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Review Article

ANTIBIOTIC RESISTANCE IN AQUACULTURE AND THE SCOPE OF PROBIOTIC APPROACH: A REVIEW

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Abstract

Antibiotic resistance has become a critical challenge in the aquaculture industry. Besides devastating economic losses, the alarming rate of antibiotic resistance poses a significant threat and is not limited to aquatic organisms but also affects human and other animal health through environmental and food chain transmission. Aquatic microorganisms can acquire resistance via horizontal gene transfer or evolve different mechanisms (i.e., efflux and biofilm production) to counteract the antibiotic effects. The overuse and misuse of antibiotics in aquaculture accelerate this process and promote the emergence of multidrug-resistant bacteria. To combat this growing concern, alternative strategies such as phage therapy, immunostimulants, and probiotics are being explored. Among these, probiotics represent a promising and sustainable option. These probiotic microorganisms, when administered in adequate amounts, can confer health benefits to the host, like enhancing growth and stress tolerance, improving feed utilization, and boosting the immune system. Besides disease prevention, probiotics can improve water quality by breaking down organic matter and reducing ammonia levels, thereby fostering a healthier rearing environment for aquaculture. Therefore, it can lead to a significant reduction in antibiotic use. The strategic integration of probiotics into aquaculture practices represents a promising approach to addressing antibiotic resistance and a crucial step toward sustainable and eco-friendly fish farming.

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Introduction

Antimicrobial resistance among pathogenic bacteria has emerged as a major concern in aquaculture, threatening fish health, farm productivity, and food safety (Ajitha et al., 2004). The spread of antibiotic resistance genes from one bacterium to another, either through horizontal or vertical gene transfer, accelerates the problem. Antimicrobial resistance in aquaculture varies across regions, with high levels reported in developing countries and warm climates, where pathogenic bacteria often exhibit multidrug resistance (Preena et al., 2020). Consequently, treating infectious fish diseases has become complicated, since the causal agents do not respond to conventional antibiotics (Tamminen et al., 2011).

Common bacterial diseases in aquaculture include vibriosis, furunculosis, salmon rickettsia syndrome, salmonoid rickettsia septicaemia, edwardsiellosis, columnaris disease, yersiniosis, and lactococcosis (Bondad-Reantaso et al., 2023). These are traditionally treated using a wide range of antibiotics, such as

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tetracyclines, quinolones, β-lactams, macrolides, sulfonamides, diaminopyrimidines, and amphenicols (Arthur et al., 2019). For example, oxytetracycline is commonly used against ulcer disease (*Hemophilus piscium*), tenacibaculosis (*Tenacibaculum maritimum*), and furunculosis (*Aeromonas salmonicida*) (Fraser, 2002), while amoxicillin, cephalosporins, penicillin, ampicillin, cephalexin, cefradine, and cefotaxime are used to treat salmon rickettsia syndrome, salmonoid rickettsia septicemia (*Piscirickettsia salmonis*) (Tandberg et al., 2016). Quinolones are used to treat columnaris (*Flavobacterium columnare*) (Lulijwa et al., 2020). Aminoglycosides (neomycin, gentamycin S, kanamycin, and apramycin) have been reported to treat *Pseudomonas septicemia* (Noone, P. 1978). Erythromycin & penicillins are highly used in the treatment of gram-positive bacterial diseases. Sulphonamides (like sulfadiazine) are used to treat vibriosis and salmonellosis (Sakai et al., 1995). In Bangladesh, oxytetracycline, ciprofloxacin, and amoxicillin are among the most frequently used antibiotics for both therapeutic and prophylactic purposes (Chowdhury et al., 2022).

However, the extensive and indiscriminate use of antibiotics in aquaculture accelerates resistance development. Plasmids carrying antibiotic resistance genes have been identified in marine *Vibrio* spp., where horizontal gene transfer enables the rapid emergence of resistant strains (Balcázar et al., 2006). Moreover, the overuse of antibiotics in aquaculture leads to more resistance development (Munita & Arias, 2016).

To address these challenges, alternative strategies to antibiotics are urgently needed for the prevention and control of bacterial diseases in aquaculture. Promising alternatives include phage therapy, immunostimulants, improved aquaculture practices, and most importantly, probiotics (Karunasagar, 2012). Among these, probiotics have received growing attention as a sustainable and eco-friendly option. These beneficial microbes can inhibit pathogens through competitive exclusion, antimicrobial production, and quorum quenching, while also improving immunity, restoring gut microbiota balance (Balcázar et al., 2006; Gatesoupe, 1999). Common probiotics, such as *Lactobacillus acidophilus*, *Pediococcus pentosaceus*, and *Bacillus subtilis*, have been shown to improve growth, immunity, digestion, and disease resistance in fish species, including carp, tilapia, trout, and shrimp (*Litopenaeus vannamei*) (Rahman et al, 2019; Ringø et al., 2010). Moreover, probiotics can positively influence intestinal morphology, feed utilisation, and overall performance (Adel et al., 2017; Ahmadifar et al., 2020; Gonzalez et al., 1999; Xia et al., 2020).

Despite global initiatives to regulate antibiotic residues and encourage the use of vaccines, prevention through probiotics remains one of the most sustainable strategies. Ongoing efforts include the establishment of maximum residue levels (MRLs), strengthening of surveillance systems, and promoting alternatives like vaccines to reduce antibiotic dependence. Coordinated global action, stronger regulatory frameworks, and increased investment in research are urgently required to monitor, manage, and mitigate drug resistance in aquaculture. However, the most effective lies in preventive measures, which minimize the need for treatment or disease management. As a valid and sustainable preventive tool, probiotics meet these criteria and hold strong potential to overcome the challenges of antibiotic resistance while supporting a healthier and more resilient aquaculture management system.

Therefore, this review aims to assess the challenge of antibiotic resistance in aquaculture and to emphasize the potential of probiotics as a viable alternative strategy for promoting fish health, reducing antibiotic dependence, and ensuring long-term sustainability in the aquaculture industry.

Antimicrobial Resistance in Aquaculture

Antimicrobial resistance (AMR) is a survival trait developed by disease-causing microorganisms, enabling them to survive and proliferate even in the presence of antimicrobial agents. This creates a critical challenge for disease control, as the available treatment options for infectious diseases are steadily decreasing (Abushaheen et al., 2020). Globally, causes an estimated 700,000 deaths annually and is projected to reach 10 million by 2050, with severe economic losses estimated at 100 trillion USD (Inoue, 2019). Aquaculture includes several management processes for the prevention and control of diseases. Antibiotic therapy has long been used in fish and shrimp farming for rapid disease control. But indiscriminate use has accelerated

the development of antibiotic resistance in aquatic pathogens and facilitated resistance transfer to other organisms. Therefore, limiting the overuse of antibiotics is essential to protect the environment and public health (Jayaprakashvel and Subramani, 2019).

Dynamics of Antibiotic Resistance: Ranges and Mechanisms

Range of antimicrobial resistance

Antibiotic resistance exists on a spectrum from narrow resistance, where a pathogen withstands one or a few antibiotics, extensively drug-resistant (XDR), or even pan-drug resistance (PDR), where nearly all treatments become ineffective (Ventola, 2015). In aquaculture, several major pathogens demonstrate these alarming traits. *Vibrio* species, common in marine environments affecting fish and shrimp, have shown increasing resistance to tetracyclines and quinolones (Cabello, 2006). Hannan et al. (2019) reported multidrug resistance in shrimp pathogenic *Vibrio alginolyticus* strains isolated from the south-west region of Bangladesh, showing resistance to multiple commonly used antibiotics, including erythromycin, penicillin, amoxicillin, vancomycin, ampicillin, and cefradine. *Aeromonas hydrophila*, a widespread freshwater pathogen, frequently displays multidrug resistance, complicating disease management in finfish culture (Defoirdt et al., 2011). *Streptococcus agalactiae*, a serious pathogen in tilapia, has been reported to resist macrolides and sulfonamides. Akter et al. (2023) and Rahman et al. (2017) documented *Enterococcus faecalis* from diseased fish in Bangladesh, exhibiting resistance to ampicillin, amoxicillin, cefradine, erythromycin, and penicillin. Recently, extended-spectrum beta-lactamases (ESBLs) producing *Salmonella* spp. have also been found to be present in shrimp (Afrin et al. 2023). Understanding this range of resistance in aquatic pathogens is essential for guiding responsible antibiotic use and developing alternative strategies.

Mechanism of antibiotic resistance

Antibiotic resistance undermines our ability to treat infections by enabling certain bacterial strains to survive and multiply despite medication. This adaptive phenomenon is influenced by selective pressures in hospitals, agriculture, aquaculture, and natural environments (Martínez & Baquero, 2014). To survive in the presence of antibiotics and spread these characteristics, bacteria employ various defence mechanisms (Cantón et al., 2023; Davies & Davies, 2010).

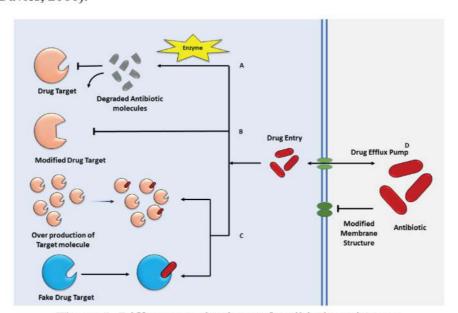


Figure 1. Different mechanisms of antibiotic resistance.

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Understanding these diverse strategies is pivotal for developing next-generation therapies, such as β -lactamase inhibitors, efflux pump antagonists, and agents that disrupt plasmid stability, to preserve existing antibiotics and curb the rise of untreatable infections (Cantón et al., 2023).

As depicted in Figure 1, gram-negative bacteria modify outer-membrane porins to restrict the entry of antibiotics, and upregulate efflux systems in the MFS (Major Facilitator Superfamily), ABC (ATP-Binding Cassette), RND (Resistance Nodulation Division), SMR (Small Multidrug Resistance), and MATE (Multidrug and Toxic compound Extrusion) families to actively expel drugs, often resulting in multidrug resistance (Li & Nikaido, 2009; Li, Plésiat, & Nikaido, 2015). Certain species of bacteria also reduce antibiotic efficacy by altering target pathways or producing decoy proteins that bind to the antibiotics (Blair et al., 2015; Munita & Arias, 2016). These resistance factors are acquired through transformation, transduction, and conjugation processes. Conjugation uses some mobile genetic elements like plasmids, transposons, integrons, and bacteriophages, which include gene clusters for β-lactamases, aminoglycoside modifiers, and Qnr proteins (Martínez & Baquero, 2014; Halawa et al., 2024).

Table 1. Drug resistance mechanisms of different fish pathogens

Fish Species	Pathogen	Drug(s)	Resistance Mechanism	Reference
Tilapia (Oreochromis niloticus)	Aeromonas hydrophila	Oxytetracycline, Tetracycline	Efflux pumps, beta-lactamase enzymes, and tetracycline resistance genes.	(Lukkana et al., 2012)
	Salmonella spp.	Amoxicillin	Beta-lactamase enzyme production, drug efflux.	(Oliveira-Ferreira et al., 2021)
	Escherichia coli	Ciprofloxacin	Plasmid-mediated quinolone resistance, enzyme inactivation.	(Rocha et al., 2014)
	Streptococcus agalactiae	Penicillin	Altered drug-binding proteins, macrolide resistance genes.	(Osman et al., 2017)
Rohu (Labeo rohita)	Aeromonas hydrophila	Gentamicin, Ampicillin	Aminoglycoside-modifying enzymes, extended-spectrum beta-lactamases (ESBLs).	(Ramesh & Souissi, 2018)
	Aeromonas veronii	Ampicillin	Beta-lactamase production, drug efflux systems.	(Behera et al., 2023)
Mrigal (Cirrhinus cirrhosus)	Aeromonas hydrophila	Oxytetracycline	Efflux pumps, enzymatic inactivation of tetracyclines.	(Bhuvaneswari et al., 2022)
	Pseudomonas sp.	Florfenicol	Overexpression of efflux pumps; ribosomal protection proteins	(Samal et al., 2009)
Salmon (Salmo salar)	Aeromonas salmonicida	Oxytetracycline	Tetracycline efflux pumps, plasmid-mediated resistance.	(Miranda & Zemelman, 2002)
	Yersinia ruckeri	Florfenicol	Ribosomal RNA mutations, chloramphenicol exporter genes.	(Huang et al., 2014)
Catfish (Pangasianodon hypophthalmus)	Edwardsiella ictaluri	Enrofloxacin	DNA gyrase mutations, quinolone resistance.	(Dung, 2010)
Seabass (Lates calcarifer)	Vibrio harveyi	Oxytetracycline	Ribosomal protection proteins, efflux pumps.	(Hamdan et al., 2017)
Catla (Catla catla)	Aeromonas hydrophila	Oxytetracycline, Enrofloxacin	Efflux pumps, beta-lactamase enzymes.	(Deshmukh et al.)
Stinging Catfish (Heteropneustes fossilis)	Aeromonas hydrophila	Ampicillin	Aminoglycoside-modifying enzymes, ESBLs.	(Bhuvaneswari et al., 2022)

Key Factors Behind Antibiotic Resistance in Aquaculture

The major cause of antimicrobial resistance in bacteria is the unnecessary, inappropriate, and uncontrolled (overdose) use of antibiotics in aquaculture. Horizontal gene transfer through mobile genetic elements like transposons, plasmids, integrons, etc., is the most potent method by which aquatic bacteria acquire antibiotic-resistant genes (ARGs), including gyrA, qnrB, parE, tetA, tet34, strA, and floR. These genes can then be stably inherited through vertical transmission in subsequent generations (Zhang et al., 2024). The aquatic microorganisms can develop complex communal structures (i.e., biofilms) where the rate of horizontal genetic transmission is much higher compared to free-living cells (Tucker et al., 2020). Biofilm-producing microbes are highly resistant to antibiotics due to their protective matrix and complex microbial interactions, allowing resistant strains to persist and spread (Jayaprakashvel & Subramani, 2019). Antibiotic resistance genes (ARGs) encoding resistant proteins and enzymes in aquatic environments can be transmitted to human bacterial pathogens without phylogenetic or species-specific barriers (Huang et al., 2014). The soil particles or sediments in aquaculture environments assist the interactions among bacteria and the development of antibiotic resistance, as sediments have 10 times higher bacterial populations than surrounding water (Peñarubia et al., 2020; Sivaraman, 2022; Fabra et al., 2021; Michael-Kordatou et al., 2018). ARB strains enter the aquaculture systems through multiple pathways: contaminated fish fry or larvae, manure used for fertilizing ponds, water exchange with natural water bodies, commercial feed and feed supplements, and unhygienic handling by farm personnel (Rao et al., 2021; Sivaraman, 2022). Antibiotic-resistant bacteria can enter fish and fish products when contaminated water or ice is used during culturing, cleaning, processing, or preservation (Sivaraman, 2022). Antibiotic resistance is generated through horizontal and vertical transmission of ARGs. Moreover, bacteria associated with humans have a 25-fold greater likelihood of exchanging genetic material compared to those in other environments, highlighting the role of zoonosis in the transfer of antibiotic resistance from aquatic organisms to humans (Rabetafika et al., 2023).

Multidimensional Effects of Antibiotics and Antibiotic Resistance

Antibiotic-resistant bacteria (ARB) and Antibiotic resistance genes (ARGs) in aquatic environments pose major risks to aquaculture productivity, ecosystems, and public health (Larsson et al. 2018). Up to 30–90% of ingested antibiotics are excreted unchanged, releasing substantial amounts of these drugs into water bodies through hospital, animal, and aquaculture effluents (Sarmah et al., 2006; Wang et al., 2015).

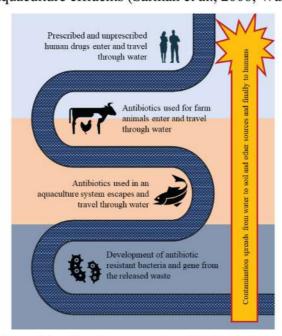


Figure 2. Overview of the development of antibiotic resistance and its effects.

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This leads to high concentrations of ARGs, particularly near discharge zones and intensive aquaculture farms, where over 70% of administered antibiotics can diffuse into the environment (Giang et al., 2015; Rowe et al., 2016). These residues disrupt aquatic microbial communities by impairing key processes like nitrification and mineralisation, while also reducing survival of algae, zooplankton, and other aquatic organisms (Samuelsen et al., 2014; Tamminen et al., 2011; Yasser and Adli, 2015; Song et al., 2016; Park and Kwak, 2018). The spread of ARBs and ARGs further amplifies the problem, as resistant strains persist in sediments and water, circulate within cultured fish, and enter the wider food chain. This bioaccumulation increases the risk of chronic toxicity in humans and accelerates the spread of antibiotic resistance, with particularly severe consequences for vulnerable populations (Jangra et al., 2022; Tang et al., 2020; Nasr-Eldahan et al., 2021).

Global Status of Antimicrobial Resistance in Aquaculture

Antimicrobial resistance (AMR) is a growing concern in aquaculture worldwide (Hoque et al., 2021). Studies have shown that up to 90% of aquatic bacteria exhibit resistance to at least one antibiotic, and approximately 20% exhibit multi-antibiotic resistance (Pepi and Focardi, 2021). In the Mediterranean region, misuse of antibiotics in aquaculture has led to their accumulation in sediments and the water column, exhibiting the spread of resistant strains (Pepi and Focardi, 2021). In Asia, responsible for two-thirds of the world's fish production, an analysis from 2000-2019 showed that resistance to antimicrobials exceeded 50% (P50) in one-third of surveys (Vaiyapuri et al., 2023). China alone represented 37.9% of such surveys, underscoring its central role in the global aquaculture industry (Schar et al., 2021). Moreover, the global multi-antibiotic resistance index averaged 0.25 was significantly higher (> .35) in low- and middle-income countries of Asia, reflecting weaker regulation and more intensive antibiotic use (Schar et al., 2021).

Aquaculture studies involving the assessment of antibiotic usage and bacterial antimicrobial resistance (AMR) were conducted in 61 different countries across various WHO regions, including multiple environmental compartments, such as water, sediment, biofilms, feed, and organisms. The study again highlighted China's dominance, with 115 studies conducted over the past 25 years. Globally, antibiotic resistance genes (ARGs) linked to a single class of antibiotics represented 75% of all detections, with five classes accounting for over 85%: tetracyclines (39%), sulfonamides (22%), aminoglycosides (13%), diaminopyrimidines (6%), and phenicols (6%).

Regarding the type of organisms, 76% of identified antibiotic resistance genes (ARGs) were linked to finfish aquaculture, 22% to crustacean aquaculture (of which 64% originated from ponds), and the remaining either pertained to combined fish/crustacean aquaculture or lacked provided data. Small but notable proportions were linked to ornamental culture (6%), marine aquaculture (11%), and freshwater aquaculture (17%). There were A total of 418 distinct antibiotic resistance genes (ARGs) were identified, with only 60 accounting for more than 75% of all reported detections. The Salmonidae family was the most frequently associated with ARGs, representing 22% of all identified cases, followed by Penaeidae (15%), Cyprinidae (7%), and the Cichlidae (6%). In nearly 46% of the detections, it was not possible to associate ARGs with a specific bacterial genus. Among the genera that could be identified, the most frequently reported were *Aeromonas* (27%), *Vibrio* (10%), *Escherichia* (8%), *Pseudomonas* (7%), and *Enterococcus* (5%) (Kemp et al., 2021).

Probiotics: A Revolutionary Replacement for Antibiotics

The term Probiotics is derived from the Greek *pro* ("for") and *bios* ("life"), and is considered the opposite of antibiotics ("against life"). Lilley and Stillwell (1965) first used the term probiotic to describe substances secreted by one microorganism that stimulate the growth of another (Fuller, 1992). Later, Montanaro et al. (1971) applied it to characterize "tissue extracts which stimulated microbial growth". Probiotics are described by the Food and Agriculture Organization of the United Nations/World Health Organization (FAO/WHO) as live microorganisms that, when administered in adequate amounts, confer health benefits to the host's health (FAO/WHO, 2001). More recently, Lazado and Caipang (2014) extended the definition in the context of aquaculture as live or dead, or even a component of the microorganisms that act under different modes of action in conferring beneficial effects to the host or its environment.

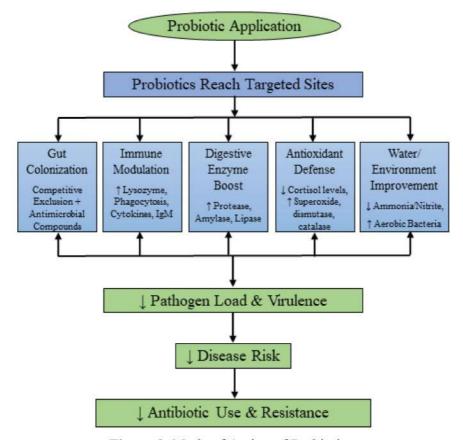


Figure 3. Mode of Action of Probiotics.

When applied in aquaculture, probiotics induce several beneficial changes in the aquatic environment. Upon reaching the target site, the gastrointestinal tract, probiotic species such as *Lactobacillus plantarum* and *Bacillus subtilis* colonize the gut epithelium and compete with-pathogens (e.g., *Aeromonas hydrophila*) for nutrients and binding sites by adhering to the gut lining. In addition, they produce antimicrobial substances (such as bacteriocins) and organic acids, thereby creating unfavorable conditions for the pathogens (Balcázar et al., 2006; Sahu et al., 2015). Thus, decreasing the pathogen load and virulence, probiotics reduce the dependence on antibiotics and mitigate the risk of antibiotic resistance.

Benefits of Probiotics in Aquaculture

Probiotics have emerged as a crucial component in aquaculture, offering multifaceted benefits including feed utilization, growth promotion, disease resistance, immune response enhancement, and stress tolerance (Austin et al., 1995).

Growth Promotion and Feed Efficiency

Probiotic supplementation has been shown to enhance digestive enzyme activities, such as amylase, lipase, and protease, leading to improved nutrient utilization and growth performance in the host (Rahman et al., 2019). For instance, inclusion of heat-killed *Lactobacillus plantarum* at 50, 100, or 1000 mg/kg for 12 weeks significantly enhanced the amylase, lipase, and protease activities in Nile tilapia (Dawood et al., 2019). Similarly, feeding fish with *Bacillus* strain promotes growth and the production of anti-oxidative enzymes such as catalase, glutathione, and peroxidase (Vine et al., 2006). Inclusion of gut-derived probiotic bacterial strains significantly improved the weight gain, specific growth, and feed conversion ratio of *Barbonymus*

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gonionotus compared to untreated controls (Salam et al., 2021). Probiotic *Pediococcus acidilactici* also enhanced the growth of ornamental fish (*Danio rerio*) (Ahmadifar et. Al., 2020). In shellfish cultivation, probiotics are frequently utilized as growth promoters. *Bacillus* sp. improves the growth of white-leg shrimp (*Litopenaeus vannamei*) by increasing lipase and cellulase activity (Zokaeifar et al., 2012). Supplementation of *Bacillus subtilis* at 10⁷ and 10⁹ CFU/kg meal greatly enhanced the growth of *L. vanname* (Kewacharoen & Srisapoome, 2019). Most recently, Rahman et al. (2025) reported enhanced growth of tiger shrimp (*Penaeus monodon*) following the application of two *Bacillus* strains.

Reproductive Enhancement

Probiotics play a crucial role in improving reproductive performance by enhancing gamete quality, fertilization rate, and larval survival (Ochoa and Olmos, 2006). During the reproductive period, female fish require more energy (in terms of protein, lipid, and carbohydrate) to increase their fecundity (egg-producing capacity). Currently, there is a huge increase in probiotics in water bodies to improve the reproduction rate of fish (Table 2). *Bacillus subtilis* (isolated from the intestine of *Cirrhinus mrigala*), when incorporated at different concentrations and applied to ornamental fish species: *Poecilia sphenops, Xiphophorus maculates, Poecilia reticulate,* and *Xiphophorus helleri*, resulted in increased fecundity and fry production (Ghosh et al., 2007). Gioacchini et al. (2012) reported *Lactobacillus rhamnosus* as the most widely used potential probiotic for gamete and larval quality in fish.

Table 2: List of different probiotic strains applied in fish for improved disease resistance and increased immunity

Probiotics Species	Pathogen	Fish species	Impact on fish	Reference
Lactobacillus acidophilus	Pseudomonas luorescens and Streptococcus iniae	Nile tilapia	Improve immune function and disease resistance	Aly et al., 2008a; Aly et al. 2008b
Lactobacillus rhamnosus	Edwardsiella tarda	Tilapia	Reduced mortalities	Pirarat et al., 2006
Bacillus subtilis	A. hydrophila	Indian major carp	Control of infection	Kumar et al., 2006
Bacillus pumilus	A. hydrophila.	Tilapia	Enhance immune and health status and improve disease resistance	Aly et al., 2008
Pseudomonas aeruginosa	A. hydrophila	Rohu	Significantly higher post- challenge survival rates	Giri et al., 2012
Aeromonas veronii	A. hydrophila	Common carp	Enhance disease resistance enhance disease resistance	Chi et al., 2013
Lactobacillus acidophilus, Streptococcus cremoris, Lactobacillus bulgaricus	Vibrio alginolyticus	Indian white shrimp (Penaeus indicus)	Higher survival rate	Ajitha et al., 2004
Lactobacillus plantarum AH 78		Nile tilapia (Oreochromis niloticus)	Significantly up-regulated the expression of cytokine genes, IL-4, IL-12, and IFN-γ	Ajitha et al., 2004

Disease Resistance

Probiotic microorganisms have the capacity to produce compounds that may have a bactericidal or bacteriostatic effect on pathogenic bacteria present in the host's gut (Cruz et al., 2012). For example, Nile tilapia (*Oreochromis niloticus*) exhibited enhanced resistance against *Staphylococcus aureus* after being administered *Lactococcus garvieae* isolated from raw cow milk at a concentration of 10⁷ cells/gm for ten days (Abdelfatah & Mahbouh, 2018). Similarly, dietary supplementation of *Bacillus haynesii* and *Advenella mimigardefordensis* also suppressed the streptococcosis infection in Nile tilapia (Rahman et al., 2022). *Aeromonas veronii* and *Flavobacterium sasangense*, two isolated gut probiotic bacteria, improved disease resistance in common carp against *Aeromonas hydrophila* (Chi et al., 2013). Paul et al. (2021) showed that extracellular products of *Bacillus subtilis* strains WS1A and YBS29 significantly protected *Labeo rohita* fingerlings against motile *Aeromonas* septicaemia.

Immune Modulation

Probiotics Lactobacillus plantarum and Bacillus velezensis enhanced innate immune defenses of Nile tilapia, including skin mucus lysozyme and peroxidase activities, serum lysozyme, serum peroxidase, elective supplement, phagocytosis, and respiratory burst responses (Doan et al., 2018). Lactobacillus sp. produced various compounds such as organic acids, hydrogen peroxide, and bactericidal proteins. These compounds activated the immune systems of fish and rendered them more resistant to infections by viruses, bacteria, fungi, and parasites or inhibited the bacterial pathogens in aquaculture systems (Balcazar et al., 2006).

Stress Tolerance Enhancement

Stress is a significant factor contributing to disease outbreaks and mortality in aquaculture. Supplementation of probiotics improves the stress tolerance of aquaculture species. For instance, *Lactobacillus plantarum* supplementation boosted fish tolerance to ammonia and induced a lower increase in cortisol (a stress hormone) level (Nguyen et al., 2019). According to Dawood et al. (2019), *Aspergillus oryzae* as a probiotic improved the Nile tilapia's hypoxic stress.

Pathogen Inhibition and Water Quality Improvement

Aquaculture systems can benefit from the presence of probiotic bacterial species because they promote the breakdown of organic matter, lower phosphate and nitrogen levels, and regulate ammonia, nitrite, and hydrogen sulfide, all of which prevent pathogen growth (Boyd and Massaut 1999; Ma et al., 2009; Cha et al., 2013). *Enterobacter*, *Nitrobacter*, *Pseudomonas*, *Cellulomonas*, and *Rhodopseudomonas* are a few examples of bacteria that are useful in preserving the quality of water, especially when it comes to eliminating organic debris from pond bottoms (Srirengaraj et al., 2023).

Probiotics as a Sustainable Alternative to Antibiotics in Aquaculture

The overuse of antibiotics in aquaculture has led to the alarming rise of antibiotic-resistant bacteria, posing serious risks to both aquatic organisms and human health (Cabello, 2006; Miranda & Zemelman, 2002). In contrast, probiotics offer a promising, sustainable alternative that improves fish health by supporting gut microbiota and boosting immunity, while also helping to limit the spread of resistant bacteria (Balcázar et al., 2006). Studies in Nile tilapia (*Oreochromis niloticus*) and rainbow trout (*Oncorhynchus mykiss*) demonstrate that dietary supplementation with beneficial strains such as *Bacillus subtilis and Lactobacillus plantarum* can reduce incidences of infectious diseases, improve feed conversion ratios, and promote overall growth performance (Ringø et al., 2010). In recirculating aquaculture systems (RAS), the application of probiotics has been associated with improved water quality through the breakdown of organic matter and reduction of ammonia levels, thereby creating a healthier rearing environment (Kesarcodi-Watson et al., 2008; Merrifield et al., 2010). Moreover, probiotics can mitigate stress responses and strengthen the immune system, enabling

fish to better tolerate environmental challenges while reducing dependence on antibiotics and limiting the risk of resistant pathogens transfer to humans (Martinez & Baquero, 2014). Collectively, these multifaceted benefits highlight probiotics as not only an effective strategy to address antibiotic resistance but also a cornerstone of sustainable and eco-friendly aquaculture (Cabello, 2006; Balcázar et al., 2006).

Conclusion

Investigating probiotics as sustainable alternatives to antibiotics offers a promising approach to enhancing aquaculture health and productivity. Probiotics are increasingly investigated for their therapeutic potential in response to rising concerns about antibiotic resistance and the adverse effects of long-term antibiotic use. Probiotics provide a more focused and sustainable way of treating certain infections by supporting a healthy microbial ecosystem in the body. Probiotics hold potential in maintaining health and treating infections, although further research is required to fully understand their effectiveness and modes of action. Probiotics thus stand out as a viable supplemental or alternative strategy, offering significant promise for advancing sustainable health management in aquaculture.

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