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COMPREHENSIVE ASSESSMENT OF BACTERIAL PATHOGENS AFFECTING NILE TILAPIA AND THEIR CONTROL STRATEGIES: IMPLICATIONS FOR AQUATIC AND PUBLIC HEALTH

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Abstract

Aquaculture is one of the fastest-growing food production sectors and plays a crucial role in meeting the demand for nutritious and affordable food for billions of people worldwide. Nile tilapia is an economically important fish species that is widely farmed in over 140 countries. However, diseases affecting Nile tilapia significantly hinder the expansion and development of sustainable aquaculture. Recently, the industry has faced serious bacterial infections that have resulted in substantial losses for Nile tilapia farmers. These bacterial infections –including *Aeromonas hydrophila*, *Yersinia ruckeri*, *Escherichia coli*, *Streptococcus aureus*, *Flavobacterium columnare*, *Pseudomonas aeruginosa*, *Streptococcus agalactiae*, *Streptococcus iniae*, and *Edwardsiella tarda* affect various parts of the fish such as the skin, eyes, kidneys, gills, and liver. The absence of effective disease prevention and appropriate biosecurity measures makes these infections a major threat to global Nile tilapia farming. Moreover, factors such as high nutrient levels, elevated water temperatures, and high fish density can promote bacterial growth, including that of potentially pathogenic bacteria. Strategies employed to combat diseases in tilapia include the use of feed supplements, herbal extracts, and vaccines. This review aims to provide an updated overview of the disease risks affecting Nile tilapia production, emphasizing the challenges related to these diseases and their treatment approaches. Moreover, it seeks to enhance understanding of country-specific bacterial diseases and addresses a critical gap in knowledge regarding health and disease pathways for sustainable aquaculture and the control strategies implemented thus far.

Key words: *Oreochromis niloticus*, bacterial fish pathogens, treatments, current trends, future prospects in disease management

The aquaculture sector, one of the food production technologies with the greatest growth rate in the world in recent decades, has revolutionized the seafood production industry (Hassan et al., 2025; Verdegem et al., 2023). Consequently, globally, fish is becoming an increasingly important food source (Verdegem et al., 2023). By 2050, there will be 10 billion people on the globe, and to feed this growing and increasingly affluent population. Aquatic food production can be increased by aquaculture in response to the growing demand for protein. Aquaculture is crucial for ensuring global food security, particularly in low-income and food-deficit countries (Khan et al., 2023; Hassan et al., 2025). Aquaculture profitability is directly associated with the health of fish but unfortunately, the mismanagement of fish rearing like overstocking, overfeeding, environmental variation, and contaminated water quality causes disease outbreaks (Verdegem et al., 2023).

The fish industry is a rapidly growing food sector in the world that comprises many cultivable commercially important species (Huicab-Pech et al., 2017; Hassan et al., 2022). Nile tilapia, one of the most popular species, is also called aquatic chicken (Abdel Aziz et al., 2021; Hassan et al., 2024). Nile tilapia is widely grown due to its ease of production, tolerance to various environmental conditions, rapid growth, and high nutritional content (Syed et al., 2022). Nile tilapia, once thought to be a disease-resistant species, are becoming more susceptible to disease, and posing a threat to the industry as production increases (Abdel Aziz et al., 2023; Hassan et al., 2024). By supplying an important source of proteins, tilapia yields 4.5 million metric tons annually to the global foods industry (Kuebutornye et al., 2020). Nile tilapia is perfect for aquaculture production due to its unique characteristics such as diverse feeding habits and high disease resistance (Kuebutornye et al., 2020). Its products are highly accessible and its widespread yield is mostly attributable to its rapid development, susceptibility to a range of climatic conditions, tolerance to disease, and capacity to breed in captivity (Mugwanya et al., 2021).

Tilapia production has expanded dramatically in recent years because of the deployment of aquaculture technology. These farming practices, however, have exposed fish to distressing environments, subjecting them to a variety of infections (Mugwanya et al., 2021). Bacterial contamination causes over 600 million foodborne illnesses, including 420,000 fatal infections annually (World Health Organization, 2015). Treatment costs around USD 110 billion annually, placing a significant economic burden on low- and middle-income countries. Foodborne diseases are mostly caused by pathogenic bacteria that produce toxins, particularly in animal-derived foods (Abebe et al., 2023). Novotny et al. (2021) identified fish as a reservoir for pathogenic microorganisms associated with human disorders. Fish has been a staple in the human diet for decades due to its numerous health benefits, including animal protein, omega-3 fatty acids, vitamin D, selenium, and iodine. Nile tilapia (*Oreochromis niloticus*) has grown in popularity, as evidenced by increased levels of consumption (Munguti et al., 2022). Raw or undercooked fish may include harmful germs from the aquatic environment or post-harvest handling (Baliere et al., 2016). Pathogenic bacteria can enter fish at any stage of the production and supply chain.

Diseases severely affect sustainable aquaculture. Globally, in aquaculture, the unidentified pathogen appears, spreads quickly, and causes major losses in production (Haenen et al., 2023). Fish are infected by opportunistic bacteria and pressures in the surroundings, such as those found in intensive aquaculture (Derome et al., 2016). Stressors (for example, high stocking density, poor nutrition, and poor water quality and disease treatment) are the factor that creates physiological conditions beyond the tolerance rate which increases fish susceptibility to pathogens (Wang et al., 2023). Tilapia at once is susceptible to harmful bacteria, although its skin surfaces and parts of gills and alimentary tract, confer the latent defense due to mucus against pathogens. Fish mucus over the skin and gills contains blood ingredients such as natural killer and phagocyte cells are important innate immune components (Elavarasi et al., 2013). However, the bacterial infections still remained one of the limiting factor in tilapia farming affecting its population, causing gross economic loss to its global industry (Thanh et al., 2014). Consuming infected fish with pathogenic bacteria also affects human health. Infected fish also affect healthy fish.

Bacteria cause hemorrhagic septicemia, red disease and dropsy in fish (Khatun et al., 2011). Bacteria of particular importance in freshwater fish tilapia include *Aeromonas* spp., *Streptococcus* spp., *Edwardsiella* spp., *Flavobacterium* spp., *Vibrio* spp., *Pseudomonas* spp., and *Mycobacterium* spp. (Wamala et al., 2018).

This study is essential as bacterial infections in tilapia can cause serious mortalities, impacting fish farmers, and livelihood and food security. Additionally, some bacterial strains are zoonotic and they may pose a risk to human health. There are a lot of bacterial diseases and bacterial outbreaks reported in tilapia aquaculture and farming, however, the knowledge is widely dispersed. Herein, integrated information regarding the bacterial load in tilapia fish is presented along with the geographical distribution, etiology, epidemiology, diagnosis, pathology, and control strategies. Moreover, practices used in the isolation of the bacteria from diseased fishes were also integrated. These potent reports directly highlight the bacterial diseases while indirectly being helpful for further studies concerning fish infection.

This review covers the most prevalent Gram-positive and Gram-negative bacterial infections in tilapia, including clinical manifestations, etiology, epidemiology, treatment methods for resilient farming, vaccination, disease detection technology, and use of symbiotics for preventing infections. By collecting data on these various aspects, this study is specifically aimed at contributing to a better understanding of the hazards posed by pathogenic bacteria and identifying the key areas of focus for research on the influence of probiotics, and vaccines and improving biosecurity measures in aquaculture. This review will help fish farmers, researchers, and policymakers adopt efficient strategies to protect tilapia populations.

Review

Data with references have been cited for this review.

Gram-positive bacteria

***Streptococcus* spp.:** Streptococcosis is caused by *S. agalactiae*, *S. iniae*, and *S. parauberis*. *O. niloticus* is particularly vulnerable to streptococcosis, which is the name of the disease rather than the genus causing it (Abdallah et al., 2024). *Streptococcus* is a rapidly growing Gram-positive bacterium in marine and freshwater cultured fish (Kümmerer, 2009). Infections due to *Streptococcus* were reported with elevated frequency among cultured freshwater tilapia fishes, particularly in the summer seasons.

Streptococcal disease has been reported on all continents (Americas, Asia, Europe, Africa, and Australia) and in at least 15 countries. Among the nearly 500 streptococcal isolates recovered from tilapia between 2001 and 2009, epidemiological investigations were conducted in the major tilapia-producing regions of Asia and Latin America (Abdallah et al., 2024). From published literature, four strains of *Streptococcus* were documented (*S. iniae, S. agalactiae*, *S. anginosus*, and *S. iniae*), among them *S. agalactiae* has been frequently reported in Indonesia, Brazil, Egypt, and North America as the causal agents of streptococcosis disease in tilapia fishes (Table 1). Many experiments have been conducted to determine how *Streptococcus* sp. spreads.

Table 1. Major bacterial diseases, vector, influence, treatments of economically important fish O*reochromis niloticus*

Disease	Causative agents	Clinical signs	Stressor contributing to diseases	Treatments	Country	References
1	2	3	4	5	6	7
Motile *Aeromonas septicaemia* (MAS)	*Aeromonas hydrophila* and other related *Aeromonas* species	Loss of body balance; lethargic swimming; gasping at the water surface; external hemorrhage; exophthalmia; swollen abdomen; frequent high mortalities, ulcer, congestion hemorrhagic, skin darkness fin rot, stunted growth, exophthalmos, skin ulcers	Stress caused by high water temperature, water pH changes, low dissolved oxygen, high levels of ammonia and nitrites, high stocking density, parasitic infections, rough handling and transportation	Disinfectants ($KMnO_4$ at 4–10 mg/L for 1 h or 2–4 mg/L indefinite immersion), antibiotics (oxytetracycline as feed additive at 50 mg/kg fish/d for 12–14 d, 21 d withdrawal, probiotics (*Enterococcus faecium* at 8 g/kg feed for 45 d) *Saccharomyces cerevisiae* at 5 g/kg feed for 12 weeks), and various vaccines	Egypt Malaysia	Monir et al. (2020) Prabu et al. (2019) Stratev and Odeyemi (2017)
Streptococcosis	*Streptococcus* spp. including *S. agalactiae, S. iniae, S. dysgalactiae* and *Enterococcus* spp.	Red discoloration of the skin; lethargic; erratic swimming; exophthalmia with corneal opacity and hemorrhage in eyes; abdominal distension; skin hemorrhaging around the anus, the base of fins and anus, around the mouth, and in operculum; enlarged and nearly black spleen; and high mortality	Introduction of contaminated water and/or fry, high stocking density, high water temperature, high ammonia, low dissolved oxygen, unsuitable pH, poor husbandry management	Antibiotic in feed: erythromycin at 50 mg/kg fish/d for 12 d; oxytetracycline at 75–100 mg/kg fish/d for 14 days. Various commercial vaccines	Colombia Thailand Egypt Malaysia	Prabu et al. (2019), Zamri-Saad et al. (2014)
Columnaris	*Flavobacterium columnare*	Fin rot; necrotic lesions on skin and gills; irregular whitish to grey patches on the skin and/or fins; high mortality rates	Poor environmental conditions, high stocking densities, high organic load, and high-water temperature	$KMnO_4$ to the water at 2 mg/L; 20 min bath in $CuSO_4$ at 37 mg/L or depending on alkalinity, indefinite immersion with $CuSO_4$ at 0.5–3 mg/L	Brazil	Declercq et al. (2013); Prabu et al. (2019)
Vibriosis	*Vibrio* spp.	Septicemia; lethargy; anorexia; hemorrhages along the external body surface and the base of the fins; and high mortality	Caused by stress, poor water quality, low water temperature, and bad management practices	Dietary inclusion of antibiotic	Egypt	Prabu et al. (2019)
Edwardsiellosis	*Edwardsiella ictaluri, E. tarda*	Abnormal swimming; hemorrhages at the base of fins, operculum, belly, mouth, and vent; exophthalmia; bloody fluid in body cavity; swollen, dark red spleen; pale, mottled liver; and swollen, soft kidney	Imbalanced environmental conditions, such as high temperature, high organic load, and poor water quality	Dietary inclusion of antibiotic	United States, Venezuela, Taiwan and Japan, Norway	El-Yazeed and Ibrahem (2009); Nhinh et al. (2022); Park et al. (2012)
Yersiniosis	*Y. ruckeri*	Focal hyperplasia, desquamation in the secondary lamellae and hemorrhages in the gill arch, skin injuries, acute or chronic enterosepticemia and hemorrhagic zones	Overcrowding of fish and water quality	Antimicrobial drugs, pesticides, probiotics phytogenic agents, yeast products, Omega 3-chitosan nanoparticles and antiseptics	Egypt	Kumar et al. (2015); Aly et al. (2012); Rutherfurd-Markwick and Gill (2004); Selim and Reda (2015); Alemayehu et al. (2018); Eissa et al. (2020)
Francisellosis	*Francisella noatunensis* and subsp. *orientalis*	Splenomegaly and granulomas, bleeding around the pectoral fins, anorexia, erratic swimming and exophthalmos	Poor management of pond and high stocking densities	Autogenous whole cell-adjuvanted intravenous vaccine	United Kingdom and Taiwan	Shahin et al. (2019); Pulpipat et al. (2019)

Table 1 – contd.

1	2	3	4	5	6	7
Summer syndrome	*Citrobacter freundii*	Hyperplasia, desquamation in the secondary lamellae and hemorrhages in the gill arch, pale liver, distended abdomen, watery kidney, focal hyperplasia, desquamation in the secondary lamellae and hemorrhages in the gill arch	Contaminated water and high stocking densities	Bacteriophage therapy	India and Brazil	El Asely et al. (2020); Jia et al. (2020)
Pseudomonad septicemia	*Pseudomonas fluorescens* and *Pseudomonas aeruginosa*	Exophthalmia, red spot on skin	Overpopulation, low temperature and injuries	Yucca extract (feed additive)	Egypt	Hal and Manal (2020); Osman et al. (2021); El-Keredy and Naena (2020)
Piscirickettsiosis (salmonid-septicemic disease)	*Piscirickeittsia salmonis*	Necropsy, occasional cutaneous hemorrhage, exophthalmia, enlarged spleens with multiple white granulomas, gills epithelial hyperplasia and loss of interlamellar spaces, anorexia, lethargy, respiratory distress, skin darkening and surface swimming	Water temperature fluctuations and strong storms	Tetracycline, and clarithromycin	Taiwan	Toranzo et al. (2005); Mauel et al. (2003)
Staphylococcosis	*Staphylococcus aureus*	Red spots on the skin	Water temperature fluctuations and pH of water	Phytogenic feed additives and *Boswellia serrata* resin extract (BSRE) supplementation	Pakistan Kenya	Montaser et al. (2021); Fatima (2014); Pridgeon and Klesius (2012)
Flexibacteriosis	*Flavobacterium columnare*	Necrosis	Overpopulation, splenomegaly infected fish tissue, skin, gills and fins	*Centella asiatica* aqueous extract and β-glucan	Egypt	El-Tawab et al. (2020); Amphan et al. (2019)

The recently introduced fish, according to Nguyen et al. (2002), is the chief element that brought *S. iniae* and *S. agalactiae* into the farm. The germs are released in the affected fish's feces, live in the water, and can attack other healthy fish (Nguyen et al., 2002). *Streptococcus* spp. are transmitted primarily horizontally through water and can also infect fish through injuries and mucosal surfaces (Yue and Guo, 2025).

According to an experimental investigation, the coexistence of dead or sick fish with healthy fish results in infection of the healthy fish. Meanwhile, horizontal pathogen transfer amongst fish is thought to be the most common mode of transmission (Amal and Zamri-Saad, 2011). Streptococcosis is the major infection affecting most of the *Tilapia* spp. and other fish species widely distributed in Indonesia and worldwide (Figueiredo et al., 2012). Characteristic signs of streptococcosis, include bilateral exophthalmia, nodules in the spleen, hemorrhagic brain, hepatomegaly, spleen congestion and accumulation of fluid in the abdominal cavity (Paredes-Trujillo and Mendoza-Carranza, 2024). *Streptococcus iniae* is a sphere-shaped, catalase-negative, Gram-positive, oxidase-negative, bacterium (Rattanachaikunsopon and Phumkhachorn, 2010 a).

S. iniae infects the brain and kidneys of tilapia fish, causing meningoencephalitis and septicemia (Figueiredo et al., 2012). *S. agalactiae* infects the liver, eyes, brain, spleen, and kidney tissues of *O. niloticus* and causes diseases like gross lesions, and white fibrinous exudates in Colombia (Hernández et al., 2009). A study reported that both *S. iniae* and *S. agalactiae* cause infection on the skin, mouth, anus, and visceral organs of *O. niloticus* in Thailand. The most common signs and symptoms of septicemia and anorexia are seen in tilapia fish (Jantrakajorn et al., 2014).

Similarly, in Egypt, *S. anginosus* infects the eyes, skin, gills, heart, kidney, spleen, and liver of *Tilapia* spp.; additionally, exophthalmia, pericarditis, and enlargement of the liver are the major diseases caused by *S. anginosus* in *Tilapia* spp. (Osman et al., 2017). A study reported that *S. agalaciae* infection might be transmitted through different routes via feces and living in water with infected fish. *S. iniae* can be transferred through oral and spatial ways in the pool of water and can increase the horizontal spread of the bacteria (Anshary et al., 2014). Hemolytic anemia, eye hemorrhage, skin ulcers, blurred and damaging changes, and skin hemorrhage, particularly at the base of the tail and fins, were the normal indications of streptococcosis in tilapia (Table 1). The emerging new diseases that were uncommon in tilapia are another alarming signal of the close aquaculture environment with human wastes and fish (Duran et al., 2012).

The methods used for the diagnosis of *Streptococcus* spp. are Gram staining, general and specific agars, biochemical tests, PCR amplification, species-specific PCR, species-specific qPCR, loop-mediated isothermal amplification (LAMP) and matrix-assisted laser desorption ionization (MALDI)–time of flight (TOF) mass spectrometry (Abdallah et al., 2024). Among these techniques, 16S rRNA gene sequencing and specific PCR have been widely employed for a conclusive diagnosis of the disease. It is feasible to compare the DNA sequence of an identified isolate with others stored in public databases such as the NCBI (www.ncbi.nlm.nih.gov/BLAST) by PCR amplification of the universal 16S rRNA gene in bacterial pathogens and sequencing of the obtained amplicons (Nguyen et al., 2016).

Antibiotic resistance has been observed in *Streptococcus* species, specifically to antibiotics such as kanamycin, penicillin, nitrofurantoin, oleandomycin, sulfamethoxazole, ampicillin, erythromycin, florfenicol, and oxytetracycline. Despite this, antibiotic therapy continues to be the primary strategy for farmers to prevent significant economic losses during outbreaks of bacterial illnesses. Antimicrobial peptides (AMPs) are among the most effective methods for reducing antibiotic use in aquaculture. In tilapia species, LL-37 has shown only minor side effects, suggesting it could be a viable antibacterial candidate to combat bacterial infections in aquaculture (De Sousa et al., 2021).

Additionally, dietary supplements such as coenzyme Q10 (CoQ10) and vitamin C serve as natural immunostimulants and antioxidants, promoting better health and performance in aquatic animals. The antioxidant properties of CoQ10 and vitamin C, both individually and in combination, enhance resistance to *S. agalactiae*. Furthermore, CoQ10 and vitamin C have been shown to improve resistance to *S. agalactiae* in *Oreochromis* species (De Sousa et al., 2021). Since 2011, Merck Animal Health's commercial AQUAVAC® Strep Sa vaccine has been accessible in numerous nations. Against *S. agalactiae* biotype II, this inactivated oil adjuvant vaccine can promote active immunity (Fyrand et al., 2024).

Currently, DNA vaccines are being formulated in China against the *S. iniae* and *S. agalactiae* strains, encoding the bacteria's surface protein into plasmid vectors. Live, attenuated vaccines are also being produced (Rathor and Swain, 2024).

Reducing congestion and enhancing water quality and environmental conditions are standard proactive measures to limit *S. agalactia* infection in intensively farmed tilapia. Also, avoiding excessive feeding, minimizing needless handling or transportation, and removing dead and moribund fish as soon as possible to reduce the risk of disease outbreaks and the spread of pathogens. All production units and utensils should be properly disinfected and tanks should be cleaned regularly. Streptococcosis in Nile tilapia is a serious global obstacle, characterized by a lack of extensive prior data and a partial grasp of current dynamics. The disease's notable features include histopathological impairment, persistent infections, and targeted mortalities, all of which raise concerns about the fish population's health. Streptococcosis epidemics have serious consequences on the environment, human health, and socioeconomic status. However, there is a substantial lack of information regarding the disease's epidemiology in specific regions. Given this scenario, it is critical to step up scientific research to gain precise understanding of the strains present and their propagation dynamics, as well as to propose efficient prevention and eradication strategies.

***Staphylococcus* spp.:** Staphylococcosis is caused by *Staphylococcus* spp. in tilapia. *Staphylococcus aureus* is the etiological agent responsible for a range of morbidity and mortality worldwide (Pridgeon and Klesius, 2012). Staphylococcal food poisoning is the main cause of gastroenteritis and the second most frequently recorded foodborne illness globally. *S. aureus* number of extracellular poisons, staphylococcal enterotoxins (SEs), is released by *S. aureus*, indicating emetic activity. *Staphylococcus* spp. induced a clinical manifestation that included neurological symptoms, modulation or inflammation in various areas, granulomatosis, erratic swimming, bilateral exophthalmia with or without corneal opacity and periocular hemorrhage congestion or enlargement of internal organs, and disorders of appetite. In juvenile specimens, hemorrhagic septicemia was a characteristic symptom of providenciosis (Rajme-Manzur et al., 2023). In order to overcome those obstacles, 16S rRNA sequencing has emerged as a key component of accurate and dependable identification for quick bacterial disease detection and diagnosis.

The high salt concentration (up to 10% NaCl) and osmotic pressure are tolerated by *S. aureus* strains, with bacterial growth. Control of temperature below 10°C can hinder SE production. A report was done in Kenya to assess the frequency of foodborne disease caused by *S. aureus* in tilapia fish (Table 1). A study undertaken in Pakistan showed the presence of *S. aureus* causing red spots on the skin of *Oreochromis niloticus* (Fatima, 2014). Recently, *Staphylococcus haemolyticus* was isolated from tilapia farms in Chiapas, Mexico (Rajme et al., 2023).

Staphylococcus aureus is a harmful bacterium that has been identified in health facilities all over the world. It is commonly known that *Staphylococcus aureus* can develop resistance to antibiotics, both historically about penicillin, erythromycin, and tetracycline and more recently with regard to methicillin and vancomycin (Soliman et al., 2014). The fast growth of antibiotic resistance in the majority of *S. aureus* strains, as well as the production of virulence factors that contribute to their severity and ability to cause disease, has contributed to their prominence. Because antibiotics are no longer permitted as feed additives, research on alternative feed additives in aquaculture diets has intensified and resulted in significant studies. Herbs, resins, and spices, for example, are phytogenic feed additives that provide a variety of volatile and aromatic compounds to the diet. These nutrients boost fish health, development rate, and immunity. *Boswellia serrata* resin extract (BSRE) supplementation to *O. niloticus* can improve its antioxidant activity, immunological status, and disease resistance to *S. aureus* infection (Montaser et al., 2021).

The prompt implementation of control and preventive measures depends on the early diagnosis of these procedures and a determination of the causative agents that impact aquaculture in particular geographic areas. Additionally, the success of aquaculture industries depends on the detection of unexpected emerging pathogens in areas that are vulnerable to epidemics. Although *Staphylococcus* spp. are not prevalent pathogens in Nile tilapia aquaculture, reports indicate that they are not only found in farms but also have a high virulence, resulting in higher mortalities than anticipated for a fish like Nile tilapia. As a result, it should be labeled an emerging threat in fish farming that requires further investigation. Furthermore, for efficient farm management, the underlying causes of fish pathogens must be accurately identified. Because numerous bacterial pathogens can produce comparable clinical symptoms, this identification is difficult. The accurate diagnosis of *S. epidermidis* and the avoidance of false positives depend on the combination of clinical and biochemical identifications with 16S rRNA sequencing.

***Micrococcus* spp.:** *Micrococcus luteus* is an emerging opportunistic fish pathogen. Gram-negative bacteria are still the dominant fish pathogens, Gram-positive bacteria have been observed in recent years (Saleh et al., 2021). *Micrococcus* belong to the family Micrococcaceae, are aerobic coccoids, and are Gram-positive. These bacteria are frequent in mammalian skin, often occur in various habitats, live in the soil, and can occur in many other biological niches such as marine residues, meat products, freshwater, or fruit. A study conducted in Mexico showed signs of disease such as intestine and vesicle inflammation, corneal opacity, distended gallbladder, body depigmentation, corneal opacity, and liver discoloration caused by *Micrococcus* spp. in tilapia fish (Huicab-Pech et al., 2017) (Table 1).

Histopathological changes included expanded hepatocytes, fatal renal tubules, fibrous lesions, elliptic enlargement of white pulp, and degeneration of splenic tissue, melanoma-macrophage centers, and hyperplasia and fusion of gill lamellae. Characterization of *Micrococcus spp.* was done by using cultural, and biochemical characteristics and 16 S rRNA gene sequence (Suresh et al., 2025). A study by Siamujompa et al. (2023) identified *Micrococcus* spp. from Nile tilapia culture in Zambia. Another study also investigated the identification of *Micrococcus* spp. from Nile tilapia (Ayoub et al., 2021). The authors (Chitambo et al., 2023) demonstrated the isolation of zoonotic strains of *Micrococcus* spp. from Nile tilapia. *M. luteus* improves fish growth and health and it is suggested to use *M. luteus* as a probiotic *in vivo* (Abd El-Rhman et al., 2009; Ridha and Azad, 2012).

Chemical additives such as growth regulators, anabolic steroids, and some antibiotics are widely used as feed ingredients in aquaculture to optimize growth performance and prevent the spread of different diseases. Mistreatment of antimicrobial agents, on the other hand, can result in the evolution of resistant bacterial strains. In recent years, research has focused on the use of a class of beneficial living bacteria that colonize the animal's digestive tract, fighting with other pathogens for resources, area, and adhesion sites, and attempting to enhance the animal's associated microbiota balance. Probiotics are microbes that are thought to be a harmless and easy substitute for the chemicals described above (Mukherjee et al., 2019). In tilapia, a variety of commercial probiotics containing one or more bacteria such as *Bacillus, Lactobacillus, Streptococcus*, or the commercial yeast *Saccharomyces* were used, and it was confirmed that the treated fish had higher productivity and immune responses than the raw fish (Lara-Flores et al., 2003). A report demonstrated the potential and beneficial effect of using *Lactobacillus* sp. and *B. amyloliquefaciens* added with forage in improving the growth performance and the immune response in tilapia against *Micrococcus* spp. (Ridha and Azad, 2012). Good aquaculture practices (GAP), safety, monitoring of diseases, and the One Health Initiative are critical for addressing disease concerns in aquaculture.

***Lactococcus* spp.:** *Lactococcus garvieae* is the primary cause of piscine lactococcosis, which is common in many freshwater fish species worldwide (Wongkaew et al., 2025). The lactic acid bacteria (LAB) are cocci or bacilli and Gram-positive bacteria that do not form spores, have an optimum temperature of ±40°C, are usually anaerobic, oxidase-positive, non-motile, catalase-negative (Shabirah et al., 2019). Direct contact between susceptible and infected fish, consumption of tainted water or feed, and an infestation of feces in the system are the three ways that the bacterium spreads horizontally. Transportation, high stocking density, and poor water quality are examples of stressors that can make fish more vulnerable to *Lactococcus* infection (Vaneci-Silva et al., 2025).

The most important fish pathogen is *Lactococcus garvieae*, which has frequently been recognized as a human pathogen triggering diskospondylitis, cholecystitis and endocarditis. Initially, *L. garvieae* was derived from bovine mastitis cases, primarily as *Streptococcus garvieae,* and was isolated from hot water fish, mainly as *Enterococcus seriolicida,* which was eventually confirmed as a synonym for *L. garviea* (Gauthier, 2015).

Infections of *L. garvieae* in tilapia are the cause of an emerging disease that has become very important in the last decade (Bwalya et al., 2020). A study in Indonesia isolated *Lactococcus gravies* from *Oreochromis* spp. (Anshary et al., 2014). Another study in Brazil reported pathogenic *L. garvieae* causing mortalities in Nile tilapia (Evans et al., 2009). Human disease with *L. garvieae* has been linked with the consumption of raw fish (Chan et al., 2011). Typing of RFLP showed remarkable variability among *L. garvieae* and has been linked with illness in fish (Gauthier, 2015). The genomics comparison of isolates of *L. garvieae* did not show strong relations between fish strains and other sources (Ferrario et al., 2013). Fish with chronic illnesses exhibit symptoms like exophthalmia or corneal opacity, irregular swimming, scale loss, and skin hemorrhage (Wongkaew et al., 2025). Antimicrobial susceptibility testing, histopathological analysis, 16S ribosomal RNA (rRNA) gene sequencing, matrix-assisted laser desorption/ionization (MALDI), time-of-flight (TOF) mass spectrometry (MS), and phenotypic testing are used to identify bacterial isolates (Jantrakajorn et al., 2024).

Subsequent losses can be as high as 50% to 80% of the total production. The role of outer membrane proteins (OMPs) in harmful bacteria has been discovered, and they show promise in protecting diseased fish. Bacterial GAPDH should be considered a multi-purpose vaccination candidate against a variety of harmful bacteria (Tsai et al., 2013). In a challenge with *L. garvieae*, GAPDH of *L. garvieae* can efficiently defend tilapia. Through an antibody-mediated reaction, an oil-adjuvant, inactive whole cell auto-vaccine can defend tilapia against *L. garvieae* disease (Bwalya et al., 2020). To better our understanding, we need further research on microbiological and molecular diagnoses in addition to necropsy and histopathology.

***Arthrobacter* spp.:** The *Arthrobacter* genus comprises a group of rod-shaped, asporogenous bacteria that exhibit a coryneform morphology. They are catalase-positive and strictly aerobic (Osorio et al., 1999). The species *Bacterium globiforme* was initially identified, which later became known as *Arthrobacter globiformis*. Members of the *Arthrobacter* genus are widely distributed, particularly in soil, and have only recently been isolated from clinical sources (Storms et al., 2003).

A study conducted in Mexico reported various health issues in tilapia linked to *Arthrobacter*, including body ulceration, frayed fins, skin bleeding, liver discoloration, inflammation of the intestine and vesicles, body depigmentation, corneal opacity, and a distended gallbladder (Huicab-Pech et al., 2017) (see Table 1).

The use of probiotics in aquaculture feed has been recognized for its positive effects on the host, leading to effective disease control and increased production. These live microorganisms enhance immune response and strengthen disease resistance against pathogenic bacteria such as *Arthrobacter* spp. in Nile tilapia (Kuebutornye et al., 2020). Additionally, the seeds of pawpaw (*Carica papaya*) have been shown to have beneficial effects in controlling *Arthrobacter* in tilapia (Omeje, 2016).

Gram-negative bacteria

A. hydrophila: Motile *Aeromonas* septicemia (MAS), which is caused by various *Aeromonas* species, is one of the most significant bacterial diseases in aquaculture and causes significant financial losses. MAS has a complex pathophysiology, meaning that multiple factors must interact for the disease to manifest. Numerous virulence genes and extracellular enzymes secreted by *Aeromonas* species allow bacteria to evade the host's immune system and cause serious illnesses (Elgendy et al., 2024 a).

A. hydrophila's pathogenicity resulted in the development of an aerolysin-related cytotoxic enterotoxin that can destroy erythrocytes, disintegrate cell walls, and cause efflux and pore formation. Symptoms of *A. hydrophila* include tissue obstruction, dropsy, necrosis, bleeding, and ulcers (Hal and Manal, 2020).

A. hydrophila is the most dreadful bacteria that can survive in both aerobic and anaerobic conditions. *A. hydrophila* is a bacterial pathogen that was found to be highly infectious in juvenile *O. niloticus* and a causative agent of several pathological conditions such as *Aeromonas* septicemia (Roque et al., 2009). This disease can kill fish in large numbers, as well as cause ulceration and hemorrhages on the skin. Fish infected with the disease may die, resulting in significant losses in fish culture (Riauwaty et al., 2021).

The infections caused by *A. hydrophila* lead to fatal diseases such as dropsy, epizootic ulcerative syndrome (EUS), and eye lesions (Roque et al., 2009). The EUS caused by *A. hydrophila* is a condition characterized by large cutaneous ulcerative lesions that periodically result in deaths in tilapia species. This condition is considered an epidemic disease and is distributed worldwide, particularly in Southeast Asia, distressing various types of cultured and wild fishes (Abdul Kader Mydeen and Haniffa, 2011).

A. hydrophila infection can grow very quickly in aquaculture due to high temperatures, high ammonia and nitrite levels, lower dissolved oxygen (DO) levels, high carbon dioxide (CO_2) levels, organic emissions, and malnutrition (Sughra et al., 2021).

According to the study, *A. hydrophila* species are associated with skin hemorrhages, loss of strength, loss of eyesight due to broken orbital eyeballs, and eating disorders (Yardimci and Aydin, 2011). Some bacteria are laterally transferred and employ water as an intermediary vehicle, resulting in fish-to-fish outbreaks due to close contact (Mauel et al., 2007). The gills, liver, heart, kidneys, spleen, muscles, stomach, and eyes are all affected by these bacteria (Sanyal et al., 2018).

The genetic heterogeneity of the genus *Aeromonas* makes it difficult to identify strains down to the species level. *Aeromonas* strains are phenotypically identified using physiological, morphological, and biochemical traits. To accurately identify and classify the *Aeromonas* genus, molecular biology methods are the most effective. This involves amplifying and sequencing the constitutive housekeeping genes (*gyrB* and *rpoD*) using a polymerase chain reaction (Haenen et al., 2023). To validate the genus and species, as well as the strain viability, biochemical tests (Simmons citrate, Kligler iron agar, motility, indole, ornithine, lysine iron agar, methyl red, and Voges-Proskauer) are performed for diagnosis of *A. hydrophila* (Elgendy et al., 2024 a; Bernal et al., 2025 a).

Molecular methods for identifying and genotyping *Aeromonas* include the enterobacterial repetitive intergenic consensus-PCR (ERIC-PCR), the 16S rRNA typing method, and the amplified fragment length polymorphism (AFLP) (Haenen et al., 2023).

In Egypt, *Aeromonas* septicemia poses a huge economic threat, causing significant losses in cultivated freshwater fish, *Oreochromis* spp. (Aboyadak et al., 2015). Another study in Egypt showed the isolation of *A. hydrophila* complex in cultured *Oreochromis* spp. (Algammal et al., 2020). *A. hydrophila* causes huge losses to *Oreochromis* spp. fish resources in natural water and aquaculture systems (Sanyal et al., 2018). Aquaculture expansion has been implemented to fulfill the increased population need for fish output; nevertheless, this intensification amplifies stressful situations, affecting growth, and immunity, and increasing disease risk. In many countries, bacterial infections are seen as a major impediment to the aquaculture industry's economic prosperity. One of the medicinal plants being studied for its nutritional effects on fish health is *Salvadora persica* (also called "arak" or "miswak" in Arabic dialects).

In addition, miswak supplementation increased hematoma immunological indices and antioxidant activities in reared tilapia, as well as protecting against *A. hydrophila* infection (Abd El-Latif et al., 2021). Nanoparticles of silver in tilapia, AgNPs, are non-cytotoxic and give an alternate antibacterial weapon to *Aeromonas hydrophila* (El-Houseiny et al., 2021). Spirulina, also known as *Arthrosis platensis*, is a freshwater blue-green filamentous alga that is high in protein (60–70%), minerals, vitamins, and important fatty acids like linolenic acid, palmitic acid and linoleic acid. As a result, it has been utilized to feed fish larvae (Lu et al., 2002).

A phage is a virus that targets bacteria and can either instantly disintegrate the bacterial cell or transfer its DNA into the host bacterial chromosome. Bacteriophage ΦZH1 and ΦZH2 persuade mortalities in *Tilapia* spp. against motile *Aeromonas* septicemia caused by *Aeromonas hydrophila* (El-Araby et al., 2016). Honey bee pollen (HBPs) is made up of the anthers of flowers that foraging bees gather and carry to the colonies, pollen agglutinates with bee discharges and nectar. HBP improves growth performance metrics [length, body weight, specific growth rate (SGR), average daily gain (ADG), and feed efficiency ratio (FER)] as well as immunological response (phagocytic activity). Honey bee pollen assimilation into the diet improves growth rate, enhances non-specific immunity, and helps manage *A. hydrophila* infections in tilapia (El-Asely et al., 2014). According to the study, feeding Nile tilapia Ecobiol Plus® enhances their immune systems, improves their development performance, and makes them more resistant to disease, particularly when exposed to *A. hydrophila* (Omar et al., 2025).

Recently, the aquaculture industry has become more interested in using new natural compounds as part of safe, antibiotic-free, and environmentally friendly diets. A possible option is the metabolic itaconate molecule, which has anti-inflammatory, immunomodulatory, and antioxidant qualities (Mathew et al., 2025). Another study evaluated how dietary *Chenopodium album* leaf powder affected the growth performance, hematological and biochemical profiles, levels of antioxidants, vague immunity, and resistance to *Aeromonas hydrophila* infection of Nile tilapia (*Oreochromis niloticus*). In Nile tilapia, supplementing with 20–30 g/kg of *C. album* enhanced growth, immune response, and disease resistance. Additionally, this diet improved general health by lowering stress markers (Ujan et al., 2025).

Fish MAS can be treated with florfenicol (FFC), an approved therapy. FFC's viability effectiveness against *A. hydrophila* infection in fish in tropical settings was shown in this study. In *A. hydrophila*-challenged *O. niloticus*, the dietary FFC administration reduced stress and altered the histoarchitecture of vital organs while also increasing survival, biomass, and feed intake. Furthermore, it assisted the fish in overcoming erythromorphology, hematology, and wounds caused by pathogens (Sharon et al., 2025). Multiple virulence and antibiotic-resistance genes are present in motile aeromonads. Safeguarding the health of farmed tilapia in aquaculture requires proper oversight and biosecurity procedures. Identification of *Aeromonas* at wide ranges, which is essential for determining the pathogen and the management of epidemics of illnesses in aquaculture, depends on routine monitoring of fish farms. Further research into the mechanisms leading to these beneficial impacts could help optimize the use of *C. album* and Ecobiol Plus® etc. in aquaculture practices. Moreover, research should be conducted to evaluate the efficacy of *C. album,* Ecobiol Plus®, and other extracts against other bacterial strains in aquaculture.

E. coli: *Escherichia coli* has been discovered to be a crucial pathogenic bacterium linked to freshly harvested or treated fish, posing a substantial global public health hazard and being the principal source of the majority of bacterial food-borne infections. The most common mode of transmission is through the intake of infected food and water, but dissemination can also occur directly from person to person and from animal to person. It was mostly detected in the *Tilapia* spp., specifically in muscles, as muscles might be infected during harvesting due to stressful conditions. Similarly, several studies reported that gills were also infected with *E. coli* due to their direct interaction with the water in *Tilapia* spp. Typically, *E. coli* causes lesions on gills, muscles, liver, stomach, body surfaces, eyes and skin tissues (Rocha et al., 2014; Elhadi et al., 2016). Lesions, hemorrhagic eyes, focal hyperplasia, desquamation in the secondary lamellae, hemorrhages in the gills and infected eyes are diseases caused by *E. coli* in *Tilapia* spp. (Aly et al., 2012; Takyi et al., 2012; Rocha et al., 2014; Elhadi et al., 2016). Triple sugar iron (TSI), methyl red (MR), Voges-Proskauer (VP), citrate utilization (CIT), urease (URE), catalase (CAT), oxidase (OX), and hydrogen sulfide (H2S) production tests were among the biochemical tests conducted for the diagnosis of *E. coli* (Mumbo et al., 2023).

E. coli causes diseases in *Tilapia* spp. and in other fish species in different regions of the world, such as Brazil (Rocha et al., 2014), Egypt (Aly et al., 2012), Saudi Arabia (Elhadi et al., 2016), the Philippines (Kang et al., 2020) and Trinidad (Newaj-Fyzul et al., 2008). Antibiotics and chemotherapy have been used in aquaculture for a long time to avoid infectious diseases and limit pathogen multiplication, resulting in the spread of antibiotic-resistant microorganisms (Taoka et al., 2006). *E. coli* could be observed in *Tilapia* spp. due to contamination of cultured water by animal waste, as well as the use of contaminated water in fish processing (Saqr et al., 2016).

In a study by Lee et al. (2019) the oral injection of *B. subtilis* T1 and T13 transgenic strains was employed to suppress harmful bacteria in tilapia fish fry. Transgenic *B. subtilis* strains T1 and T13 not only displayed greater bactericidal effectiveness against *E. coli*, but they also had relatively steady plasmid propagation. They were also used in *in vivo* studies. This finding implies that sequential repetitions of transgenic lactoferricin synthesized by transgenic strains going through the gastrointestinal tract of tilapia would generate cleaved functional lactoferricin that would kill the intestinal pathogen, lowering pathogen-infected fish death rates. In another investigation, the human probiotic bacterium *Escherichia coli* Nissle 1917 was employed to regulate *E. coli*. *Escherichia coli* Nissle 1917 has a good effect on *Tilapia* spp. efficiency and immunological responses to *E. coli* (Zein et al., 2022). These economic effects of *E. coli* are attributable to a lack of management practices, disease control knowledge and sustaining of excessively high densities. Deaths are determined by the level of infectivity that relies on the modification and development of the host physiological conditions under the effect of ecological variables, state of health and disease virulence (Huicab-Pech et al., 2016). There is a need for research on antibiotic susceptibility tracking in aquatic environments where fresh and marine fish are harvested for human consumption.

***Edwardsiella* spp.:** Edwardsiellosis is one of the most common bacterial diseases in fish. It is caused by *Edwardsiella piscicida*, a Gram-negative, facultative anaerobic bacterium from the Enterobacteriaceae family. Enteric septicemia of catfish (ESC), also known as hole-in-the-head disease, is caused by *Edwardsiella ictaluri* (Rathor and Swain, 2024). *Edwardsiella tarda* is a common fish pathogen, causing septicemic diseases and formidable economic losses in freshwater fish farming (Algammal et al., 2022). The genus comprises four species: *E. ictaluri, E. tarda, E. anguillimortifera,* and *E. hoshinae*. *E. tarda* exists in areas with poor water quality and elevated temperatures that permit its devotion to and propagation within fish cells.

E. ictaluri can quickly adhere to and pierce host mucosal membranes to cause a systemic infection. Additionally, it is a facultative intracellular pathogen that may be able to survive inside phagocytic cells, which may serve as a means of transmission. This trait contributes significantly to the disease's quick spread. The pathogen could be transferred horizontally between fish and spread by the water flow (Haenen et al., 2023). Edwardsiellosis generates a medical diagnosis of septicemia, including organs such as the liver, kidney, and spleen, as well as external organs such as the rectum, abdominal dull and pupils bump, skin, and fins (bleeding). Symptoms of exophthalmos, spiral movements, and irregular swimming also occur in diseased fish (Huicab-Pech et al., 2016). The most common lesions that were reported were exophthalmia and liver granulomas. An outbreak of edwardsiellosis in tilapia shows ocular lesions (corneal opacity, eye loss, and exophthalmia), hemorrhagic ulceration of the urogenital orifice, and abdominal distension in the caudal fin caused by *E. tarda* (Miyazaki and Kaige, 1985).

The study reported lesions in the eyes (i.e., ocular edema and opacity of the cornea), hemorrhage, ulcer, and splenomegaly (Huicab-Pech et al., 2017) (Table 1). For the initial detection, gross signs with white spots on the head kidney, and spleen are essential. Additionally, the liver's decreased fat reserve and pale gills from anemia are useful indicators for identifying afflicted fish (Haenen et al., 2023). The initial step in confirming the existence of *Edwardsiella* spp. from fresh fish tissue, such as kidney or spleen, is wet-mount Gram staining with the presence of a rod-shaped, Gram-negative intracellular bacterium. *Edwardsiella* species can be accurately identified using an array of 16S rRNA sequencing, essential genes like gyrB for a phylogenetic study, and a particular PCR-based assay (Haenen et al., 2023).

Edwardsiella is an *Enterococcus* fish pathogen that triggers edwardsiellosis in a variety of marine and freshwater fish taxa in Norway (Abayneh et al., 2012). Edwardsiella is prevalent in the United States, Venezuela, Taiwan and Japan (Burr et al., 2012; Park et al., 2012). *Edwardsiella anguillarum* was reported from the spleen, intestine, posterior kidney, and gonads of *Oreochromis spp.* cultivated in the biofloc system in Lima, Peru (Sierralta et al., 2020). Another study characterized virulent *Edwardsiella anguillarum* from *Tilapia* spp. (Oh et al., 2020).

Florfenicol is an antibiotic that is commonly used in the aquaculture industry to fight bacterial infections around the world. Florfenicol is approved as a feed premix for the treatment of pathogenic bacteria in a variety of fish species in several countries, including Egypt, the United Kingdom, Norway, the United States, Canada, and several other Asian and South American countries. *Lactobacillus plantarum* is a probiotic that has immunomodulatory effects. *Oreochromis* spp. health was enhanced by *L. plantarum. L. plantarum* feeding may improve the health and immunological state of *Oreochromis* spp. more effectively (Sherif et al., 2021).

The study by Kwon et al. (2006) showed the vaccination efficacy of *Edwardsiella tarda* ghosts generated by gene E-induced lysis in tilapia. Tilapia inoculated with both *E. tarda* ghosts (ETG) and formalin-killed *E. tarda* (FKC) vaccines had considerably greater serum agglutination titers. There were no significant changes in serum agglutination titers between fish inoculated with ETG and fish immunized with FKC, but ETG showed substantially greater bactericidal action. Furthermore, fish inoculated with ETG outperformed fish immunized with FKC. In recent years, probiotics, particularly lactic acid bacteria, have been used as food additives to protect fish from a variety of diseases. *Lactobacillus rhamnosus* was evaluated for its ability to protect tilapia against experimental *Edwardsiella tarda* infection. Overall mortality in probiotic-supplemented fish was much lower than in control fish. In a histological study, pyogranulomatous responses were detected in the probiotic-supplemented fish at an earlier stage and to a greater extent than in the control fish. *L. rhamnosus* enhanced the fish's potential inflammatory response by facilitating phagocytic cell aggregation, increasing phagocytosis, and therefore protecting the fish against *E. tarda* infection (Pirarat et al., 2006).

Antibiotics are widely used to treat diseases. Nevertheless, misuse of antibiotics is responsible for significant antibiotic susceptibility among *Edwardsiella* spp. in aquaculture. Alternatives to antibiotics should be further explored to tackle this emerging, highly pathogenic bacterium. Furthermore, it is strongly advised to implement biosecurity measures and early diagnostic screening to stop the pathogen's detrimental effects and transboundary spread.

***Flavobacter* spp.:** Flavobacteriosis is caused by bacteria in the Flavobacteriaceae family, and impacts both farmed and wild fish (Rathor et al., 2024). There are three *Flavobacterium* spp. *Flavobacterium psychrophilum* triggers bacterial cold-water disease, *Flavobacterium columnare* is the cause of columnar disease, and *Flavobacterium branchiophilum* triggers bacterial gill disease, being the major pathogens of freshwater-reared and wild fish populations. *F. columnare* is a Gram-negative, motile rod-shaped bacterium, characteristically 0.5 µm wide and up to 3 µm long. *Flavobacterium columnare* is the bacterium causing columnaris disease, a contagious bacterial infection that occurs globally. A few other terms, such as gliding bacterial diseases of sea fish black patch necrosis and eroded mouth conditions were used to characterize the inaction triggered by this bacterium (Toranzo et al., 2005). The *F. columnare* isolated from tilapia was recently renamed to *F. oreochromis* (LaFrentz et al., 2022). 330 species in the Flavobacterium genus are officially recognized by the International Code of Nomenclature of Prokaryotes. *Flavobacterium columnare* has been reclassified into four new species: *Flavobacterium columnare*, *Flavobacterium davisii*, *Flavobacterium covae*, and *Flavobacterium oreochromis* (Janampa-Sarmiento et al., 2025). In combination, mortality, and diseases caused by these pathogens represent the largest host and geographic distribution of any bacterial pathogen for fish (Starliper, 2011). As they are widespread in freshwater and soil, *Flavobacteria* are important and are known for their novel gliding motility.

Additionally, due to the fast mortality rate and widespread occurrence of this bacterial disease, it has caused an enormous economic impact on fish production. *F. columnare* is known to be an opportunistic bacterium and forms part of the normal microbiota in soil and water, as well as in the intestines, and gills of fish (Sebastião et al., 2011).

Since marine flexibacteriosis may affect both adults and juveniles, fingerling fish experience a more serious type of disease. An improvement in the intensity of the disease has been confirmed at extreme temperatures. In addition to water temperature, the disorder is affected by a broad array of environmental pressure and host-linked variables. As an initial stage for the suspected screening of marine flexibacteriosis, clinical signs can be used along with the microscopic identification of long rod deposits in Gram-stained preparations obtained from gills or wounds. This preliminary analysis must be followed by pathogen isolation in a suitable medium or by the use of an advanced molecular DNA-based technique implemented directly on fish tissues (Toranzo et al., 2005). It is the second most ubiquitous pathogen after *Edwardsiella* to trigger an infection in *Oreochromis* spp. Columnaris disease has been reported in different fish species around the world, including economically valuable species of *Oreochromis* spp. (Declercq et al., 2013).

A study reported in Uganda identified the *Flavobacterium* spp. infecting *Oreochromis* spp. (tilapia) (Wamala et al., 2018). It was also reported from Nile tilapia in Egypt (El-Tawab et al., 2020). They are required for innate immunity to function. TLR25 is a newly discovered fish-specific TLR1. Toll-like receptors (TLR25) are thought to play a function in the innate immune system's antimicrobial defenses to *Flavobacter* spp. of Nile tilapia (Lee et al., 2020).

The survey performed in Brazil confirmed the clinical signs begin with corrosion of the dorsal and tail fins, and this progresses to exterior infection in which grey spots or yellowed erosion appear on the body surface and gills of tilapia (Sebastião et al., 2011). *Flavobacterium* infects the skin, gills, fins, eye, spleen, internal organs, brain, and liver tissues of tilapia, causing diseases like skin lesions, fin erosion, gill necrosis, and splenomegaly (Huicab-Pech et al., 2017). multiplex PCR, matrix-assisted laser desorption ionization-time of flight (MALDI-ToF MS) method have been proposed as methods for distinguishing *Flavobacterium* species associated with columnaris disease (Janampa et al., 2025). *F. columnare* was isolated from skin, and gills, and rare in internal organs of *Oreochromis* spp.in Egypt (El-Tawab et al., 2020).

A pathogenic *Flexibacter* spp. was isolated from tilapia var. Stirling culture (Huicab-Pech et al., 2017). The most common treatments for columnaris illness involve adding chemicals to the culture water or providing antibiotic-medicated feed to the fish. To treat columnaris by bath, copper sulfate ($CuSO_4$) and potassium permanganate ($KMnO_4$) are regularly employed chemicals; oxytetracycline and similar antibiotics are among the medications of choice for feed. Antibiotic use for an extended period may promote the establishment of antibiotic-resistant strains, lowering therapeutic efficacy. Natural compounds to manage diseases of aquatic animals are required to establish antibiotic-free and chemical-free aquaculture. Natural products have recently gained popularity as alternatives to antibiotics in the treatment of bacterial infections in aquaculture. The use of Asiatic pennywort *Centella asiatica* aqueous extract as a bath treatment has the potential to control disease caused by *F. columnare* (Rattanachaikunsopon and Phumkhachorn, 2010 b). β-glucan is a powerful immunostimulant that boosts innate immunological function, disease resistance, and growth in a variety of aquatic organisms. Tilapia's inherent immunity to *F. columnare* is enhanced by β-glucan supplemented feeding regimens (Amphan et al., 2019).

In intensive aquaculture, it is important to determine novel natural sources from the marine environment that have unique immunomodulatory and antioxidant properties. In this regard, a marine sponge extract derived from *Smenospongia* (SS-extract) was investigated for its potential anti-inflammatory, antioxidant, and antimicrobial activities in Nile tilapia during a simultaneous infection with *Flavobacterium columnare.* Supplementation with marine sponges *Smenospongia* extract was found to strengthen Nile tilapia's immune and autophagy defenses in skin and gill tissues, thereby preventing infection of *F. columnare*. Additionally, SS-extract addition substantially lowered the exaggerated immune response and endoplasmic reticulum stress-related gene expression. Furthermore, antimicrobial defense peptides and the antioxidant barrier in skin tissues were enhanced (Ibrahim et al., 2024).

The high genetic diversity within *F. columnare* has been highlighted by prior studies that used genome-wide comparisons and phylogenetic analysis of 16S rRNA and housekeeping genes, indicating the need for further research on taxonomy revision. To establish efficient prevention and control measures in aquaculture, columnaris disease, particularly in newly infected fish species, should be described not only by pathogenicity but also by their genetic diversity information. Further research is recommended to evaluate the effects of plant extracts against *Flavobacterium* spp.

***Yersinia* spp.**: It is a Gram-negative bacterium, known for causing enteric red mouth disease and yersiniosis as a result of severe economic loss in freshwater *Oreochromis* spp. The prevalence and mortality rate of yersiniosis disease in the entire *Oreochromis* spp. was almost 77%, as well as the sternness of the skin injuries on the individual fish, showing the elevated pathogenicity of *Yersinia ruckeri* (Kumar et al., 2015).

Y. ruckeri is described as oxidase-negative, catalase-positive, glucose-fermentative, b-galactosidase, and nitrate-reductive with the potential to release decarboxylases of lysine, but neither hydrogen indole nor sulfide. This pathogen can be spread by direct interaction between fish that are infected and fish that are not infected. A carrier condition for this pathogen has been shown to endure for 2 months after both laboratory and natural infections by infected fish. Studies have reported that *Y. ruckeri* infects the liver, kidney, spleen, lower part of the intestine, and heart in *Oreochromis* spp. The major signs and symptoms include acute or chronic enteric septicemia and hemorrhagic zones (Kumar et al., 2015).

Y. ruckeri affects the parts of the intestine, liver, gills and spleen of *Oreochromis* spp. and causing diseases like focal hyperplasia, desquamation in the secondary lamellae and hemorrhages in the gill arch (Aly et al., 2012). *Yersinia ruckeri* was reported in tilapia from an earthen pond at a semi-intensive fish farm in Sharkiya Province, lower Egypt, in 2007 (Eissa et al., 2008).

Traditional disease control methods include the use of chemicals such as antimicrobial drugs, pesticides, and antiseptics, which are harmful to fish and trigger immune suppression, gastrointestinal bacterial population disturbances, and decreased disease resistance (Rutherfurd-Markwick and Gill, 2004). Probiotics are useful microbial cells that are often used to modulate the immune system. *Bacillus* sp., *Lactobacillus* sp. and *Saccharomyces* sp. are the most widely used probiotics in aquaculture. *Bacillus amyloliquefaciens* improved the immune responses of tilapia against *Y. rukeri* (Selim and Reda, 2015).

The specific dietary supplements improved the fish's growth, immune response, metabolic responses, and health performance over the standard feed additives. Phytogenic agents, yeast products, probiotics, prebiotics, and enzymes were also used as functional feed additives (Alemayehu et al., 2018). Chitosan has been used as a natural polymer to coat a variety of nanoparticles (NP) because of its special and excellent bio-absorbable, biocompatible, and mucoadhesive features. Omega 3-chitosan nanoparticles have the ability to promote growth in tilapia fish by enhancing immune function to bacterial yersiniosis (Eissa et al., 2020). Because antibiotics in aquaculture cause multidrug-resistant bacteria to proliferate, there is an urgent need to create new alternatives in order to prevent and control disease. The improper use of antibiotics leads to antibiotic resistance, and to impede this issue it is essential to limit the use of antibiotics in aquaculture.

***Francisella* spp.:** Francisellosis is a chronic illness caused by the Gram-negative coccobacillus bacteria, *F. noatunensis* subsp. *orientalis* (Fno) (Xu et al., 2025). *Francisella* is a coccobacillus bacteria that is Gram-negative, intracellular, and aerobically facultative (Ottem et al., 2007; Jeffery et al., 2010). The pathogen generates persistent damage through intracellular penetration, and illnesses have been described in a range of species, especially *Oreochromis* spp. Non-specific external indications of the pathogen include bleeding around the pectoral fins, anorexia, erratic swimming and exophthalmos (Soto et al., 2009), and interior clinical signs such as splenomegaly and granulomas (Mauel et al., 2007; Ottem et al., 2007).

Clinically affected tilapia primarily manifested multifocal superficial skin ulcers, mild focal congestion, and hemorrhage in the jaws, eyes' irises, and other integumentary regions (Xu et al., 2025). A study showed exophthalmia, fungal patches, petechial hemorrhaging on the pectoral fins, and pale gills are triggered by *Francisella* spp. in tilapia fish farms in the United Kingdom (Jeffery et al., 2010). The study found that *F. noatunensis* subsp. *orientalis* can be transmitted horizontally through different routes of infection, such as injection, immersion, cohabitation of infected fish with healthy fish, or direct contact with contaminated water (Xu et al., 2025). The PCR assay is used for identification/diagnosis of *Francisella* spp. (Xu et al., 2025). In water, the pathogen is spread horizontally, invading fish through direct contact with the fish (Mauel et al., 2007).

In fish aquaculture, *Francisella* has an incidence of 85 to 90%. It is spread globally and has been recorded in Brazil, Indonesia, Japan, Egypt, Costa Rica, Chile and various European countries (Jeffery et al., 2010; Ottem et al., 2007). *Francisella noatunensis* subsp. *orientalis* was isolated from cultured tilapia (*Oreochromis* spp.) in Taiwan (Pulpipat et al., 2019), Honduras (Soto et al., 2019).

Francisellosis is a bacterial disease caused by *Francisella noatunensis* subsp. *orientalis* (Fno), which poses a serious threat to the global tilapia industry. There are currently no commercially available vaccines against francisellosis for use in farmed tilapia, and the only possible clinical strategies in the field are the use of antibiotics for long periods of time or increasing water temperature. An autogenous whole cell-adjuvanted intravenous vaccine with 100% relative survival (RPS) in tilapia was recently created. The Fno (*Francisella noatunensis orientalis*) vaccine may be used to create a broad-spectrum, highly defensive francisellosis vaccine for tilapia (Shahin et al., 2019). This novel technology has been used to create new vaccine candidates that are better than live-attenuated or DNA vaccines because they do not infect the genome of the recipient or proliferate in the environment or host. Injectable vaccines using diatoms as antigen expression vectors have demonstrated efficacy in tilapia models. When given as top-coated feed, fusion proteins made of *F. orientalis* IglC and flagellin produced in *Thalassiosira pseudonana* diatoms function as self-adjuvanting antigen delivery systems to provide tilapia with a protective immune response against *F. orientalis* (Meyer et al., 2025).

***Citrobacter* spp.:** *C. freundii* is a rod-shaped, Gram-negative, and facultative anaerobic bacteria. Significant clinical signs are caused by the infection, such as a distended belly, skin ulcerative lesions, darkened spleen, and bloody ulceration. Summer syndrome in tilapia is caused by *C. freundii* (El Asely, 2020). A study reported that these bacteria infect the intestine, liver, gills, and spleen of *Oreochromis* spp. with major signs and symptoms, e.g., focal hyperplasia, desquamation in the secondary lamellae, and hemorrhages in the gill arch. The study carried out in Egypt shows vacuolar disintegration in the hepatocytes, leukocytic infiltration in the primary gill lamellae, mucinous relapse in the epithelial lining, and cloudy swelling of the hepatocytes due to the infection caused by *C. freundii* in tilapia (Table 1) (Aly et al., 2012).

Citrobacter freundii pathogenic effects on tilapia fingerlings taken from an Indian fish farm revealed signs such as septicemia, tail necrosis, destruction of primary and secondary lamella, severe gill damage, reddening and bleeding of the body (Thanigaivel et al., 2015). A report carried out in Brazil confirmed outbreaks of *Oreochromis* spp. caused by *Citrobacter freundii* with clinical signs, such as pale liver, distended abdomen, watery kidney, skin ulcerative lesions, darkened spleen, and bloody exudates in the gastrointestinal system (Molinari et al., 2003).

Citrobacter freundii is a fish pathogen that has been widely documented to cause damage in fish. Phage therapy is a method of controlling infectious diseases and contamination differently. A bacteriophage, also known as a phage, is a form of virus that can infect bacteria. Bacteriophages with high virulence can trigger bacteria to lyse. Bacteriophages are said to be the biosphere's utmost varied species. In contrast to broad-spectrum antibiotics, bacteriophage-specific bactericidal activity has no impact on the body's normal flora (Oliveira et al., 2016). Bacteriophage therapy is very effective at treating bacterial infections, and phages are extensively used as antibacterial agents in the food and aquaculture industries. *In vitro* and *in vivo*, the bacteriophage IME-JL8 was found to effectively lyse *Citrobacter freundii* in tilapia (Jia et al., 2020).

***Pseudomonas* spp.** Pseudomonas is a group of rod-shaped, Gram-negative, and aerobic bacteria. The disorder exists during the winter months. *Pseudomonas* septicemia is characterized by elevated mortality associated with a decline in the water temperature below 11–12°C (Pridgeon and Klesius, 2012). *Pseudomonas* species (including *P. aeruginosa, P. putida*, and *P. fluorescens*) are zoonotic bacterial pathogens that cause disease and high mortality rates in both cultured and wild fish around the world (Kebede Abdi et al., 2024). Abdominal obstruction and hemorrhages in the internal organs are the major clinical symptoms of the fish impaired by this septicemia (Toranzo et al., 2005). *Pseudomonas fluorescens* has been discovered as a causal agent of *Pseudomonas* septicemia disorders in several species of fish, causing clinical symptoms such as skin bleeding and exophthalmia (Hal and Manal, 2020).

Pseudomonas septicemia has been widely spread in the environment and has been recognized as a cause of bacterial hemorrhagic septicemia in fish. This pathogen is typically linked with ecologically unfavorable conditions such as overpopulation, low temperature, and injuries. The causative agent of red spot disease, *P. fluorescens*, is known to infect all forms of cultivated fish where the disease has occurred in running water ponds, standing water ponds, and cages (Fatima, 2014). *Pseudomonas* spp. is diagnosed through the conventional PCR method (Kebede Abdi et al., 2024). API 20E or API 20NE may be used for the diagnosis of *Pseudomonas* spp. (Haenen et al., 2023).

Pseudomonas spp. were reported from *Tilapia* spp. in Egypt (Hassan et al., 2020; Hal and Manal, 2020; Osman et al., 2021). Because of the enormous economic impact of the diseases they create, bacterial infections pose a substantial risk to global fish farming. The use of veterinary drugs is becoming more limited as a result of their various environmental and health-related side effects. The yucca has also been suggested as suitable for water quality management in aquaculture systems: yucca extract as a dietary feed additive to enhance disease resistance in tilapia against *Pseudomonas aeruginosa* infection (El-Keredy and Naena, 2020). In fish infected with *P. putida*, titanium dioxide nanogel (TDNG) reduces oxidative stress, mortality, and hepato-renal dysfunction. Additionally, it can be used as an antioxidant and immunomodulatory agent because it regenerates the histopathological alterations brought on by bacterial infection and increases activity on immune-antioxidant parameters (Rahman et al., 2024). More research is needed to evaluate the nutritional supplementation of TDNG and its impact on other fish species.

***Piscirickettsia* spp.:** *Piscirickettsia salmonis* is an obligate intracellular, Gram-negative, and non-motile bacterium. It was the first bacterium resembling *Rickettsia* to be recognized as a fish pathogen. Anorexia, lethargy, respiratory distress, skin darkening and surface swimming are documented clinical symptoms of affected tilapia fish impaired by piscirickettsiosis. The presence of white patches or superficial hemorrhagic sores on the skin may be the first physical signs of the illness. Sometimes, however, the fish die without any obvious clinical signs. Piscirickettsiosis is a salmonid-septicemic disease. *Piscirickettsia salmonis* is the potential cause of piscirickettsiosis. Many studies have been reported identifying *Rickettsia* disease as causing epizootic outbreaks in freshwater tilapia species in Taiwan (Toranzo et al., 2005).

A study undertaken in the USA confirmed outbreaks caused by *Piscirickettsia* with clinical signs such as emaciation, swam, necropsy, occasional cutaneous hemorrhage and exophthalmia, enlarged spleens with multiple white granulomas, gills epithelial hyperplasia and loss of interlamellar spaces noted in tilapia fish (Mauel et al., 2003). Piscirickettsiosis is caused by stress caused by a range of reasons, such as water temperature fluctuations and strong storms. Thus, stress reduction (i.e., by lowering fish density, the number of net changes, and the number of size gradings) has been proven to be beneficial in minimizing *P. salmonis* epizootics (Branson and Diaz-Munoz, 1991). *In vitro*, *P. salmonis* was found to be susceptible to tetracycline, clarithromycin, erythromycin, streptomycin, and oxytetracycline and resistant to penicillin and lincomycin. Antibiotics' failure to cure piscirickettsiosis could be related to variations in antibiotic dosage per fish when given orally, antibiotics failing to implement effective levels in the bacteria's intracellular site, bacterial resistance to medications, and/or seawater cation suppression of antibiotics (Mauel and Miller, 2002). Although more research is needed, the preventive effect is hopeful for the designing of an *O. niloticus* vaccine (Mauel and Miller, 2002).

***Vibrio* spp.:** Numerous *Vibrio* species, such as *V. harveyi, V. parahaemolyticus, V. alginolyticus, V. anguillarum*, and *V. vulnificus*, are responsible for fish vibriosis, which is a widespread infection. The main cause of human infections associated with seafood is *Vibrio* spp. (Haenen et al., 2014). One of the most commonly reported species is *Vibrio parahaemolyticus* found in tilapia (Hamad et al., 2024). Vibriosis is among the most common diseases leading to massive mortality of cultured shrimp, fish, and shellfish in Asia (Ina-Salwany et al., 2019). *Vibrio* are bacteria with motile bipolar flagella. *Vibrio* are widely distributed in brackish and/or coastal waters. Epidemics of clinical disease only occur when fish are susceptible to infectious agents (Gibello et al., 2019; Hamada et al., 2025). Based on growth parameters and serology, *Vibrio vulnificus* is isolated from fish and oysters and categorized into three biotypes. Vibriosis is a well-known disease that affects a variety of domesticated species all over the world (El-Sayed et al., 2019). In tropical countries, the ulcerative skin lesions, hemorrhagic septicemia, exophthalmia, and abdominal distension in the gills and intestinal tract of *Oreochromis* spp. are caused by *Vibrio* spp. (Table 1) (Younes et al., 2016). To analyze vibriosis microbiologically, isolate bacteria on a general medium like TSA-1 (1% NaCl) with TCBS or VVM agar. Pure culture can be obtained through a commercial phenotypic API 20E system (bioMérieux). PCR- or protein-based (like MALDI-TOF) methods should be used to confirm species. PCR targeting *vvhA*, *fpcrp*, and *seq61* genes allows identification of strains to species (Haenen et al., 2023).

A study conducted in Egypt reported *V. alginoltyicus* from *Oreochromis* spp. (El-Sayed et al., 2019). Both marine and freshwater fish may be infected with *V. alginolyticus,* resulting in a high mortality rate. The mortality rate of infected Nile tilapia fish is reduced when they are treated with florfenicol, enrofloxacin, or oxytetracycline (El-Gohary et al., 2020). Fodder additives based on medicinal plants or plant extracts are a new trend for controlling fish diseases, to achieve the same results as antibiotics but avoid the issue of antibiotic resistance. *Spirulina platensis* (*Sp. platensis*) belongs to the phytobiotics community since it can be used as a food supplement since it is high in vitamins, minerals, carbohydrates, and α-linolenic acid, as well as a source of protein. Spirulina or Ropadiar powder can help *O. niloticus* develop faster by improving muscle protein content, serum antioxidant activity, and immune status (Abdel-Latif and Khalil, 2014).

Vaccination, instead of antibiotics, is an alternate approach to combating fish infections. Formalin-killed *V. harveyi* strain Vh1 offered stronger protections against vibriosis in a tilapia model by eliciting a higher immune response and more effective innate defence, resulting in formalin-killed fish. *Vibrio harveyi* (FKVh) vaccine is a viable vibriosis vaccine candidate in Nile tilapia. (Abu Nor et al., 2020). Extracts from plants bearing polyphenols include *Cassia glauca* and Brazilian peppertree. Brazilian peppertree and *Cassia glauca* mixture extracts have high phenolic and flavonoid content, as well as high antioxidant effects, so the mixture displayed greater antibacterial activity against *Vibrio parahaemolyticus* with a larger barrier when compared to synthetic antibiotics, and this mixture extract substantially decreased *Vibrio parahaemolyticus* growth in tilapia (Hamad et al., 2024).

Inactivated whole-cell bivalent vaccines were tested for their ability to protect against *Vibrio alginolyticus*. Vaccinated tilapia showed higher survival rate, decreased mortalities, normal growth patterns, no clinical signs and high antibody level. Bivalent vaccines are extremely protective and safe, and they may be used as promising candidate vaccines to make Nile tilapia more resistant to *V. alginolyticus* (Abotaleb et al., 2024).

Advances in diagnosis of bacteria

Disease diagnostics play a crucial role in biosecurity and health management to mitigate disease loss and improve animal welfare in aquaculture (Dong et al., 2023). Bacterial strains are recognized based on biochemical properties. Diagnosis for such characteristics gives an approach to the capacity of pathogens to modify precise substrates and reconstruct different items (Abdullah et al., 2013). Bacterial isolation requires the use of specific culture media described as having nutrient compositions that bacteria need to grow and expand colonies (Abdel-Tawwab et al., 2008). Because of the proliferation of cutting-edge molecular methods in aquaculture, researchers and users have shifted away from basic approaches and toward molecular diagnostics (Dong et al., 2023).

Molecular diagnostic approaches are more precise and faster than traditional approaches for identifying septicemic bacterial pathogens. Rapid identification of diseases would assist commercial aquaculturists and fish pathologists in developing efficient control strategies for their farms (Abdelsalam et al., 2023, 2024). Although traditional diagnostic methods like visual diagnosis and histopathology are still widely used, technological advancements like next-generation sequencing (NGS) and artificial intelligence (AI) are being tested for early diagnosis (MacAulay et al., 2022). Some of the modern molecular diagnostics include polymerase chain reaction methods (conventional, quantitative, digital), isothermal amplification methods (loop-mediated isothermal amplification, LAMP), recombinase polymerase amplification (RPA), clustered regularly interspaced short palindromic repeats (CRISPR)-based detection and lateral flow immunoassays (Dong et al., 2023).

Various nucleic acid-based amplification techniques are commonly used in detecting aquatic pathogens, including conventional PCR, qPCR, dPCR, LAMP, and CRISPR. Developments of technologies in aquamedicine, such as sequencing, biosensors, and CRISPR, have enabled rapid disease detection within minutes. Use of cutting-edge tools like nanopore sequencing, biosensors, CRISPR, environmental DNA/RNA (eDNA/eRNA) analysis, matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI TOF MS), sensors, artificial intelligence (AI) and drones are poised to reshape disease diagnosis and monitoring in aquaculture (Bohara et al., 2024).

To gain a better understanding of how to increase fish resistance to pathogen infection, multi-omics platforms have been employed. Finding possible biomarkers for a range of infectious fish diseases in the aquaculture system requires the use of multi-omics techniques like transcriptomics, proteomics, and metabolomics, which offer details on their molecular mechanisms of action. High-throughput omics techniques are emerging as a potent multidisciplinary tool for life science research, including studies of fish diseases. Investigating the relationship between fish immune systems and pathogen infections requires the use of omics techniques to examine DNA variations (genomics), gene expressions at the mRNA level (transcriptomics), protein expression (proteomics), and metabolite concentration (metabolomics) (Natnan et al., 2021). Additionally, these methods enable the identification of molecular pathways and gene networks linked to the immune response of fish to infections (Martin and Król, 2017).

High-throughput data from omics studies can help develop vaccines and immunostimulants for avoiding and controlling disease in fish. Modern technology, such as next-generation sequencing, can detect infections in fish before signs of illness appear (Shivam et al., 2021). High-throughput technology has frequently been employed in proteomics research to find novel antigens for the creation of new vaccines. The transcriptomic approach has been extensively applied in many fish disease studies such as tilapia (Zhu et al., 2015). Data analytics tools like artificial intelligence, 5G networks, cloud computing, robotics, machine learning, big data, and the Internet of Things (IoT) enable farmers to proactively monitor their farms and identify possible disease outbreaks before they occur, which is crucial for disease management in aquaculture. Aquaculture disease management can be greatly impacted by cutting-edge technologies like image-based machine learning, augmented reality (AR), surface-enhanced Raman scattering (SERS), and sensor technology. It is feasible to diagnose fish illness using machine learning quickly (Islam et al., 2024). However, large-scale training at the farmer level is required to understand these technologies

PCR-based methods are highly reliable and more sensitive, because of their rapid results and easy handling. Therefore, several scientists have devised such methods for the rapid detection of bacteria using the 16S rRNA technique (Lau et al., 2015).

Therapeutic and non-therapeutic preventive measures of pathogenic bacteria in Nile tilapia culture

Aquaculture of fish is an estimated billion-dollar business and one of the most rapidly expanding sectors in animal food production. Beyond supplying a stable source of income for millions of people, it plays a critical role in ensuring food safety and promoting economic development (Rathor and Swain, 2024). Fish can become stressed by conditions in the culture environment, such as poor water quality, high stocking density, and low oxygen levels, which increases their susceptibility to infectious diseases (Wanja et al., 2020). Infectious diseases cause the loss of over 10% of cultured fish annually. Fish diseases continue to have a significant global impact on the aquaculture sector, costing more than USD 10 billion. This issue causes substantial declines in aquaculture production and economic concerns in the developing world, which accounts for 90% of the industry (FAO, 2012). To prevent disease in tilapia farming systems, researchers are keen to discover long-lasting, eco-friendly alternatives. Fish health, fish's ability to resist disease can be improved by modulating the immune system of fish (Wang et al., 2023).

Farmers can increase the viability and profitability of the tilapia aquaculture sector by lowering disease outbreaks. Antibiotics, probiotics, vaccination, improving farm management, and eradicating diseased fish populations are the recent control measures in tilapia farming. Probiotics, prebiotics, medicinal herbs, and other immunostimulatory products have been demonstrated to stimulate the fish's immune system during immunosuppression or before the fish reaches full immunocompetence. Vaccines, on the other hand, use built-in immunity to protect against subsequent infections (Figure 1) (Wang et al., 2023).

Serious consequences have resulted from the careless use of antibiotics, such as the emergence of resistant pathogens, disturbances in fish metabolism, deterioration of the aquatic environment, drug residues in aquatic products, and a possible risk to human health. To get past these obstacles, several efficient bio-based and immunoprophylactic alternative treatments have been created. Phytotherapeutics, nanotherapeutics, probiotics, prebiotics, synbiotics, phage therapy, vaccination, quorum quenching, antimicrobial peptides, biosurfactants, bacteriocins, stem cells, and diagnostic-based therapy are some of the recent alternative remedies to fish diseases (Elgendy et al., 2024 b).

Antibiotics are used for treating various human and fish diseases. Extensive use of these antibiotics leads to various antibiotics resistance bacteria (ARB) which have adverse effects on both humans and fish as this is becoming the most threatening and alarming global issue, which is confirmed by most research reports (Caruso, 2016). Antibiotics have been the most widely used compounds in aquaculture for more than a half-century. Antibiotics are a class of organic or chemical substances that kill or hinder the growth of microorganisms. They are also used to boost growth and treat or prevent disease. Lulijwa et al. (2020) examined the global usage of antibiotics in aquaculture and discovered that 11 nations used 67 antibiotic compounds from 2008 to 2018. They reported that florfenicol, sulphadiazine, and oxytetracycline were the most often used antibiotics in aquaculture (Lulijwa et al., 2020).

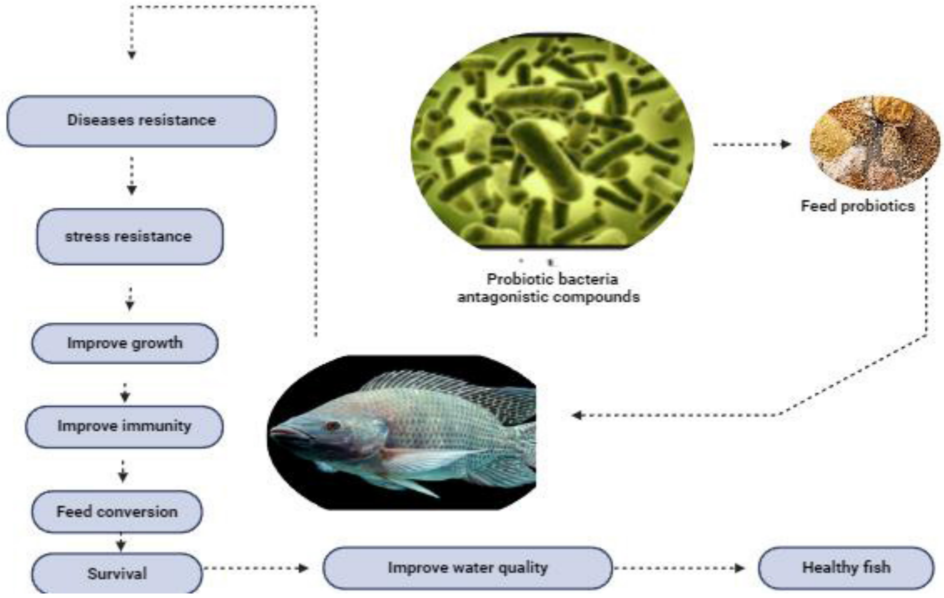

Figure 1. Dietary supplementation of probiotics live microorganisms used against different bacterial diseases

Indiscriminate utilization of modern antimicrobial medicines for all antimicrobial diseases leads to the serious threat of resistance (Alagesaboopathi and Kalaiselvi, 2012). Ampicillin, tetracycline, oxytetracycline, and florfenicol have the highest rates of antibacterial resistance, whereas kanamycin, gentamycin, and enrofloxacin have the lowest rates of resistance (Caruso, 2016). According to recent research, probiotics have a vital role in the management of bacterial infections. Many questions remain unsolved in the probiotic industry; a rapidly expanding research area suggests that they may be effective in the treatment and prevention of a range of infections (Parthasarathy et al., 2012). A carotenoid product (Lycogen™) derived from the photobacterium *Rhodobacter sphaeroides* WL-APD911 supplemented at 1.0% in feed can improve tilapia (*O. mossambicus* and *O. niloticus*) growth performance via immune function modulation (Chiu and Liu, 2014). A range of microorganisms have been used as probiotics in aquaculture, and these include *Enterococcus*, *Pseudomonas*, *Bacillus*, *Lactobacillus*, *Lactiplantibacillus*, *Lactococcus*, *Clostridium*, *Carnobacterium*, *Shewanella*, *Vibrio*, *Aeromonas*, *Enterobacter*, *Leuconostoc*, and *Saccharomyces* species (Lulijwa et al., 2020). Abdel-Tawwab et al. (2008) reported the benefits of feeding probiotics to tilapia. They observed that Nile tilapia fed spirulina (*Arthrospira platensis*) had increased red blood cell and white blood cell counts as compared to control fish. After clinically infecting fish with *A. hydrophila* and *S. iniae*, the overall mortality was decreased in the fish given these probiotics ($P<0.05$) (Iwashita et al., 2015).

Genetically modified microorganisms (GMMs) have been explored for their ability to produce beneficial compounds, such as enzymes and antimicrobial peptides, which can improve fish health and reduce the need for chemical treatments (Amillano-Cisneros et al., 2025). The term “probiotics” comes from the Greek words “pro” and “bios,” which mean “for life”; hence, probiotics aid in the survival of life. Probiotics are described by the Food and Agriculture Organization (FAO) and the World Health Organization (WHO) as “live bacteria that, when supplied in sufficient quantities, confer health advantages on the host” (Merrifield et al., 2010). Probiotics can be fed to tilapia to alter the composition of the gut bacterial community and keep up and improve host health. Live microbial supplements that are advantageous to their host are known as probiotics (Wang et al., 2023).

Probiotics have been employed in aquaculture to control the fish’s immunological response. Nile tilapia’s innate immunity has been demonstrated to be improved by *Bacillus subtilis*, and the stress brought on by dense stocking has been found to reduce immunosuppression. Fish treated with the substance had higher mean corpuscular hemoglobin and higher lysozyme and phagocytic activity (Telli et al., 2014). To increase fish survival, lactic acid bacteria, and other probiotic microorganisms modify the immunological processes of their hosts. *P. fluorescens*, a probiotic, also decreased the death rate in Nile tilapia exposed to *A. hydrophila* (Ridha and Azad, 2014). Nile tilapia were administered *B. pumilus* as a probiotic for 1 or 2 months and during this time they showed a considerable rise in total leucocyte counts as well as lymphocyte and monocyte populations in the fish’s blood (Aly et al., 2008).

Like all other microbes, probiotics have microbe-associated molecular patterns (MAMPs). MAMPs comprise lipopolysaccharides, microbial nucleic acids, and flagellin. Following recognition and adhesion, a signal transduction channel is started, leading to the release of certain mediators, chemokines, and other activator agents, thereby promoting the immunological response of the host organism (Figure 2) (Ringø et al., 2010). Possible responses include phagocytosis, an elevation in pulmonary bursting activities, a rise in peroxidase and anti-protease activity, and the release of cytokines (Foysal et al., 2020). Iron is a critical mineral for bacteria to flourish, but its deficiency in animal fluids and tissues hinders their growth. As a consequence, the iron-binding siderophores assist bacteria in attaining the iron levels essential for growth (Verschuere et al., 2000). Probiotics improve dissolved oxygen, reduce nitrite toxicity, and induce bioremediation (Figure 1).

Prebiotics are characterized as "a substrate specifically exploited by host bacteria to impart a health advantage" (Hill et al., 2014). These bacteria consume prebiotics as a source of carbon in their metabolism, promoting the growth and repression of both beneficial and harmful bacteria while also creating beneficial metabolites required by the host cell (Figure 2). By promoting bacterial development and activity in the fish's gut, they have positive effects on health. Prebiotics can activate the host's innate immune responses and are metabolized by the gut bacteria (Kocher, 2004), when coupled with probiotics, they are referred to as synbiotics since they influence the probiotic's development.

Many medicinal plants have been successfully used to treat tilapia, either as whole plants, parts of the plants (leaf, root, or seed), or as extracted substances, as feed additives. Alkaloids, terpenoids, lectins, polyphenols, phenols, quinones, and polypeptides are the principal phytoadditives found in herbal remedies. Many studies used plant extracts as feed additives that can enhance fish growth, immunity, and health. Medicinal plants are an important source of bioactive chemicals that have been utilized as immunostimulants and to modulate the immune system, immune cell proliferation, and antioxidant properties in tilapia (Wang et al., 2023).

Vaccines are crucial for preventing infectious diseases in the aquaculture sector, where high population densities put people at higher risk and treatment is a difficult undertaking from a practical, procedural, and financial standpoint. Since vaccines are natural biological components that leave no residue in the product or environment and do not produce disease-resistant organisms, they are generally regarded as safe and reasonably priced preventive measures. There are a fair number of commercially available fish vaccines these days, including live attenuated, inactivated, or heat-killed vaccines, as well as genetically modified vaccines against bacterial and viral illnesses. These vaccines can be monovalent, multivalent, or mixed. The majority of commercially available vaccines used in aquaculture are currently inactivated (Sudhakar et al., 2025).

Vaccines increase immunity and memory in immunized fish. There are several commercially available bacterial vaccines for tilapia. There is a streptococcosis vaccine (AQUAVAC® MSD Animal Health) that is commonly used in tilapia farming (Zeng et al., 2021). Recently, *S. agalactiae* has emerged as the major bacterial pathogen in Nile tilapia farms. A variety of vaccines have been produced that can enhance the immune response to infection, including inactivated vaccines and live attenuated vaccines (Wang et al., 2023). Researchers reported the administration via intraperitoneal injection of attenuated *S. agalactiae* vaccine provided 100% protection in tilapia against bacterial infections (Pridgeon and Klesius, 2013). Attenuated erythromycin-resistant *S. agalactiae* vaccine (Liu et al., 2019), Freund's incomplete vaccines (Li et al., 2016), aluminum hydroxide gel vaccines (He et al., 2014) were used against bacterial diseases in tilapia. Both were potent in control of bacterial diseases in tilapia (Table 2).

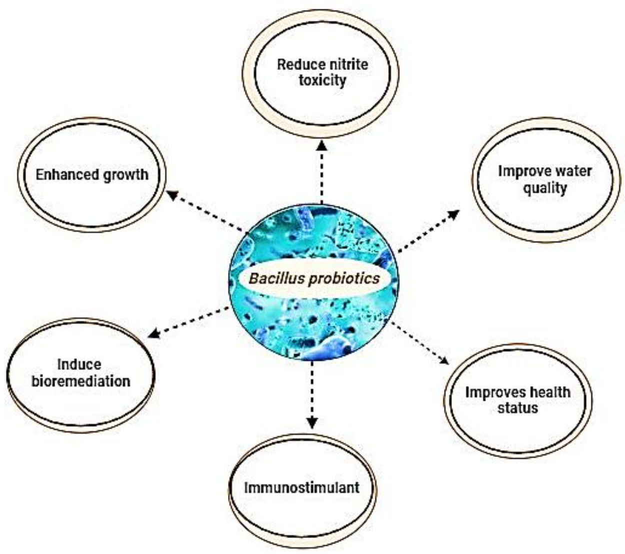

Figure 2. Use of *Bacillus* as a probiotic against pathogenic bacteria in fish

Table 2. Pathogenic bacteria, key characteristics and recent control in Nile tilapia

Pathogenic bacteria	Key characteristics	Control	References
Aeromonas hydrophila	Gram-negative, rod-shaped, motile. Causes ulcers, hemorrhages, and fin rot.	Antibiotic treatments, probiotics, immunization.	Rivas et al. (2023); Hassanin et al. (2024)
Streptococcus iniae	Gram-positive, cocci, causes systemic infections and lesions in muscle.	Vaccination, early detection, and hygiene practices.	Wang et al. (2021)
Edwardsiella ictaluri	Gram-negative, facultative anaerobe, causes septicemia.	Vaccination, environmental control, antibiotics.	Abu-Zahra et al. (2024); Ghani et al. (2024)
Vibrio alginolyticus	Gram-negative, halophilic, associated with skin lesions and fin rot.	Salt baths, antimicrobial treatments, biosecurity.	Abotaleb et al. (2024)
Flavobacterium columnare	Gram-negative, filamentous, causes columnaris disease (skin ulceration).	Immunostimulants, bacteriophage therapy, water quality management.	Zahran and Risha (2013)
Yersinia ruckeri	Gram-negative, motile, associated with red mouth disease in fish.	Antibiotics, vaccination, good water quality management.	Alemayehu et al. (2018)
Pseudomonas fluorescens	Gram-negative, motile, causes gill disease and systemic infections.	Antibiotic treatment, improving water quality, and biosecurity.	Moharam et al. (2024)
Vibrio vulnificus	Gram-negative, halophilic, associated with wound infections.	Saltwater baths, antibiotics, and early detection.	Cai et al. (2024)
Francisella spp.	Gram-negative coccobacillus, causes francisellosis	Live-attenuated or DNA vaccines	Meyer et al. (2025)
Staphylococcus aureus	Gram-positive, causes staphylococcosis	*Boswellia serrata* resin extract (BSRE) supplementation	Montaser et al. (2021)
Lactococcus garvieae	Gram-positive, causes piscine lactococcosis	Adjuvant, inactive whole cell vaccine	Bwalya et al. (2020)

Nanobubble technology is a new wastewater treatment method. This approach entails injecting nano or ultrafine bubbles (200 nm) into water using a specific gas. Unlike macro and microbubbles, these nanobubbles have neutral buoyancy and can float for days in water. The method is particularly successful at dissolving gases into the water column due to the large surface area to volume ratio of the bubbles. The NB-O_3 ozone nanobubble technology helps decrease the intensity of freshwater bacterial pathogens and is relatively healthy for tilapia (Jhunkeaw et al., 2021).

Application of biosecurity and good farm management practices, development and breading of disease-resistant fish strains, feeding fish on well-balanced diets, conducting antibiotic sensitivity testing before administering, ozone treatment of water, and enforcing legislation and policies are the non-therapeutic control measures in aquaculture (Elgendy et al., 2024 b). Furthermore, integrating molecular and immunological diagnostics with artificial intelligence-based technologies significantly enhances the accuracy of pathogen detection. Strategies for controlling risks of disease in aquaculture include good health management and responsible aquaculture practices (including the safe transportation of live aquatic animals), efficient biosecurity governance (at the farm, sectoral, industry, and legislation/policy levels), and efficient prevention technologies (e.g., use of clean seed through specific pathogen-free stocks, vaccination) supported by timely and sensitive diagnostics, surveillance, emergency preparedness, and contingency plans (Wang et al., 2023).

A blend of perfect aquaculture farming operations, strategic use of control agents, and efficient vaccination are vital to enhancing fish health, avoiding disease outbreaks, and lowering the drastic economic effects on aquaculture. Essentially, it also necessitates the implementation of efficient management and biosecurity programs, which include raising farmer awareness of disease management and improper use of antibiotics. Disease outbreaks and disease-related losses in tilapia culture can be controlled by modulating the immune system of fish. It is possible to improve fish immunity to disease by understanding how they react immunologically to pathogens and controlling these responses.

Current innovations and future horizons in aquaculture health management

Aquaculture is rapidly growing into one of the most important sectors in the farming economy, driven by rising demand for nutritious animal protein at a reasonable price, particularly as the world's population grows. However, the proliferation of high-density fish populations poses an issue: the swift dissemination and spread of pathogenic agents between them. Vaccination is an effective and controlled method to provide immunity against viral and bacterial infections.

The perfect vaccine should be easy to administer, safe, affordable, and effective. The development of vaccine formulation and efficacy is aided by the constant publication of new data on fish immunology and vaccine research by the fish vaccination industry. Advancements in technology have boosted our knowledge of fish immunology, resulting in better vaccine administration and the fabrication of novel vaccines (live attenuated, subunit, DNA, and RNA) (Rathor and Swain, 2024).

Currently, the market offers over 50 vaccines for over 30 different fish species. The majority of these vaccines are USDA-approved and produced by culturing target pathogens (Irshath et al., 2022). The optimal vaccine creates a potent defense against a particular pathogen with few adverse effects by combining the most effective adjuvant systems and antigens.

Advances in recombinant DNA technology, which uses a variety of expression systems to target particular pathogen components, are part of modern vaccine technology. Additionally under investigation are mRNA vaccines, which have been shown to boost immunity (Guo and Li, 2021). Oral vaccines, bath immersion, and mucosal vaccines are widely distributed, easy to administer, and can provide optimal administration efficacy (Rathor and Swain, 2024). Live attenuated vaccines, recombinant vaccines, and chitosan-based vaccines have all been shown to improve immersion vaccine effectiveness and long-term immunity (Li et al., 2019).

Oral vaccines are used as an alternative to commercially vaccinating fish in terms of vaccine administration. They have the added benefit of not stressing fish and being simpler for fish farmers to administer (Ma et al., 2019). Individualized nature of vaccine delivery and aqueous environment poses a potential hindrance to the optimal efficacy of the vaccines (Rathor and Swain, 2024).

Oral tolerance is another issue that hinders the efficacy of oral vaccine (Mutoloki et al., 2015). Despite the potential success of such vaccine models, further research on immunological mechanisms is necessary to understand how to develop a vaccine that can effectively produce the intended result without serious side effects, like chronic stress. The development of vaccines that produce long-term immunity should be the main goal of research.

In recent years with an increase in advances in biotechnology, the latest technology, reverse vaccinology has been brought into focus. This latest technology helps develop a vaccine against various pathogenic organisms. This software uses bioinformatics to predict immunogenic sequences and regions, which are expressed as recombinant proteins (Mondal and Thomas, 2022). The software has been used to design vaccines against *Flavobacterium columnare* and *Edwardsiella tarda*, two important intracellular infectious fish pathogens that cause columnaris and edwardsiellosis, respectively (Mahendran et al., 2016). Another recent development in molecular biology is the advancement in designing as well as developing vaccines including marker vaccines, structural vaccinology (SV), immunomics-based vaccines, designer cell lines, and dendritic cells (Mondal and Thomas, 2022).

The most important thing farmers can do to reduce fish losses is to manage fish disease. This has proven to be difficult because several pathogens are responsible for the rise in the mortality rate of fish raised for food (Ali et al., 2019).

Conclusion and future perspectives

Future global food security will be significantly impacted by aquaculture. In the coming years, freshwater aquaculture is expected to grow and intensify, with low-trophic feeding finfish such as tilapia playing a crucial role. This is largely due to their ability to thrive in less-than-ideal water conditions, their general adaptability, high nutritional value, and resilience against diseases.

However, the potential for expansion within the aquaculture industry is being hindered by the emergence and increasing prevalence of various diseases, which will have serious economic consequences. This situation is particularly acute in countries like Pakistan, where most production occurs in open-air clay ponds in rural areas with minimal biosecurity measures. To address these challenges, increased research and support are urgently needed.

The number of bacterial species associated with fish diseases has risen significantly. Our extensive review of bacterial epidemics in tilapia has concluded that the identified bacteria are highly pathogenic and can harm tilapia species worldwide. Current treatment methods are often ineffective due to a lack of knowledge regarding the biology and genetics of most fish bacteria. Therefore, comprehensive studies in this area are essential to facilitate the development of novel antiseptic drugs against bacterial pathogens.

To enhance the resistance of *O. niloticus* to infections, future research should focus on understanding the dynamics of pathogen spread. This includes the development of effective polyvalent vaccines, bacteriophage therapies, live attenuated vaccines, and the exploration of probiotic treatments. Additionally, studying the environmental factors that influence bacterial pathogenicity could provide valuable insights into disease control strategies.

Researchers should also pursue innovative approaches that utilize advanced technologies, such as surface drones for early detection of bacterial diseases, nanosensors, image-based machine learning techniques, and phytochemical drugs as alternatives to antibiotics, along with nanoparticles. Collaboration across the industry, increased funding, and sustainable practices will be crucial for the advancement of tilapia farming.

To facilitate the development of targeted treatments and vaccines, a more profound understanding of disease prevalence, bacterial adhesion routes, disease progression, and pathophysiology is essential. There is an urgent need for research and support to address emerging diseases.

Consent to participate

All people involved in this research paper are well connected with me, and I am available to all these people if anyone seeks further clarification and information.

Conflicts of interest

All authors declare no conflicts of interest.

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