Vaccination Approaches in Aquaculture against Fish-Borne Bacterial Zoonoses

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Abstract

Aquatic zoonotic infections present significant challenges to the global aquaculture and fishing industries. Fish, animals, and human health are badly affected by these infections. With the continuous growth of the global population and expansion of aquaculture trade, the risks of environmental pollution and the transmission of zoonotic diseases originating from fish and aquatic environments are increasing. These zoonoses are primarily caused by viruses, fungi, parasites, and bacteria. Although various therapeutics, including antibiotics, probiotics, edible antibodies, natural antimicrobial products and bacteriophages, are employed for disease management, vaccination remains a vital protective measure in aquaculture. The efficacy of antibiotics and probiotics has diminished over time due to the emergence of resistant strains, highlighting the urgent need for advanced vaccine development through molecular technologies. Vaccination is regarded as the most viable solution for ensuring sustainable aquaculture practices. This chapter discusses the various bacterial families associated with bacterial zoonoses in aquaculture, traditional vaccine types such as live attenuated and killed-inactivated vaccines, and progresses to contemporary approaches, including autogenous vaccines and subunit vaccines. To reduce dependence on antibiotics, vaccination strategies have the potential to minimize environmental contamination and enhance fish health and productivity.

Keywords: Zoonoses, Fish, Bacteria, Vaccine, Antibiotics

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Introduction

Zoonotic diseases are infectious illnesses that spread from animals to humans and are caused by bacteria, viruses, parasites, and fungi. In aquaculture, bacterial pathogens play a significant role in zoonoses. Common bacterial families associated with zoonotic diseases in aquaculture include Hafniaceae, Mycobacteriaceae, Erysipelotrichaceae, Streptococcaceae, Vibrionaceae, Pseudomonadaceae, Aeromonadaceae, and Enterobacteriaceae (Farzadnia & Naeemipour, 2020). Zoonotic diseases are currently recognized as critical in fish farming due to insufficient surveillance and diagnostic efforts (Shamsi, 2019). Proper diagnosis and surveillance could reveal severe consequences (Zorriehzahra & Talebi, 2021). For example, infections caused by Gnathostoma binucleatum Spotted Sleeper Perch have triggered gnathostomiasis outbreaks a fishing community in Mexico (Camacho et al., 2003). Fish and aquatic environments are key reservoirs for zoonotic pathogens capable of spreading to humans through various transmission routes. Raissy (2017) reported that forty-six percent of fish-borne infections are spread orally, while fifteen percent occur through multiple pathways. Additionally, waterborne transmission from infected organisms accounts for 24% of cases, and direct skin contact during fish handling contributes to 19% of infections. Despite the perception that zoonotic diseases in aquaculture are of minor significance, this may be an underestimation due to limited awareness and oversight. For example, contaminated fish are responsible for approximately 0.26M foodborne illnesses annually in the United States (Barrett et al., 2017). The rapid global expansion of the aquaculture industry, coupled with the presence of transmissible bacterial pathogens, underscores the importance of understanding and addressing bacterial zoonoses. This Chapter highlights the risk these diseases pose to human health and emphasizes the need for effective control and prevention strategies. Figure 1 shows the bacterial families associated with fish-borne zoonoses.

1. Mycobacteriaceae

Numerous infective bacteria that impact animals, humans, reptiles, and fish belong to the Mycobacteriaceae family. These bacteria are pleomorphic bacilli, acid-fast, gram-positive, aerobic and non-motile (Delghandi et al., 2020). A widespread disease known as mycobacteriosis affects freshwater, brackish, and marine fish, representing a significant cause of mortality in both farmed and wild populations. One hundred and twenty *Mycobacterium* species have been identified. Several species such as *M. peregrinum*, *M. marinum*, *M. avium*, *M. chelonae*, *M. gordonae* and *M. septicum* have zoonotic potential. These zoonotic species are transmitted to humans and cause severe complications for example necrotic lesions, deep infections in tendons and bone tissue and skin rasping (Hashish et al., 2018).

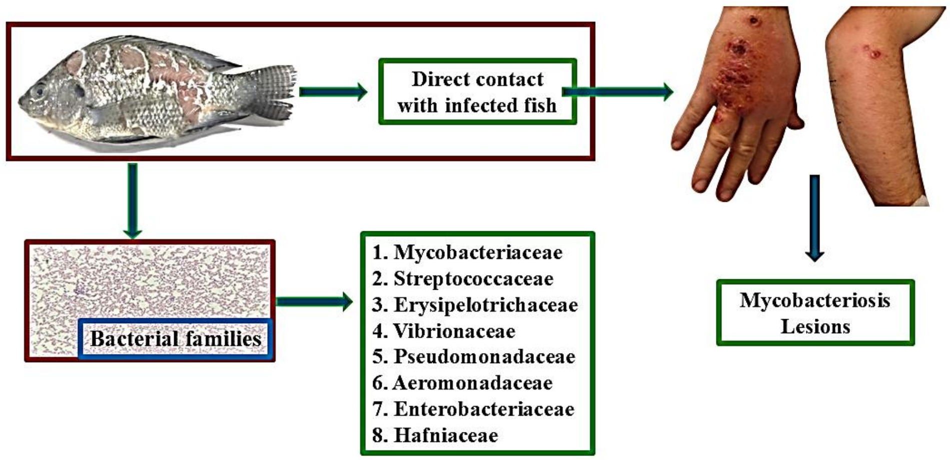

Fig. 1: Classification of bacterial families associated with fish borne bacterial zoonoses.

2. Streptococcaceae

Streptococcus is a gram-positive bacterium that is a major concern of fish aquaculture and causes systemic streptococcosis (Iregui et al., 2016). Fish streptococcosis is mostly caused by the bacteria *S. dysgalactiae, S. agalactiae, S. iniae and S. difficile* (Pradeep et al., 2016). Meningoencephalitis and fatalities in fish species are associated with streptococcosis (Novotny et al., 2004). These microbes are thought to be human pathogens and emerge as zoonotic agents when people encounter infected fish. Indirect contact with contaminated water can spread zoonoses. Management of contaminated live and dead fish can cause endocarditis, cellulite, lymphadenitis, severe systemic infections, suppurating ulcers, septicemia, meningitis, arthritis and, in rare cases, have resulted in human fatalities (Haenen et al., 2013).

3. Erysipelotrichaceae

The Gram-positive bacterium *Erysipelothrix* is associated with zoonotic infections in fish (Boylan, 2011). Among its species, *E. rhusiopathiae* is the most significant, causing disease in both humans and animals. This bacterium primarily targets arterial walls, connective tissues, and skin. While *E. rhusiopathiae* was previously considered a common fish bacterium, its role in causing mortality has been documented in several countries (Pomaranski et al., 2020). In warmer environments, *E. rhusiopathiae* functions as a soil saprophyte and can easily cause erysipeloid infections in fish handlers and sellers (Novotny et al., 2004). Humans can acquire infections through contact with live or dead fish carrying the bacterium. Infections caused by *E. rhusiopathiae* include endocarditis, septicemia, and skin lesions, particularly on the hands. Occupations such as veterinarians and fishermen are at higher risk of *Erysipelothrix* infections (Nielsen et al., 2018).

4. Vibrionaceae

The Vibrionaceae family comprises gram-negative bacteria known as a source of vibriosis in animals and act as potent zoonotic pathogens. Vibriosis is a serious illness in fish that can spread to humans through contact or eating contaminated aquatic products. Aquaculture workers and consumers of seafood are at significant risk of infection from *Vibrio* species (Austin, 2010). Notable zoonotic species include *V. alginolyticus, V. cholerae, V. damselae, V. hollisae, V. metschnikovi, V. parahaemolyticus and V. vulnificus*, all of which can cause infections in humans (Boylan, 2011).

5. Pseudomonadaceae

Pseudomonas is an opportunistic gram-negative bacillus that is a natural component of the fish microbiota but can pose a threat to fish under stressful conditions. It is zoonotic and can cause food poisoning in humans when infected fish are consumed, making it a significant public health concern (Yagoub, 2009; Fernandes et al., 2018; Algammal et al., 2020).

6. Aeromonadaceae

Aeromonas is a gram-negative fish pathogen that causes severe infections and doesn't show any symptoms until the fish's immune system is compromised. *Aeromonas* species are more common in freshwater fish (Boylan, 2011). Among the species with zoonotic potential, *A. hydrophila* is the most common pathogen, followed by *A. dhakensis, A. jandaei, A. sobria, A. salmonidae, A. caviae, and A. veronii* (Musa & Laith, 2014). Edema or swelling at the injection site is one of the disease's clinical manifestations in humans (Boylan, 2011). *Aeromonas* can also cause diarrhea, lung infections, gastroenteritis, sepsis, bacteremia, and urinary tract infections in humans. *Aeromonas's* multi-antibiotic resistance is a sign of a growing general health issue affecting both aquatic species and humans (Odeyemi & Ahmad, 2017).

7. Enterobacteriaceae

The Enterobacteriaceae family is a fish's natural microbiome. This family includes organisms that are associated with human illnesses (Oliveira & Pelli, 2017). *Escherichia coli*, *Klebsiella*, and *Salmonella* are members of this family, which are known to be potential zoonotic pathogens. The most typical way for humans to become infected with these microbes is by commencing wounds, contact with fish, or bites, which induce illness and infection at the bacterial entry site and leads to systemic diseases (Smith, 2011). Conversely, some bacteria in this family can infect humans through food sources; for example, *S. typhimurium* infection have been associated with the consumption and trade of dried fish (Bonyadian et al., 2014).

8. Hafniaceae

Hafniaceae family includes three genera *Edwardsiella, Hafnia* and *Obesumbacterium* in the order Enterobacteriales (Adeolu et al., 2016). Edwardsiella is pathogenic to fish at higher organic concentrations and ambient temperature causing Edwardsiellosis so far produced critical financial problems in the aquaculture industry (Park et al., 2012; Yu et al., 2012; Davies et al., 2018). Five species of Edwardsiella have been identified, i.e., *E. hoshnae, E. ictaturi, E. tarda, E. piscicida* and *E. anguillarum.* All these classes are infective to fish, except for *E. hoshnae* (Kerie et al., 2019).

9. Vaccination against Zoonotic Bacterial fish Diseases

Aquatic foods like fish, shrimp, prawns and lobster are the biggest source of protein for humans. Conversely, the fish trade faces significant financial losses due to zoonotic diseases. Bacteria contribution is 50% and effect all stage of fish growth (Mohamad et al., 2019). Different types of treatment strategies are used for the control of bacterial diseases in fish farming (Figure 2). Research on fish vaccines began in the 1940s when Duff (1942) successfully immunized fish with inactivated *A. salmonicida*. Since the 1980s, there has been significant progress in developing vaccines for fish diseases using methods like those for human and animal vaccines. Fish vaccines are mainly of two types: killed and live vaccines. Live vaccines, made from weakened microorganisms, are more effective as they stimulate stronger immune responses, including both cellular and humoral immunity (Levine & Sztein, 2004). Recent advances, like genome sequencing, better antigen screening, and improved understanding of fish immunity, have supported the development of better vaccines, delivery systems, and adjuvants. These advancements are expected to boost vaccine development, helping make aquaculture more sustainable and improving fish health worldwide (Priya & Kappalli, 2022).

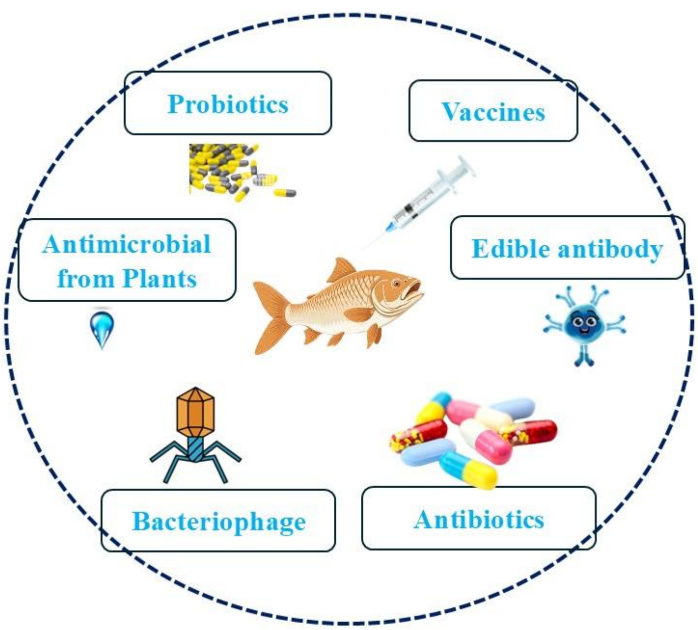

Fig. 2: Approached used for the control of bacterial infections in fish culture.

10. Vaccination types in Aquaculture

The different categories of vaccines used in managing fish diseases and health are depicted in Figure 3.

i. Live Attenuated Vaccines

Attenuated vaccines, also known as live vaccines, are created by weakening pathogens (bacteria or viruses) so they can no longer cause disease but still stimulate a strong immune response (Lin & Smooker, 2015). This is done by growing the pathogen in non-natural host cells or under unfavorable conditions, leading to reduced virulence, or by using genetic engineering to deactivate or remove virulence genes (Klesius & Pridgeon, 2011). An attenuated vaccine was developed by Shoemaker et al. (2011) for columnaris disease against *Flavobacterium columnaris* infecting all freshwater fin fish species in the USA. These vaccines are stored carefully to maintain their effectiveness. Attenuated vaccines stimulate both humoral and cell-mediated immunity, often providing long-lasting or even lifelong protection, and some can induce mucosal immunity, which is crucial for defending against pathogens entering through mucosal surfaces (Mohn et al., 2017). Research is ongoing for bacterial fish pathogens like *Aeromonas*, *Vibrio*, and *Streptococcus*, though few commercial options currently exist (Liu et al., 2018; Irshath et al., 2023). Limitations include the risk of reversion to a virulent form, short shelf life, and potential contamination during production (Pulendran & Ahmed, 2011).

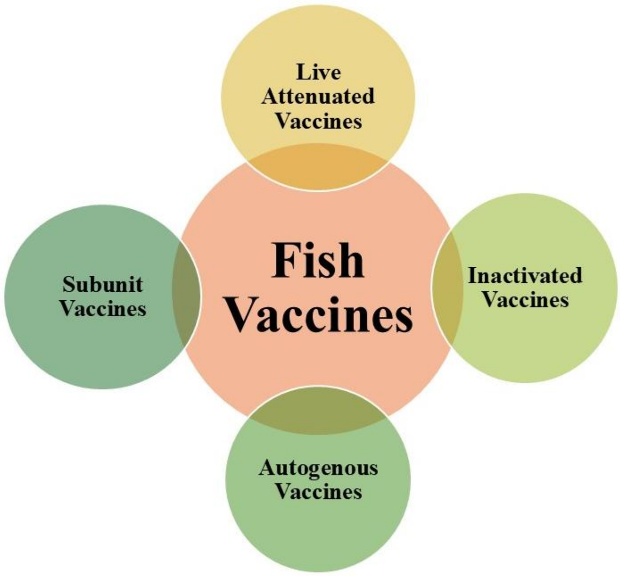

Fig. 3: Types of vaccines for fish.

ii. Inactivated Vaccines

Inactivated vaccines, also known as killed vaccines, are developed by eliminating the pathogenicity of bacteria or viruses through physical or chemical methods, rendering them incapable of causing disease while retaining their ability to elicit an immune response in the host. The target pathogen is cultivated in an appropriate culture medium. To inactivate the pathogen, the bacterial culture is treated with chemicals (such as formalin or beta-propiolactone) or exposed to physical agents such as heat (Tammas et al., 2024). Inactivated microorganisms are then purified and formulated into a vaccine that may be administered to fish. Adjuvants can be used to boost the immunological response (Lin et al., 2022). Inactivated vaccines are widely used to prevent several bacterial fish diseases caused by *A. salmonicida*, *V. anguillarum*, *Lactococcus garviae*, and *Y. ruckeri* (Austin, 2012). An inactivated vaccine developed for furunculosis disease against *A. salmonicida subsp. Salmonicida* infecting salmonids in the USA, Canada, Chile, Europe, and Australia. Inactivated vaccines are considered safe as they do not induce disease in vaccinated fish. Additionally, they offer practical advantages, including greater stability, a longer shelf life, and easier storage compared to live vaccines (Sanders et al., 2014). However, inactivated vaccines generally produce a weaker immune response than live vaccines, often necessitating booster doses. Adjuvants are frequently required to enhance their immunogenicity (Nooraei et al., 2023). Inactivated vaccine technology is well-established and widely used in both human and animal medicine, but incomplete inactivation of pathogens is possible, which could result in residual pathogenicity.

iii. Autogenous Vaccines

Autogenous vaccines are prepared using a pathogen strain isolated directly from the affected animals, which offers several advantages in disease prevention and control. Autogenous vaccines, also known as autovaccines, are a special kind of vaccine created specifically to combat a particular disease outbreak within a specific population or farm. Vaccines are used to treat several common bacterial fish diseases, including, *A. salmonicida*, *V. anguillarum*, *S. iniae*, and *Y. ruckeri* (Adams & Immunology, 2019; Putnam et al., 2024). They reduce antibiotic use and help to manage endemic diseases and adapt quickly to new threats. However, they are costlier, time-intensive to produce, have limited shelf life, and face regulatory challenges (Palic & Aksentijevic, 2022). Instead of limitations, these vaccines are suitable to combat a particular disease outbreak within a specific population or farm.

iv. Subunit Vaccines

A subunit vaccine contains only a portion of the pathogen, such as a protein or polysaccharide, rather than the full organism. These components are sufficient to elicit an immune response but cannot cause disease since they lack the whole pathogen. Subunit vaccines are thought to be safer than whole-cell vaccines because they only use specific parts of the pathogen and cannot replicate or cause illness (Austin, 2012). Subunit vaccines are widely used against several fish-borne bacterial infections including *A. salmonicida*, *V. anguillarum*, *Y. ruckeri*, and *E. ictalurid* (Xu et al., 2022; Zhang et al., 2023). The first step is to determine which component of the pathogen is most likely to elicit an immune response. This could be an outer membrane protein, flagellar protein, or a bacterial toxin. Identifying the correct antigen is critical to the vaccine's effectiveness. After selecting the suitable antigen, the gene encoding it is extracted and introduced into a host organism, such as bacteria, yeast, or mammalian cells. These cells then express the antigen. In some situations, the gene can be synthesized, particularly if the target antigen is small. Once the antigen has been produced in large enough numbers, it is purified to remove any impurities for the vaccine's safety and potency. After this, the antigen is combined with adjuvants and stabilizers to increase vaccine efficacy, storage, and administration. Subunit vaccines consist of a small portion of pathogens (e.g. Proteins or polysaccharides) that do not multiply or cause disease in the host. This characteristic of subunit vaccines makes them safer to employ in fish and humans than live or inactivated whole-cell vaccines (Heidary et al., 2022). Subunit vaccines may provide a shorter immunity duration than whole-cell immunizations. This implies that fish may need to be re-vaccinated more frequently, which could be difficult or expensive in large-scale aquaculture operations (Chen et al., 2023).

Conclusion

The usage of antibiotics doesn't always affect the quality of fish products but is also a source of the development of multidrug resistance in fish pathogens and aquatic environments. Moreover, these resistant bacterial strains can be transferred to humans and animals through the food chain. Treatment of infections due to MDR strains is a global challenge. Inexpensive vaccines are favored for use against fish infections. Long-lasting and sufficient protection cannot be obtained with killed or inactivated vaccines unless adjuvants are added to increase the formulation's potency. Currently, available commercial vaccines may or may not provide the intended level of protection. To educate consumers about the advantages of safer and more affordable vaccines, scientists and researchers must get a deeper comprehension of safety issues. Furthermore, developing several autogenous vaccines and expanding vaccine production and availability can significantly alter the direction of vaccines in the future to increase protection. Future fish vaccines against infectious diseases, such as bacteria and viruses, should be both cost-effective and environmentally friendly.

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