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CHAPTER 12

Fish Diseases in Aquaculture Due to Climate Change: Use Vaccination to Reduce Fish Diseases

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Abstract

The immune system is altered as a result of climate change and other environmental factors getting worse. This results in fresh outbreaks of diseases that are already recognised, an increase in opportunistic pathogens, and a decrease in fish resistance. The surge in aquaculture production is currently facing a concomitant rise in disease outbreaks due to the climate change, posing significant threats to the productivity, financial viability, and long-term sustainability of global aquaculture operations. This includes the enhancement of water quality, implementation of robust biosecurity measures on farms, and the utilization of disease-free sources of fish.

In this context, vaccination emerges as a highly effective, economically viable, and practically feasible solution. This article delves into the crucial realm of fish health management, focusing specifically on the development of vaccines as a key strategy to combat infectious diseases in aquaculture. By providing a comprehensive understanding of the intricacies involved in the development of fish vaccines, the article aims to shed light on the significance of immunization in preventing disease outbreaks and ensuring the overall health of aquatic populations.

The discussion encompasses various aspects, including the scientific and technological foundations of vaccine development, considerations for practical application in aquaculture settings, and economic and environmental benefits associated with widespread vaccine adoption. By addressing the challenges and opportunities in this field, the article aims to contribute valuable insights to the ongoing efforts aimed at bolstering the resilience and sustainability of the global aquaculture industry through the strategic use of vaccination as a disease management tool.

Keywords: Fish, Vaccination, licensed, Development, Constrains

Introduction

Global aquaculture is growing rapidly in the last few decades, producing a wide range of fish species, from carps and cyprinids to highly carnivorous fish like salmonids. The opportunistic infections *Aeromonas sp.* and *Flavobacterium sp.* are also significant in fish farms. When taking into account the 96 subsequent incidence of parasites of farmed fish, meteorological events are also significant. Direct cycle parasites thrive in particular temperatures and oxygen concentrations. This growth, expected to continue, reflects the industry's adaptability in the face of limited resources (Reinertsen and Haaland, 1995). Due to the climate change occurrences of different infections in farmed fish and shellfish (Goniea et al., 2006).

A changing thermal regime will have an impact on various diseases, such as those caused by bacteria (Galbreath et al., 2006), viruses (Larsson and Berglund, 2006), parasites (Levesque et al., 2005), and fungi (Claireaux et al., 1995), but the effects will be mostly unpredictable because of the uncertainty surrounding the temperature-induced fluctuations in the immunological response of the cultured species. Since the majority of fish are poikilothermic (Bond, 1996), the temperature of their surroundings has a significant influence on their physiology. Warmer water causes the fish to have a higher metabolism, which increases the amount of viral replication inside the host.

However, cultivated species are probably more prone to illness in situations when they are under heat stress. In addition, warmer weather may encourage the spread of exotic diseases, whereas cold-weather-specific illnesses—like cold water vibriosis—may become far less common. Rising temperatures would certainly prolong the sea lice season and maybe increase the infective pressure, meaning that more clinical interventions will be needed to address the issue of sea lice in salmon farming (Levesque et al., 2005). Increases in temperature, modifications to precipitation patterns (e.g., decreased snowpack, altered rainfall), adjustments to flow regimes (e.g., decreased summertime in-stream flows), an increase in the frequency of extreme weather events (e.g., droughts and floods), and other abiotic Fisheries are just a few of the effects that climate change is having on the terrestrial environment and inland waters (Claireaux et al., 1995). For instance, climate change may result in the loss of conducive thermal environments that offer protection from pathogens, increasing the occurrence of disease (Chiaramonte et al. 2016). Certain diseases may become more common if the temperature rises above a certain point. The distribution and abundance of fish that fish infections affect can be impacted indirectly by temperature changes in freshwater, or directly by changes in the biological processes of the diseases. Temperature variations can have an organismal impact on the pathogen's pathogenicity, the rate at which it replicates inside fish, the duration of its life stages outside fish, and the pathogen's ability to spread among fish (Marcogliese, 2001).

Since it was first used by Salk & Salk in 1977, the term "vaccinology" has come to refer to the multidisciplinary strategy for disease prevention that uses microorganisms to boost immune responses in both people and populations (Salk & Salk, 1977). Vaccination is now widely used in aquaculture, especially for atlantic salmon (*Salmo salar*). However, issues including low performance, expensive pricing, and vaccine shortages restrict its application to other fish species. Vaccines are seen as essential instruments for averting and managing fish illnesses, tackling apprehensions over antibiotic abuse in aquaculture in the UK and Norway (Van et al., 2015; Phu et al., 2016).

Fish immunisation attempts have been documented since 1942, when Duff worked at the Pacific Biological Station in British Columbia, Canada, to immunise cutthroat trout against *Aeromonas salmonicida* (Duff, 1942). Later research investigated immunological features in a variety of fish species, taking environmental variables and temperature into account (Snieszko, 1974; Snieszko et al., 1949). Aquaculture of Atlantic salmon and rainbow trout had an increase in the 1980s in the USA, Norway, and the UK. But this growth also meant more disease threats, particularly from bacterial infections like *Aeromonas salmonicida*, *Yersinia ruckeri,* and *Vibrio* species. The first fish vaccinations against vibriosis, Enteric Red Mouth disease (ERM), and furunculosis were developed as a result of worries about resistance brought up by overuse of antibiotics. An important development in aquaculture vaccination occurred in 1976 when the ERM vaccine for salmonid fish was approved in the United States (Gudding et al., 2013).

Recombinant vaccine (ISAV) is used in Chile as a preventative measure against the infectious salmon anaemia virus (IPNV). In Asian sea bass, oral DNA vaccinations against pathogens like *Vibrio anguillarum* have shown promise (Vimal et al., 2012).

Oral vaccinations are a substitute for commercial fish vaccinations 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).

Large-scale commercial fish farming greatly depends on the approximately 26 commercially available fish vaccines licensed by the US Department of Agriculture (USDA) that are available worldwide. Numerous investigations, such as Yang et al. (2021), have evaluated the efficacy of immersion vaccinations, so making a valuable contribution to the continuous improvement of disease prevention in aquaculture.

2. Immune System of Fish

The immune system of fish works to recognise and get rid of foreign objects. The innate and adaptive immune systems make up its two subsystems (Smith et al., 2019). Both subsystems work to keep the body safe, but adaptive immunity is a system where the organism creates an immune memory against the pathogen by recombination and genetic mutation. Specifically, it confers immunity by recognising and triggering the right antigen response via memory cell formation and certain receptors, such as immunoglobins, B lymphocytes, and T cells (Rauta et al., 2012). The body's physical and anatomical barriers, such as the mucosa and epithelium, act as a barrier against or chemically react to anything that is foreign or non-self in innate immunity, which is non-specific (Aristizábal, 2013).

There are three parts to the innate immune system: humoral, cellular, and physical (Magnadóttir, 2006). Mucosal pathways, especially those found in the gills, skin, gut, and epidermis, make up the physical barriers (Mutoloki et al., 2015). It is significant to remember that specific chemical constituents of this system are essential to the immune response. Specifically, mucosa and intestinal tract system components called lysozymes cause cell lysis to stop infected viral cells from proliferating (Swain et al., 2022). Inflammation can be triggered by cytokines, like TNF-α and IL-1β, in reaction to Gram-negative bacteria (Swain et al., 2012).

3. Types of Vaccinations for Fish

On the other hand, the presence of seasonal water impoundments could present new prospects for aquaculture due to climate change. elevated dangers of fish disease transmission through vectors and species invasions. Small farmers and impoverished fishing communities that rely on wetlands would be more susceptible to the negative effects of climate change on their economies and food security. Adaptive actions are recommended to mitigate a number of the effects of climate change. Fish vaccination employs a range of strategies, including inactivated or killed vaccines, live vaccines, subunit vaccines, and DNA vaccines, each tailored to address specific challenges in aquatic disease prevention.

3.1. Inactivated/Killed Vaccines

Vaccines rendered inactive or destroyed are typically derived from virulent microbes, neutralized by physical, chemical, or radiation methods while retaining their antigenic properties (Tlaxca et al., 2015). A kill *Yersinia ruckeri* vaccination against enteric red mouth disease administered by immersion was the first commercially licenced vaccine for fish (Gudding et al., 2013). Weak immunogenicity in fish species is a problem for inactivated vaccines, even if they induce shorter-lived or lower immunity than other vaccine types. It is frequently necessary to administer adjuvants or many booster shots in order to induce protective immunity. Immunosuppressive passenger antigens, toxicities associated with adjuvants, decreased immunogenicity from protein denaturation, and systemic reactions to certain adjuvants are among the disadvantages (Pasquale, 2015). Early aquaculture vaccine experiments focused on killed vaccines, with the first commercially approved vaccine for fish being a dead *Yersinia ruckeri* vaccine administered by immersion to combat Enteric Red Mouth disease (Gudding et al., 2013). Vibrio species, primarily *Vibrio anguillarum* and *V. alginolyticus*, are the cause of vibrio infections. vaccines that are inactive Immersion: O1, O2a, and O2b highly pathogenic serotypes of Vibrio are covered by a licenced bacterin (GAVA-3) (Woo, P.T.K. and Buchman, K., 2012). Most commercially available vaccinations seem to target serotypes O1 or O1+O2a (Aqua-Vac Vibrio, MicroVib, Alpha-Marine, and Alpha Dip) (Jones, S.R., 2001). On young Atlantic cod, a formalin-inactivated trivalent vaccine targeting sero-subgroups O2a, O2b, and O2c was tried. All sero-subgroups were effectively protected against by the vaccination (Alvarez-Pellitero, 2008).

Intraperitoneal: Vaccines against biofilm, extracellular product, and whole cell are similarly well-received by goldfish when administered IP. When biofilm were used in conjunction with immune adjuvant *Asparagus racemosus* tuber powders, the survival rate increased considerably at 25 and 50 days following immunisation (Dash et al., 2011).

3.2. Live Vaccines

Modified live vaccines are crafted using viruses or bacteria exhibiting attenuated virulence or low pathogenicity towards the target fish species. Pathogens can be attenuated through various methods, including physical, chemical, serial cell culture passage, culture under unfavourable conditions, and genetic manipulation (Desmettre et al., 1997; Swain et al., 2022). Live vaccines, composed of attenuated microorganisms, offer benefits such as prolonged effective antigen diffusion and stimulation of the immune system's cellular branch. They generally exhibit higher immunogenicity than inactivated counterparts, triggering robust cellular reactions connected to innate and adaptive immunity (Levine and Sztein, 2004). There is just a single vaccine that is marketed commercially and goes by the name Renogen. It is a live vaccination made with lyophilization that includes living microorganisms (Elliott et al., 2014). Safety, persistence, reversion to virulence, and the risk of spreading to non-target animals must be addressed before widespread use of live vaccines. Examples include Renogen against BKD and live viral vaccines against Koi Herpes Virus (KHV) and Hemorrhagic Septicemia Virus (VHSV) (Shoemaker et al., 2009; Gomez-Casado et al., 2011).

3.3. Subunit Vaccines

Escherichia coli strains are employed at the end of the fermentation cycle for the synthesis of antigens in subunit vaccines. Notable examples include *E. coli*- based subunit vaccination against infectious pancreatic necrosis in Atlantic salmon, offering advantages in ease of use and familiarity in molecular biological research. Subunit vaccines work well, despite the fact that they can be challenging to create since the proteins can degenerate quickly. One extremely effective instance is the oral Blueguard ISA vaccination (Dhar et al., 2014). Recombinant subunit vaccines, particularly valuable when growing the disease-causing bacterium is challenging, can be produced in highly characterized states, allowing non-refrigerated transit and storage. Various expression systems, including Saccharomyces cerevisiae, silkworms, cabbageworms, plants, and insect cells, have been explored experimentally for producing recombinant vaccines. Currently, several experimental investigations, including subunit vaccines against Infectious Pancreatic Necrosis (IPN) made in cabbageworms, are underway (Shivappa et al., 2005; Rappuoli et al., 2018). Numerous subunit vaccines influence cytokines, particularly interleukins, to confer immunity upon the recipient (Xi-zhi, et al., 2018). Commercially available subunit vaccines include those against IPN in Norway and the ISA virus in Chile (Dhar et al., 2014).

3.4. DNA Vaccines

DNA vaccines involve introducing a specific genetic component into an animal, allowing continuous production of a specific immune-stimulating pathogen component. Originally based on gene therapy principles, DNA vaccines offer theoretical advantages over traditional immunizations, triggering a unique immune response involving antibodies, T-helper cells, and cytotoxic cells (Kurath, 2008). DNA vaccines have demonstrated success in preventing fish from encountering internal microorganisms like *Mycobacterium marinum*. Notably, DNA vaccines have shown efficacy against Rhabdoviruses and channel catfish herpes virus infection in rainbow trout and atlantic salmon (Nusbaum et al., 2002; Weiner, 2008).

China is now developing DNA vaccines that encode the surface protein of the bacteria into plasmid vectors in order to protect against the strains of *Streptococcus iniae* and *Streptococcus agalactiae* (Liu et al., 2020). The first DNA vaccination against Infectious Haematopoietic Necrosis (IHN) was tested on rainbow trout cells, showcasing the potential of this technique in aquaculture (Kurath, 2008). In an effort to stop a KHV outbreak and lower the virus's transmission rate, DNA vaccines are being researched and developed, and *Arthrospira platensis* is being investigated as a potential substitute (Hu et al., 2020). DNA vaccines are being tested at the moment, one of which involves inserting the VP2 gene into an alginate microsphere along with a DNA vector (Ballesteros et al., 2014).

ICAR-CIBA (Central Institute of Brakishwater Aquaculture) in Chennai has recently produced an indigenous vaccine against viral nervous necrosis (VNN), a disease that affects several fish species. The vaccine was created in 2021. Dr. J.K. Jena, ICAR's Deputy Director General (Fisheries), declared that the recombinant VNN vaccine CIBA-Nodavac-R is now available. The technologies for two fish vaccines developed against two major bacterial diseases, Columnaris caused by *Flavobacterium columnare* and Edwardsillosis caused by *Edwardsiella tarda*, were transferred to Indian Immunological Private Limited

(IIL), Hyderabad today by ICAR-Central Institute of Fisheries Education, Mumbai in 2022. The commercial-scale vaccinations for freshwater fish will be developed by IIL. 2023 for the commercial development of a vaccination against hemorrhagic septicaemia in freshwater fish by the Central Institute of Freshwater Aquaculture (CIFA).

4. Current Licensed Vaccines in fish

Enteric Septicaemia of Catfish (ESC) (Abdelhamed et al., 2018), Bacterial Kidney Disease (BKD)(Elliott et al., 2014), Flavobacteriosis/ Columnaris (Gavriilidou et al., 2020), Furunculosis (Rathore, 2017), Streptococcosis (Munang et al., 2016), Enteric Red Mouth disease, also known as Yersiniosis (Darvishi et al., 2022) these are the licensed commercial vaccines available for bacterial diseases in fish. Koi Herpes Virus (Bergmann, 2020), Infectious Hematopoietic Necrosis Virus (Larragoite, 2016), Red Sea Bream Iridovirus (Thanasaksiri, 2018), Salmonid Alphavirus (Jensen, 2012), Infectious Pancreatic Necrosis Virus (Kanrar, 2018), Infectious Salmon Anaemia (Dhar et al., 2014) these are the licensed commercial vaccines available for viral diseases in fish. To cure a parasite infection, there is just one commercially available vaccination (an Aquatec sea lice vaccine) (Shivam et al., 2021).

5. Constraints in Fish Vaccine Development

Fish vaccination has become an acknowledged, proven, and economical method of reducing infectious disease outbreaks in aquaculture. When put into practice, it might drastically cut down on the need for antibiotics, which would minimise the amount of money lost to illness. Even though the existing vaccinations provide protection for fish with just one dosage until they are harvested, more research is needed to understand the underlying mechanisms of this protection (Sommerset et al., 2005).

The susceptibility of many fish species to stress and negative reactions following vaccination, especially during the larval or fry stages, presents a significant problem in the development of fish vaccines. This sensitivity restricts the range of protection by making it difficult to administer vaccinations at crucial developmental stages. Furthermore, prospects for parental immunisation to protect offspring are limited because to inadequacies in our understanding of fish maternal immunity (Bowser, 1999; Muktar et al., 2016).

The complexity of disease prevention techniques has led to an increase in the use of mixes of various vaccinations in commercial fish vaccination products over the past ten years. Nonetheless, this intricacy poses difficulties in creating safe and efficient commercial goods. The immunological dominance of antigens varies in different mixes, and not all of them generate a protective immune response. Additionally, the fish immune system's limited capability limits how well it can react to specific antigenic chemicals (Busch, 1997).

It is still an unsolved challenge to integrate vaccinations against infectious parasite illnesses and fish fungal infections. Because it frequently requires host populations for culture rather than depending only on cell cultures, cultivating parasites for the creation of potential vaccines is intrinsically complex and costly. The process of creating parasite vaccines becomes more complicated and expensive as a result. Furthermore, the development procedure is made more difficult by the fact that using natural hosts in parasite production creates questions regarding safety paperwork (Muktar et al., 2016; Sommerset et al., 2005).

The bulk of research on fish vaccines has been conducted by pharmaceutical corporations, contributing to a scarcity of scientific publications elucidating their findings (Sommerset et al., 2005). To enhance the development of live fish vaccines, there is a pressing need for robust collaboration between pharmaceutical companies and university research institutions. This collaboration would foster a deeper understanding of the intricacies of fish immune responses, paving the way for more effective and tailored vaccination strategies.

Conclusion

Temperature increases brought on by climate change have the ability to alter pathogen seasonal abundance, timing, and transmission efficiency at the population level. Vaccination is an efficient means of controlling gram-negative bacterial infections, such as those caused by *vibrio sp*., *Aeromonas sp*., and *Yersinia sp*. The evolution of fish vaccination in aquaculture represents a transformative journey, marked by historical milestones and continuous innovation. From the early attempts in the 1940s to the current array of commercially available vaccines, the industry has embraced vaccination as a crucial tool for disease prevention and sustainable aquaculture practices. Ongoing research and collaborations worldwide aim to address challenges, ensuring the efficacy, accessibility, and safety of fish vaccines, thereby supporting the growth and resilience of global aquaculture operations.

As the aquaculture industry continues to evolve, the refinement and adoption of these vaccination methods play a pivotal role in safeguarding fish health and ensuring sustainable practices. While fish vaccination has demonstrated its efficacy in disease prevention, several constraints impede its seamless integration into aquaculture practices. Addressing these challenges requires a multidimensional approach, encompassing research into the fundamental aspects of fish immunity, collaboration between industry and academia, and innovative strategies for tackling diseases currently lacking viable vaccines. As aquaculture continues to expand, overcoming these constraints will be pivotal in ensuring the sustainable and healthy growth of the industry.

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