections, inappropriate or excessive use can promote antimicrobial resistance, contribute to the occurrence of drug residues in edible fish tissues, and increase environmental contamination. Antibiotic residues may persist in aquatic organisms, water, and sediments, creating potential risks for consumers and aquatic ecosystems. Human health concerns include antimicrobial resistance, hypersensitivity reactions, disruption of the intestinal microbiota, toxicological effects, and possible long-term cumulative exposure. In aquatic environments, antibiotic residues may alter microbial communities, affect non-target organisms, and contribute to the spread of resistance genes through water, sediments, and food webs. These interconnected effects demonstrate the importance of addressing antibiotic use in aquaculture through a One Health perspective that integrates animal, human, and environmental health. Sustainable reduction of antibiotic dependence requires improved biosecurity, husbandry, diagnostics, vaccination, functional feeds, alternative biological strategies, prudent antimicrobial stewardship, and effective environmental management. This review summarizes the major pathways, risks, and preventive approaches associated with antibiotic use and residues in aquaculture.

Keywords: *Aquaculture; antibiotics; antimicrobial resistance; antibiotic residues; One Health; food safety; fish health; public health; aquatic environment; biosecurity*.

1. Introduction

Aquaculture has become an increasingly important component of global food production, driven by the growing demand for fish and other aquatic products and by the limited capacity of capture fisheries to meet the needs of an expanding population. The intensification of aquaculture production has contributed substantially to food availability and economic development, but it has also created conditions that favor the emergence and rapid transmission of infectious diseases. High stocking densities, environmental fluctuations, handling stress, and intensive feeding practices may

compromise fish health and increase the risk of bacterial infections, making effective disease prevention and health management essential for sustainable production [1–3].

Antibiotics have therefore played an important role in the prevention and treatment of bacterial diseases in aquaculture. When appropriately prescribed and correctly administered, antimicrobial therapy can reduce mortality, support animal welfare, and limit economic losses associated with infectious outbreaks. However, inappropriate, excessive, or poorly controlled antibiotic use may create several interconnected problems. Repeated exposure to antimicrobial agents promotes selective pressure on bacterial populations and facilitates the emergence, persistence, and dissemination of antimicrobial resistance. Resistant microorganisms and resistance determinants can circulate within aquaculture facilities, surrounding aquatic environments, wild animal populations, and ultimately through the food chain [4–6].

Another important concern is the occurrence of antibiotic residues in edible fish tissues. Residues may result from inappropriate dosing, repeated treatments, failure to observe withdrawal periods, or exposure to antimicrobial compounds present in contaminated water and sediments. Their persistence in aquaculture products is particularly relevant from the perspective of food safety, since consumers may be exposed to low concentrations of antimicrobial substances through the regular consumption of farmed fish. Such exposure has been associated with concerns related to hypersensitivity reactions, alterations of the intestinal microbiota, toxicological effects, and, most importantly, the wider problem of antimicrobial resistance [1,7,8].

The consequences of antibiotic use in aquaculture are not limited to farmed animals and consumers. A considerable proportion of administered antimicrobial compounds and their metabolites may enter the surrounding environment through uneaten medicated feed, fish excretion, wastewater, and aquaculture effluents. Once released into aquatic ecosystems, these substances may persist in water and sediments, modify microbial communities, exert selective pressure on environmental bacteria, and contribute to the maintenance and spread of antimicrobial resistance. Changes in microbial diversity and ecosystem functioning may consequently affect water quality, nutrient cycling, biodiversity, and the health of both cultured and wild aquatic organisms [9,10].

These interconnected pathways make antibiotic use in aquaculture particularly suitable for evaluation through the One Health perspective, which recognizes that human health, animal health, and environmental health are closely interdependent. In aquaculture, antimicrobial resistance and antibiotic residues represent a clear point of interaction among these three domains: antibiotics are administered to protect the health of cultured aquatic animals, their residues and resistant microorganisms may reach consumers through food, while antimicrobial compounds and resistance determinants can simultaneously circulate through aquatic environments. Reducing unnecessary antibiotic dependence therefore requires an integrated approach combining improved fish health management, disease prevention, responsible antimicrobial use, biosecurity, vaccination, appropriate husbandry, and alternative strategies capable of maintaining productivity without increasing antimicrobial pressure [1,11].

The aim of this review is to provide an integrated overview of antibiotic use and antimicrobial resistance in aquaculture, the occurrence of antibiotic residues in farmed fish, their potential implications for human health and aquatic ecosystems, and sustainable approaches for reducing antibiotic dependence from a One Health perspective.

2. Antibiotic Practices in Modern Aquaculture

Antibiotics remain an important component of bacterial disease management in intensive aquaculture, particularly when infectious outbreaks threaten fish health, survival, and production efficiency. Their use varies considerably among production systems, fish species, geographical regions, and levels of veterinary supervision. Among the antimicrobial groups most commonly associated with aquaculture are tetracyclines, fluoroquinolones, sulfonamides, beta-lactams, phenicols, and several other compounds used either alone or in combination. The range of antimicrobial agents available for aquatic animals differs substantially among countries, reflecting

differences in production practices, disease occurrence, access to veterinary medicines, and national approaches to antimicrobial use [4,12].

In commercial fish farming, antimicrobial treatment is most commonly administered through medicated feed, whereas direct application to water is used less frequently. Because individual treatment of fish is generally impractical in intensive production, therapy is often applied to groups of animals. Consequently, both clinically affected and apparently healthy fish may be exposed to antimicrobial agents during disease outbreaks. Although such an approach may be necessary under particular production conditions, it also increases the importance of accurate diagnosis, appropriate drug selection, correct dosing, and proper treatment duration [4,6].

The intensity and pattern of antibiotic use differ markedly between aquaculture-producing regions. In highly controlled production systems, antimicrobial use has generally shifted toward therapeutic application under professional supervision, accompanied by greater emphasis on vaccination, biosecurity, improved husbandry, and disease prevention. In contrast, some rapidly expanding aquaculture sectors continue to rely heavily on antibiotics because of high stocking densities, frequent disease outbreaks, limited diagnostic capacity, insufficient access to preventive measures, and relatively easy availability of antimicrobial products. These differences make it difficult to establish a uniform picture of global antibiotic consumption in aquaculture (Figure 1) [11,13–15].

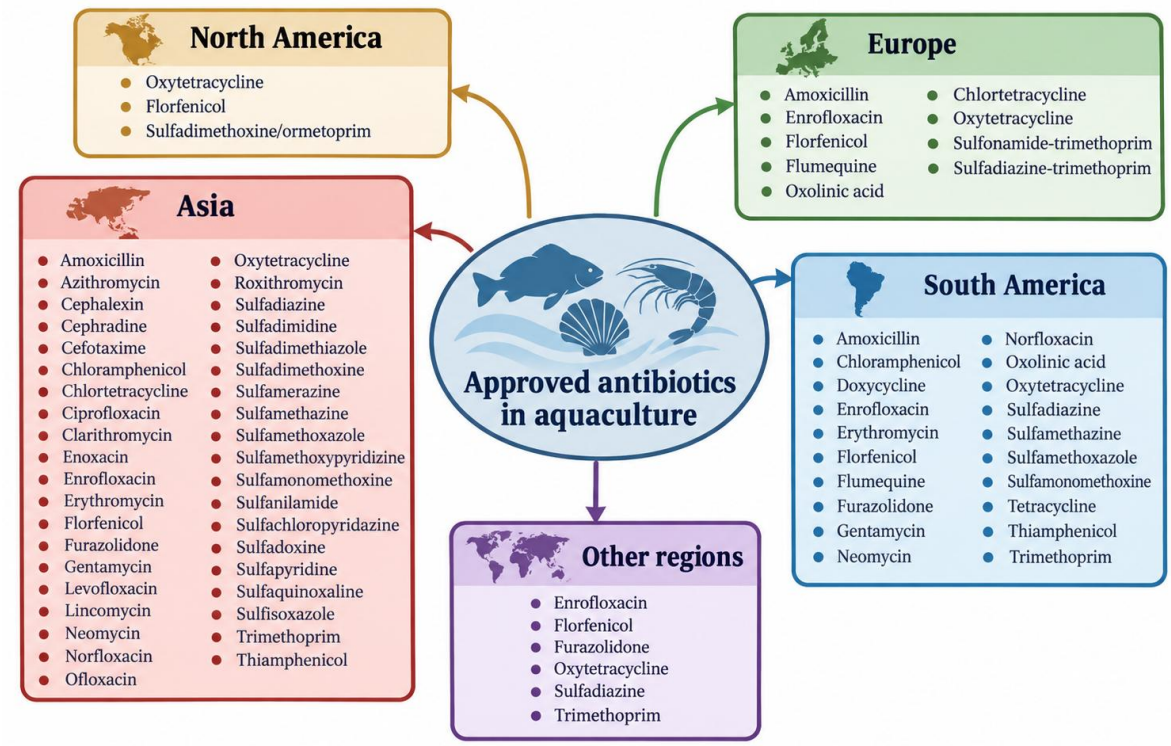

Figure 1. Regional distribution of antibiotics approved for use in aquaculture. Source data adapted from [1].

Freshwater production systems may be particularly dependent on antimicrobial therapy where effective vaccines or other preventive tools are not readily available. Under such circumstances, antibiotics may be used not only because of confirmed bacterial infections but also as a response to poorly defined disease problems. Inadequate diagnostic procedures can result in unnecessary treatment, inappropriate selection of antimicrobial agents, incorrect doses, or prolonged exposure. Such practices reduce treatment efficiency and create conditions that favor the persistence of drug residues and the selection of resistant bacterial populations [4,14].

Another important challenge is the quality and authenticity of veterinary antimicrobial products. In regions with limited pharmaceutical control, substandard or counterfeit products may contain inappropriate amounts of active compounds (Figure 2) [16].

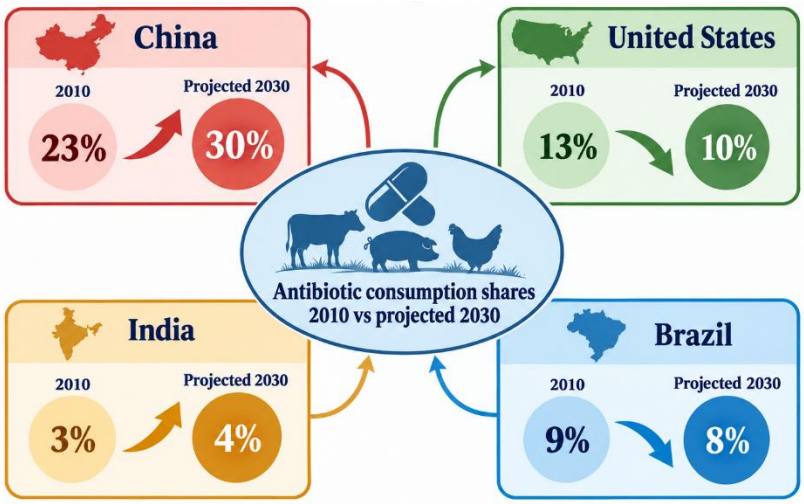

Figure 2. Schematic overview of antibiotic consumption shares in animal food production. Source data adapted from [1].

Insufficient concentrations may fail to eliminate bacterial pathogens while still exposing microbial populations to antimicrobial pressure. Persistent infections may then lead to repeated treatment, higher cumulative antimicrobial use, and an increased probability of residue occurrence in fish and the surrounding environment [16].

Antibiotic use in aquaculture therefore represents more than a question of treating bacterial diseases. The way in which these drugs are selected, administered, and managed directly influences treatment success, fish health, antimicrobial resistance, residue formation, and environmental exposure. Greater reliance on accurate disease diagnosis, professional supervision, appropriate dosing, withdrawal periods, preventive health management, and alternatives to antimicrobial treatment is essential for reducing unnecessary antibiotic exposure while maintaining productive and healthy aquaculture systems [11,12].

3. Occurrence and Persistence of Antibiotic Residues in Farmed Fish

The occurrence of antibiotic residues in farmed fish remains a relevant issue in aquaculture because these compounds may persist in edible tissues and consequently enter the human food chain. Residues have been reported in numerous cultured freshwater and marine species, which confirms that this is not an isolated problem linked to a single production system, fish species, or geographic area. Their presence reflects the close relationship between fish health management, antimicrobial use practices, environmental conditions, and the overall level of control within aquaculture production. From a food safety perspective, the detection of antibiotic residues in fish is especially important because aquaculture products are increasingly consumed worldwide, and even low-level, repeated exposure may raise concerns about long-term public health implications [7,8,17].

In aquaculture, residues may originate from both direct and indirect exposure pathways. The most common route is the administration of antibiotics through medicated feed, which is widely used for the treatment of bacterial diseases in intensive production. In some systems, antibiotics may also be introduced through the water, although this approach is generally less targeted and may increase environmental dispersion. Once administered, antimicrobial compounds are absorbed, distributed through fish tissues, metabolized to different extents, and finally eliminated. However, elimination is not always rapid or complete, and the persistence of residues depends on a variety of factors, including the chemical characteristics of the antibiotic, dosage, duration of treatment, route of administration, water temperature, fish metabolism, species-specific physiology, and the health status of the animals. As a result, antibiotic residues may remain detectable in muscle and other tissues for a period of time after treatment has ended [18,19].

The occurrence of residues is particularly associated with inappropriate or poorly controlled antimicrobial use. This includes excessive dosing, unnecessarily frequent treatments, prolonged administration, empirical treatment without proper diagnosis, and failure to observe withdrawal periods before harvest. When withdrawal periods are not respected, fish may be marketed before drug concentrations have declined to acceptable levels. In addition, inadequate treatment records, insufficient veterinary oversight, and weak monitoring systems may increase the likelihood that such practices remain undetected. In some production settings, residues may also result from the use of antimicrobials of questionable quality, including substandard or counterfeit products, which may contain incorrect concentrations of active substances and contribute to unpredictable residue patterns [7,19].

Another important source of residue occurrence is the production environment itself. Antibiotics may enter aquaculture systems not only through intentional use on the farm, but also through contaminated water sources, sediment, runoff from agricultural land, discharge from wastewater systems, and effluents associated with pharmaceutical production or other animal farming activities. These external inputs may expose fish to antimicrobial compounds even when no direct treatment is taking place. In integrated or poorly protected production systems, this environmental pathway may become especially relevant. Uneaten medicated feed, fish excretion, and poor waste management can further increase the burden of antimicrobial compounds within ponds, cages, tanks, and surrounding aquatic ecosystems, creating conditions for repeated or continuous exposure [20,21].

The persistence of antibiotic residues in farmed fish is also influenced by the behavior of these compounds in the aquatic environment. Some antibiotics are relatively unstable and degrade more rapidly, whereas others can persist in water or bind to organic matter and sediments, where they may remain available for longer periods. Sediments can therefore act as reservoirs of antimicrobial compounds, allowing re-exposure of cultured organisms over time. Environmental persistence is additionally affected by pH, salinity, temperature, light exposure, microbial activity, and water exchange. Under certain conditions, these factors may slow degradation and prolong the presence of antimicrobial residues within aquaculture systems. This is particularly concerning in intensive production systems, where repeated treatments and high stocking densities may maintain constant antimicrobial pressure [20,22].

Residue persistence should also be considered in relation to fish biology. Different fish species absorb, distribute, metabolize, and excrete drugs at different rates, which means that the same antibiotic may show different depletion profiles depending on the cultured species. Growth stage, body composition, lipid content, and feeding behavior may further influence residue dynamics. For example, compounds may persist longer in tissues when metabolism is slower or when environmental conditions reduce normal physiological activity. Stress, disease, and poor water quality may also interfere with normal elimination processes. These biological and environmental interactions make residue behavior in aquaculture complex and support the need for careful control of treatment protocols [18,23].

In practical terms, the presence of residues in farmed fish is not only a reflection of drug use, but also of the overall quality of aquaculture management. Poor biosecurity, limited disease prevention, inadequate hygiene, and insufficient monitoring often increase dependence on antibiotics and, consequently, the risk of residues. By contrast, production systems based on better husbandry, routine health surveillance, accurate diagnosis, and prudent antimicrobial use are less likely to generate residue-related problems. Residue occurrence is therefore closely linked to the broader sustainability of aquaculture and to the capacity of the sector to balance fish health protection with food safety requirements [4,24].

The actual extent of antibiotic residue occurrence in aquaculture products is often difficult to estimate with precision. In many regions, especially where surveillance infrastructure is limited, available data remain incomplete and may underestimate the true scale of the problem. Monitoring programs are not uniformly implemented, analytical capacities differ considerably among countries, and reporting systems are often fragmented. Consequently, residue occurrence may be more widespread than official records suggest, particularly in areas where aquaculture is rapidly expanding and antibiotic use remains insufficiently controlled [13].

Overall, the occurrence and persistence of antibiotic residues in farmed fish arise from the interaction of antimicrobial use practices, fish physiology, environmental contamination, and farm management conditions. Residues may originate from direct treatment, indirect environmental exposure, or a combination of both, and their persistence is shaped by multiple biological and ecological factors. For these reasons, reducing residue occurrence requires more than simple restrictions on antibiotic use; it requires a comprehensive approach that includes responsible antimicrobial administration, strict observance of withdrawal periods, better farm management, cleaner production environments, and stronger monitoring systems throughout the aquaculture chain [19].

4. Human Health Consequences of Antibiotic Residues

The presence of antibiotic residues in aquaculture products represents an important public health concern because these compounds may reach consumers through the regular consumption of farmed fish and other aquatic organisms. Although the concentrations detected in food are often low, the significance of this issue lies in the possibility of repeated dietary exposure over time, as well as in the broader biological effects that even small quantities of antimicrobial substances may have on human health. The health consequences associated with antibiotic residues are complex and may include direct toxicological effects, allergic and hypersensitivity reactions, disruption of the intestinal microbiota, interference with normal physiological processes, and, most importantly, contribution to the development and spread of antimicrobial resistance [23,25].

Among all potential consequences, antimicrobial resistance remains the most serious and far-reaching. Continuous exposure to antibiotic residues, even at subtherapeutic levels, may create selective pressure favoring the survival and persistence of resistant bacteria. This is particularly important because aquaculture environments already serve as reservoirs of diverse microbial populations, including opportunistic and pathogenic bacteria capable of carrying resistance determinants. When resistant bacteria or resistance genes circulate from aquaculture systems into the food chain, they may ultimately contribute to the wider resistance burden affecting human medicine. In that context, antibiotic residues in food are not only a chemical contamination issue, but also part of a broader ecological and epidemiological problem that weakens the long-term effectiveness of antimicrobial therapy in humans [26,27].

Another important concern is the possibility of allergic and hypersensitivity reactions. Certain antibiotics are known to trigger immune-mediated responses in susceptible individuals, and even low levels of residues may be problematic in particularly sensitive consumers. Reactions may range from mild manifestations, such as skin irritation, rashes, or gastrointestinal discomfort, to more pronounced systemic responses in predisposed individuals. Although these events may not be frequent in the general population, their clinical relevance should not be underestimated, especially when food safety systems aim to protect vulnerable individuals as well as the population at large [28].

The toxicological impact of antibiotic residues is also relevant, particularly in cases of chronic exposure. Repeated ingestion of low concentrations of antimicrobial compounds may affect various organs and physiological systems, depending on the chemical nature of the residue, the dose, the duration of exposure, and the susceptibility of the individual. Some compounds have been associated with hepatic or renal stress, while others may interfere with hematological, neurological, or metabolic processes. Even when residues remain below established safety thresholds, long-term combined exposure through multiple dietary sources remains a point of concern, especially in individuals with pre-existing health conditions or reduced detoxification capacity [25,29].

Antibiotic residues may also influence the composition and function of the human intestinal microbiota. The gut microbiome plays an essential role in digestion, nutrient metabolism, immune regulation, and overall health. Repeated exposure to antimicrobial residues may disturb the natural microbial balance, reducing beneficial bacterial populations and allowing less desirable microorganisms to proliferate. Such dysbiosis may contribute to impaired digestion, reduced

colonization resistance against pathogens, altered immune responses, and a greater likelihood of gastrointestinal disturbances. Since the intestinal microbiota is increasingly recognized as a major determinant of systemic health, the potential of antibiotic residues to disrupt this delicate ecosystem deserves particular attention [25,27].

In addition to microbiota-related effects, some antibiotic residues raise concerns regarding genotoxic, mutagenic, or carcinogenic potential. Certain antimicrobial substances or their metabolites may interact with cellular structures, induce oxidative stress, or interfere with DNA integrity and repair mechanisms. Although the extent of these effects depends heavily on the compound involved and the level of exposure, such risks are taken seriously because they relate to long-term health outcomes. For this reason, residues of substances with known carcinogenic or genotoxic properties are considered especially problematic, and their presence in food products is unacceptable in many regulatory contexts [30].

Another aspect that should be considered is the potential for endocrine and developmental effects. Some antibiotic compounds may interfere, directly or indirectly, with hormonal balance, cellular signaling, growth, or reproductive physiology. This issue is particularly important for sensitive population groups such as children, adolescents, pregnant women, and individuals with endocrine disorders. While the exact magnitude of these effects may vary and is often difficult to quantify under real-life dietary conditions, the possibility of subtle biological interference supports the need for precaution in evaluating long-term exposure to antimicrobial residues [31].

The issue of cumulative exposure further strengthens public health concerns. Consumers are not exposed to antibiotic residues from a single source only, but potentially from multiple foods of animal origin, water, and environmental contaminants. Even if residue levels in individual products are low, total cumulative exposure over time may become biologically relevant. In addition, residues may interact with prescribed medications or with other xenobiotics present in the body, potentially modifying pharmacological responses or contributing to combined toxic effects. This cumulative perspective is especially important within a One Health framework, where food safety is linked not only to immediate toxicological thresholds, but also to long-term population health and antimicrobial stewardship [25].

It is also important to recognize that the health consequences of antibiotic residues are not evenly distributed across the population. Vulnerable groups, including children, the elderly, immunocompromised individuals, and people with chronic diseases, may be more susceptible to adverse effects. Likewise, populations with high fish consumption may experience greater exposure than those in whom aquaculture products are consumed only occasionally. For this reason, the evaluation of public health risk should consider not only average exposure, but also differences in dietary habits, physiological vulnerability, and cumulative lifetime intake (Figure 3) [23].

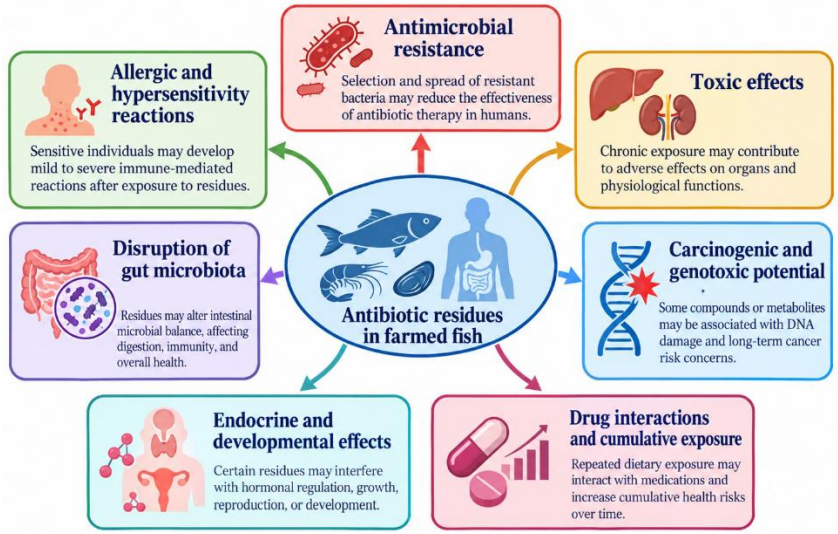

Figure 3. Adverse effects of antibiotic residue on human health.

Overall, antibiotic residues in aquaculture products represent a multifaceted human health issue that extends far beyond the simple presence of chemical traces in food. Their significance lies in the possibility of repeated exposure, their contribution to antimicrobial resistance, their capacity to alter the intestinal microbiota, and their potential to cause toxic, allergic, endocrine, or genotoxic effects. From a public health standpoint, this problem highlights the importance of prudent antibiotic use in aquaculture, strict adherence to withdrawal periods, effective monitoring systems, and broader preventive strategies aimed at reducing unnecessary antimicrobial dependence across food production systems [23,26].

5. Environmental Fate and Ecological Impact of Antibiotic Residues

Antibiotic residues released from aquaculture systems represent an important environmental concern because their effects are not limited to the cultured animals for which they were initially intended. Once introduced into production systems, these compounds may be dispersed into surrounding aquatic environments through uneaten medicated feed, fish excretion, suspended particles, wastewater, and farm effluents. As a result, antibiotic residues may enter ponds, rivers, lakes, estuaries, and coastal waters, where they can remain biologically active and influence a wide range of ecological processes. Their environmental fate depends on the physicochemical properties of the compounds, the characteristics of the receiving ecosystem, and the intensity and frequency of their use in aquaculture practice [32,33].

After entering the aquatic environment, antibiotics may remain dissolved in the water column, adsorb to organic particles, or accumulate in bottom sediments. This distribution pattern is important because it determines how long these compounds persist and which organisms are most likely to be exposed. Some antibiotics are relatively unstable and undergo degradation more rapidly, while others can remain in the environment for prolonged periods, especially under conditions that limit photodegradation, microbial breakdown, or dilution. Sediments are of particular importance because they may act as long-term reservoirs of antibiotic residues. Once deposited, these compounds may persist in production areas and surrounding habitats, allowing repeated exposure of benthic organisms and creating a source of chronic environmental contamination even after direct treatment has ended [22].

The presence of antibiotic residues in water and sediments may strongly influence aquatic microbial communities. Microorganisms are among the first biological targets of these compounds, and even low concentrations may modify the structure, diversity, and activity of microbial populations. Since microbial communities are essential for nutrient cycling, organic matter degradation, primary productivity, and the self-purification capacity of aquatic ecosystems, any disturbance in their balance may have broader ecological consequences. Altered microbial activity can affect nitrogen and phosphorus transformations, change decomposition processes, and interfere with the natural functioning of food webs. In this way, antibiotic residues do not merely contaminate the environment chemically, but may also disrupt its biological stability and resilience [34].

One of the most serious environmental consequences of antibiotic residues is the selection and spread of antimicrobial resistance. When aquatic microorganisms are repeatedly exposed to antimicrobial compounds, selective pressure favors the survival of resistant bacteria. Over time, this may lead to the enrichment of resistance genes within microbial communities and facilitate their transfer among environmental, animal-associated, and potentially human-associated bacteria. Aquatic environments influenced by aquaculture may therefore become reservoirs and transmission pathways for antimicrobial resistance. This problem extends beyond the farm itself, because resistant bacteria and resistance determinants may move through water currents, sediments, wild aquatic species, and connected ecosystems. From a One Health perspective, such environmental dissemination is especially important, as it links fish production, ecosystem health, and human health through a shared resistance burden [32,34].

Antibiotic residues may also affect non-target aquatic organisms that are not the intended recipients of treatment. These include plankton, benthic invertebrates, mollusks, crustaceans, algae,

aquatic plants, and wild fish species living in or near aquaculture systems. Exposure may influence growth, reproduction, behavior, physiology, and survival, depending on the compound, concentration, and duration of contact. In sensitive species, even sublethal exposure may produce biologically relevant effects, such as reduced feeding activity, impaired reproduction, oxidative stress, tissue alterations, or weakened immune responses. Because many of these organisms occupy key ecological roles, their impairment may indirectly affect higher trophic levels and contribute to broader ecosystem dysfunction [35,36].

Another important ecological dimension of antibiotic residues is their potential to propagate through food webs. Once residues affect microorganisms, plankton, or small invertebrates, the consequences may extend upward through trophic interactions. Sensitive organisms may decline, resistant or opportunistic populations may proliferate, and predator-prey relationships may be altered. Such shifts can influence community composition and reduce biodiversity. In addition, chronic contamination may weaken ecosystem services such as nutrient recycling, water purification, biological productivity, and ecological resilience. In highly connected aquatic environments, even localized sources of antimicrobial contamination may therefore contribute to more diffuse ecological changes over time [34,36].

Environmental effects are often further intensified in intensive production systems, especially where high stocking densities, repeated antimicrobial treatments, and insufficient waste management are present. Under such conditions, aquaculture operations may become continuous points of release for antibiotic residues into the environment. Poorly controlled discharge of sediments, sludge, and farm effluents can increase local contamination and prolong exposure in adjacent habitats. In open-water systems, residues may disperse more widely, whereas in pond-based or enclosed systems they may accumulate more readily. The ecological consequences therefore vary according to the type of farming system, hydrological conditions, and the capacity of the environment to dilute, transform, or remove contaminants [33].

The environmental fate of antibiotic residues is also shaped by several abiotic factors, including temperature, pH, salinity, dissolved oxygen, sunlight, and microbial activity. These parameters influence degradation rates, chemical stability, sorption behavior, and mobility within aquatic systems. For example, some compounds degrade more slowly at lower temperatures, while others bind more readily to sediments under specific pH conditions. Seasonal variation and local environmental conditions can therefore determine whether residues disappear relatively quickly or persist long enough to create long-term ecological pressure. This variability makes the environmental assessment of antibiotic residues particularly complex and highlights the need for site-specific understanding of contamination dynamics [22].

From a broader ecological perspective, antibiotic residues in aquaculture should not be viewed as isolated pollutants, but rather as part of a network of interacting stressors affecting aquatic systems. Their effects may be amplified when combined with other pressures such as eutrophication, organic loading, heavy metals, pesticides, habitat modification, and climate-related changes in water quality. In such circumstances, antibiotic residues may contribute to cumulative ecological stress and reduce the capacity of aquatic ecosystems to recover from disturbance. This is especially relevant in regions where aquaculture is expanding rapidly and environmental safeguards may not be equally developed [36].

Overall, the environmental fate and ecological impact of antibiotic residues in aquaculture involve a series of interconnected processes that begin with antimicrobial use on the farm and continue through water, sediments, microorganisms, non-target organisms, and food webs. These compounds may persist in the environment, alter microbial balance, promote antimicrobial resistance, affect aquatic biodiversity, and compromise essential ecosystem functions. For that reason, the environmental dimension of antibiotic use in aquaculture must be considered a central component of sustainable production. Reducing these risks requires prudent antimicrobial use, improved waste management, better farm design, stronger environmental monitoring, and the wider adoption of preventive health strategies that lower dependence on antibiotics while protecting both aquatic animal production and ecosystem integrity. [32,34]

6. Sustainable Approaches to Reduce Antibiotic Dependence within a One Health Framework

Reducing antibiotic dependence in aquaculture is an essential objective for the long-term sustainability of the sector and for the protection of animal health, human health, and the environment. Within a One Health framework, this issue cannot be approached solely as a matter of limiting antimicrobial use, but rather as a broader effort to improve fish health management, strengthen disease prevention, minimize environmental contamination, and reduce the selective pressure that drives antimicrobial resistance. Sustainable aquaculture therefore depends on the transition from a reactive model based primarily on therapeutic intervention toward a preventive model in which antibiotics are reserved for situations in which they are truly necessary and justified [37,38].

At the core of this transition is the recognition that antibiotic use in aquaculture is often a consequence of underlying weaknesses in production systems. Disease outbreaks are more likely to occur when fish are exposed to chronic stress, poor water quality, inappropriate stocking densities, inadequate nutrition, or insufficient hygiene. Under such conditions, antibiotics may be used as a short-term solution to problems that are fundamentally managerial or environmental in nature. Sustainable reduction of antibiotic dependence therefore begins with the improvement of basic production conditions. Good husbandry practices remain one of the most effective strategies for disease prevention because they strengthen fish resilience, improve welfare, and reduce the probability of infection. Appropriate stocking densities, balanced feeding, careful handling, regular health observation, and the maintenance of optimal water quality all contribute to healthier production systems in which the need for antimicrobial treatment is substantially lower [39,40].

Biosecurity is another essential pillar of antibiotic reduction. Effective biosecurity aims to prevent the introduction, circulation, and amplification of pathogens within aquaculture facilities. This includes measures such as the controlled movement of animals, quarantine of new or returning stock, disinfection of equipment, restriction of unnecessary farm access, separation of age groups or production units, and proper disposal of dead animals and waste. In well-managed systems, biosecurity reduces the risk of introducing infectious agents and limits the spread of disease once a problem emerges. By lowering pathogen pressure, it decreases the need for emergency antibiotic use and supports a more stable and predictable production environment. From a One Health perspective, strong biosecurity also reduces the release of pathogens, resistant bacteria, and antimicrobial residues into surrounding ecosystems [39].

Vaccination represents one of the most valuable alternatives to routine antibiotic use in aquaculture, particularly in production systems where important bacterial diseases can be prevented immunologically. When effective vaccines are available and properly applied, they can significantly reduce disease incidence, mortality, and the frequency of antimicrobial treatments. Vaccination not only protects fish populations directly, but also helps stabilize productivity and improve animal welfare. In addition, successful immunoprophylaxis reduces the burden of resistant bacteria by decreasing the need for antimicrobial exposure in the first place. Despite these advantages, the use of vaccines in aquaculture may still be limited by cost, species specificity, labor requirements, technical barriers related to administration methods, and variable farmer acceptance. Expanding vaccine accessibility and improving confidence in vaccination programs therefore remain important components of sustainable aquaculture development [41].

Alongside vaccination, several biological and nutritional strategies have gained attention as supportive or alternative tools for disease prevention. Probiotics, prebiotics, and synbiotics are increasingly explored for their capacity to improve gut health, support microbial balance, stimulate immune responses, and enhance disease resistance. By promoting a more favorable intestinal and environmental microbiota, these approaches may strengthen host resilience and reduce susceptibility to infection. Phytogenic compounds, plant extracts, essential oils, and other natural bioactive substances have also been investigated for their antimicrobial, antioxidant, anti-inflammatory, or immunomodulatory properties. Although their efficacy may vary depending on formulation, species, dose, and farming conditions, such interventions reflect a broader movement toward preventive health management that relies less on conventional antibiotics [37,42,43].

Immunostimulants and functional feeds provide another promising area for reducing antibiotic dependence. Nutritional interventions that improve immune competence, reduce stress, and support intestinal integrity may play an important role in preventing disease under commercial farming conditions. Since fish immunity is strongly influenced by nutrition and environmental stability, well-designed feeding strategies can improve the natural capacity of fish to resist pathogens (Table 1). In this context, antibiotic reduction should not be viewed only as a pharmacological challenge, but also as a question of optimizing the biological robustness of cultured animals through feeding, breeding, and environmental management [37,42,44].

Table 1. Sustainable strategies used to reduce antibiotic use in aquaculture within a one health framework. Content adapted and reorganized from [1].

Domain	Strategy	Practical role in aquaculture	Contribution to One Health
Foundational prevention	**Biosecurity**	Prevents pathogen introduction and spread through quarantine, disinfection, stock control, and movement restrictions.	Lowers disease pressure, reduces antibiotic need, and limits environmental dissemination of pathogens.
	Good husbandry	Maintains appropriate stocking density, water quality, nutrition, handling, and routine health observation.	Improves fish welfare and resilience, reducing disease outbreaks and treatment frequency.
	Improved farm management	Optimizes hygiene, waste handling, environmental control, and daily management practices.	Supports healthier production systems and lowers contamination risks.
Host-supportive and biological alternatives	**Vaccination**	Prevents important bacterial diseases and reduces reliance on therapeutic antimicrobials.	Protects animal health while reducing residues and resistance pressure.
	Immunostimulants	Enhances innate defense mechanisms and stress tolerance in cultured fish.	Strengthens disease resistance and decreases treatment demand.
	Probiotics	Promotes beneficial microbial communities in fish and culture systems.	Supports gut health, water quality, and lower pathogen dominance.
	Prebiotics	Stimulates beneficial intestinal microbiota and improves immune function.	Favors host resilience and may reduce antibiotic dependence.
	Phytogenics	Uses plant-derived bioactive compounds with antimicrobial, antioxidant, or immunomodulatory effects.	Provides supportive disease control with a reduced chemical burden.
Responsible use and system support	**Selective breeding**	Favors stocks with improved resistance to common pathogens.	Builds long-term resilience and reduces antimicrobial reliance.
	Antibiotic stewardship	Restricts antibiotic use to justified cases with correct drug choice, dose, duration, and withdrawal period.	Preserves antimicrobial efficacy and improves food safety.
	Governance and oversight	Strengthens farm rules, monitoring, and compliance for prudent antimicrobial use.	Supports responsible production and protects public and environmental health.
	Research and innovation	Advances diagnostics, vaccines, functional feeds, and sustainable production technologies.	Enables long-term reduction of antimicrobial dependence across aquaculture systems.

Accurate and timely diagnosis is equally important in limiting unnecessary antimicrobial use. In many aquaculture systems, antibiotics may be administered empirically, without clear confirmation of the causative agent or without distinguishing bacterial diseases from viral, parasitic, or environmental disorders. This practice not only reduces treatment efficiency, but also promotes inappropriate drug selection and avoidable antimicrobial exposure. Improved diagnostic capacity, including better access to laboratory support, pathogen identification, and health surveillance, allows more rational decision-making and helps ensure that antibiotics are used only when bacterial infection is clearly indicated. In this sense, strengthening diagnostic infrastructure and professional veterinary involvement is fundamental for antimicrobial stewardship in aquaculture [24].

Prudent antibiotic stewardship should be considered a central component of sustainable disease management. Even in systems where alternative measures are improved, antibiotics may still be necessary in some circumstances to protect animal health and prevent severe production losses. However, their use should be guided by clear principles: treatment should be based on appropriate diagnosis, the selected drug should be suitable for the target pathogen, dosing and duration should be correct, withdrawal periods should be respected, and treatment records should be maintained accurately. Antibiotics should not function as substitutes for poor husbandry or weak biosecurity, and they should not be used indiscriminately as routine preventive tools. Stewardship therefore does not imply absolute elimination of antibiotics, but rather their responsible, limited, and evidence-based use within a broader preventive framework [37].

Improved farm design and system management can also help reduce antimicrobial dependence. Production systems that maintain better water exchange, effective waste removal, lower organic loading, and improved separation between culture units are generally less prone to disease pressure. Recirculating aquaculture systems, integrated management approaches, and other technologies that allow greater environmental control may contribute to lower pathogen exposure and more targeted health management. Likewise, better sludge handling and effluent treatment can reduce the release of antibiotics and resistant microorganisms into the environment, thereby supporting both farm-level and ecosystem-level sustainability. These management improvements are especially important from a One Health perspective because they address the environmental pathways through which antimicrobial residues and resistant bacteria can spread beyond the farm [38,40,45].

Selective breeding for disease resistance offers additional long-term potential. By favoring fish lines with improved resistance to common pathogens, aquaculture operations may gradually reduce their reliance on pharmaceutical disease control. Genetic improvement cannot replace good management, but it can complement other preventive approaches and contribute to more resilient production systems. In the future, breeding programs that integrate health traits, growth performance, and environmental adaptability may become increasingly important in the design of low-antibiotic aquaculture [37].

Education and capacity building are also critical for sustainable change. Farmers, technicians, aquatic animal health professionals, and decision-makers all play a role in determining how antimicrobials are used in practice. Training in disease prevention, biosecurity, responsible medicine use, water quality management, and early recognition of health problems can significantly improve farm-level decision-making. In regions where aquaculture is expanding rapidly, improving practical knowledge may be one of the most cost-effective ways to reduce unnecessary antibiotic use. This is particularly important in low-resource settings, where access to sophisticated technologies may be limited but improvements in management practice can still produce substantial benefits [37].

A One Health approach requires that these strategies not be considered separately, but as interconnected elements of a common objective. Healthier fish reduce the need for antibiotics; lower antibiotic use decreases the probability of residue occurrence in food; reduced environmental release lowers ecological exposure and selective pressure for resistance; and improved food safety ultimately benefits consumers. In this way, interventions directed at aquaculture management can generate simultaneous benefits across animal, human, and environmental health domains. The reduction of antibiotic dependence therefore represents more than a technical improvement in fish farming; it is part of a broader commitment to sustainable food production and responsible antimicrobial stewardship [37,38].

Ultimately, sustainable approaches to reducing antibiotic dependence in aquaculture rely on prevention, not correction. Systems that emphasize biosecurity, husbandry, vaccination, nutrition, diagnostics, stewardship, environmental control, and farmer education are far more likely to achieve lasting reductions in antibiotic use than systems that depend primarily on therapeutic intervention. Within a One Health framework, such strategies provide the most balanced and scientifically sound path forward, allowing aquaculture to remain productive and economically viable while minimizing risks to public health and aquatic ecosystems [37,39].

Conflicts of Interest: The authors declare no conflicts of interest.

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