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Current Execution of Autogenous Vaccine for Health Management in Tilapia (Oreochromis Niloticus) Aquaculture - A Review

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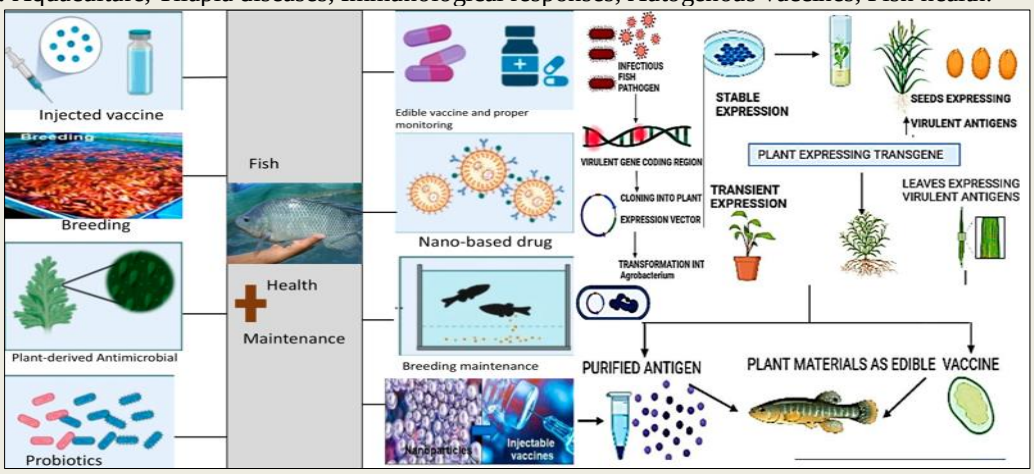
Abstract **Review Article**

Tilapia (*Oreochromis spp.*) Aquaculture has become a major industry in the world's fish production and is an essential source of protein for human consumption. However, the industry confronts various obstacles, including disease outbreaks, which can result in severe economic losses. Fish infections are mostly controlled by drug administration, immunoprophylaxis, ecologically integrated control, etc. Chemical medications and a variety of antibiotics have long been the mainstays in the prevention and treatment of aquatic diseases. However, prolonged usage of chemical inputs harms fish and aquaculture environments in addition to increasing the resistance of pathogenic bacteria. The use of autogenous vaccines has drawn interest recently as a potential method of treating health problems in tilapia agricultural practices. The safest and most efficient methods for preventing infections in aquatic animals and maintaining the sustainability and well-being of aquaculture are the creation and application of autogenous vaccines. This review study delves deeply into the application of autogenous vaccines in tilapia, including their development, mechanisms of action, methods of administration, effectiveness, challenges, and future prospects. The aim of this review is to provide perspectives on the current potential of autogenous vaccines in improving the sustainability and health of tilapia aquaculture by utilizing the most recent research findings and practical applications.

Keywords: Aquaculture, Tilapia diseases, Immunological responses, Autogenous vaccines, Fish health.



Graphical Abstract

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INTRODUCTION

Aquaculture is one of the most dynamic food producing industries, and it plays a major role in nourishing the need for healthy and cheap food for billions of people worldwide (Tigchelaar *et al.*, 2022). Currently, aquatic foods constitute at least 20% of the animal protein consumed by 3.3 billion people per capita, 17% of animal protein worldwide, and 7% of all protein sources (Fisheries, 2007). Tilapia (*Oreochromis spp.*) are one of the most extensively used culture species in freshwater earthen ponds, where most aquaculture production takes place. Tilapia is one of the second most important species of fish group that is cultivated worldwide, producing more than 4.5 million tons of fish annually (Action, 2020).

The Nile tilapia (*Oreochromis niloticus*), is the most widely farmed species of tilapia. It is cultivated in over 120 countries worldwide and ranks third in terms of production volume, with 4.6 million tonnes produced in 2019 (Tang *et al.*, 2021). Unfortunately, a number of bacterial and viral diseases, notably infectious spleen and necrosis virus (ISKNV) infections, (Surachetpong *et al.*, 2020) tilapia lake virus (TiLV) disease, and streptococcosis, (Zhang, 2021) have resulted mass fatalities in tilapia farms. These diseases have negatively impacted the global tilapia industry, particularly over the last decade (Tang *et al.*, 2021). The negative effects of these infectious disease on the tilapia cultivation are still growing despite the fact that several strategies, including the use of antibiotics and other treatments, improved farm management and biosecurity procedures, and restricting animal movements, have been employed to suppress outbreaks of these diseases, and identifying and eradicating infected fish populations (Peeler and Ernst, 2019). Enhancing tilapia health by vaccination modulation is viewed as a compelling substitute to prevent disease outbreaks and lessen the economic costs incurred by tilapia farmers due to diseases.

Potential drawbacks of traditional techniques, such as the use of commercial vaccines and medicines, include the emergence of antimicrobial resistance and insufficient defense against infections that are developing. Autogenous vaccines are a viable substitute in this regard, since they offer specialized remedies tailored to certain pathogenic problems observed in tilapia farming.

Overview of Tilapia Diseases

First, it was believed that tilapia could readily adapt to a variety of rearing habitats, even those with unfavorable environmental circumstances, and were generally resistant to diseases. However, viral and bacterial infections have lately emerged as a serious danger to the tilapia farming sector (Wangkahart *et al.*, 2022). Streptococcosis is a bacterial infection that is most commonly observed in tilapia aquaculture and is mostly found in temperate and tropical climates. During rather warm seasons, especially summers, the mortality rate may increase to 50–70%. Exophthalmos, meningitis, and aberrant behavior are the typical clinical manifestations of streptococcal infections in tilapia (Zhang, 2021). Skin damage, gill necrosis, and fin erosion are signs of exterior lesions that are often the only pathological alterations linked to this illness (Wahli and Madsen, 2018).

It has been reported earlier that some species of *Francisella* can kill farmed finfish (Sridhar *et al.*, 2012). The majority of the available data to date concerns tilapia illness brought on by an infection with F. noatunensis subsp. orientalis, which results in granulomatous inflammatory responses. The species may have significant mortality rates, and live fish migrations are probably a common way for the disease to spread (Birkbeck *et al.*, 2011). Moreover, a variety of fish species, including Nile tilapia, are frequently afflicted by aeromonad-related infections in tilapia farming. In the most affected tilapia farms, the most common clinical symptoms are hemorrhages, sluggish swimming, pop-eye, and skin reddening (Rodrigues *et al.*, 2019). Apart from bacterial infections, substantial mortality rates and detrimental effects on the worldwide tilapia sector are caused by viral illnesses such as TiLV (Behera *et al.*, 2018), ISKNV (Girisha *et al.*, 2021), and Tilapia parvovirus (TiPV) (Yamkasem *et al.*, 2021). TiLV, also known as Tilapia tilapinevirus, has been widely investigated for the past 5 years. It has already been recorded in sixteen countries and across 4 continents and harms both indigenous and cultured tilapia (Jansen *et al.*, 2019).

When fry and juveniles are infected with TiLV within one month after being transferred to grow-out ponds, the condition known as "tilapia 1-month mortality syndrome" can result in up to 90% umulative mortality (Surachetpong *et al.*, 2017). Furthermore, substantial rates of TiLV-associated mortality in several tilapia species have been documented in a number of investigations (Waiyamitra *et al.*, 2021). TiPV, an newly discovered virus, has been identified and extracted from mature tilapia (Liu *et al.*, 2020). Later, concurrent TiLV and TiPV infections were discovered when studying the disease in cultured red hybrid tilapia (Yamkasem *et al.*, 2021). Moreover, there are several accounts of numerous infections in farmed tilapia resulting in serious pathology (Abdel-Latif *et al.*, 2020). Even while these developing diseases have been the subject of recent, substantial study, no practical solutions, such as the creation of effective vaccinations, have been created to control them (Wangkaghart *et al.*, 2021). As a result, these infections are still wreaking havoc on tilapia cultures across the world, posing a threat to food security due to loss of productivity and causing socioeconomic difficulties (Wangkahart *et al.*, 2022).

Due to the overuse of antibiotics in agriculture and aquaculture, concerns have been raised about potential health impacts on humans and animals, possible

harm to the environment and ecology from products containing antimicrobial residues, and the emergence of antimicrobial resistance (AMR) in bacteria. The 68th World Health Assembly in 2015 resulted in the creation of the Global Plan of Action (GAP) on AMR. A National Action Plan on AMR has been prepared and executed by World Health Organization members using a "One Health" concept. Members present at the 39th Conference of the Food and Agriculture Organization (FAO) and the 83rd General Assembly of the World Organization for Animal Health (WOAH) pledged to support the GAP (Talaat *et al.*, 2022). In tilapia aquaculture, vaccinations and antibiotics are two options for managing new disease issues. Since infectious disease issues have grown as a result of the industry's explosive growth, vaccination usage in the tilapia industry has surged recently. Drug-resistant bacteria would be less likely to emerge if vaccinations were administered properly, which would also improve treatment outcomes (Schar *et al.*, 2020). Effective vaccinations and quick detection of pathogens are essential to stop and manage disease outbreaks in the future, as there are currently no particular therapies available for viral infections in tilapia farming.

Immune System in Tilapia

Tilapia are protected from invasive infections by a strong immune system that consists of both innate and adaptive immune responses (Riera Romo *et al.*, 2016). The innate immune response triggers the adaptive immune response, which reacts to certain infections and creates an immunological memory that can react to a re-exposure to the pathogen later on (Smith *et al.*, 2019). Figure 1 shows a basic overview of tilapia's immunological response to infection.

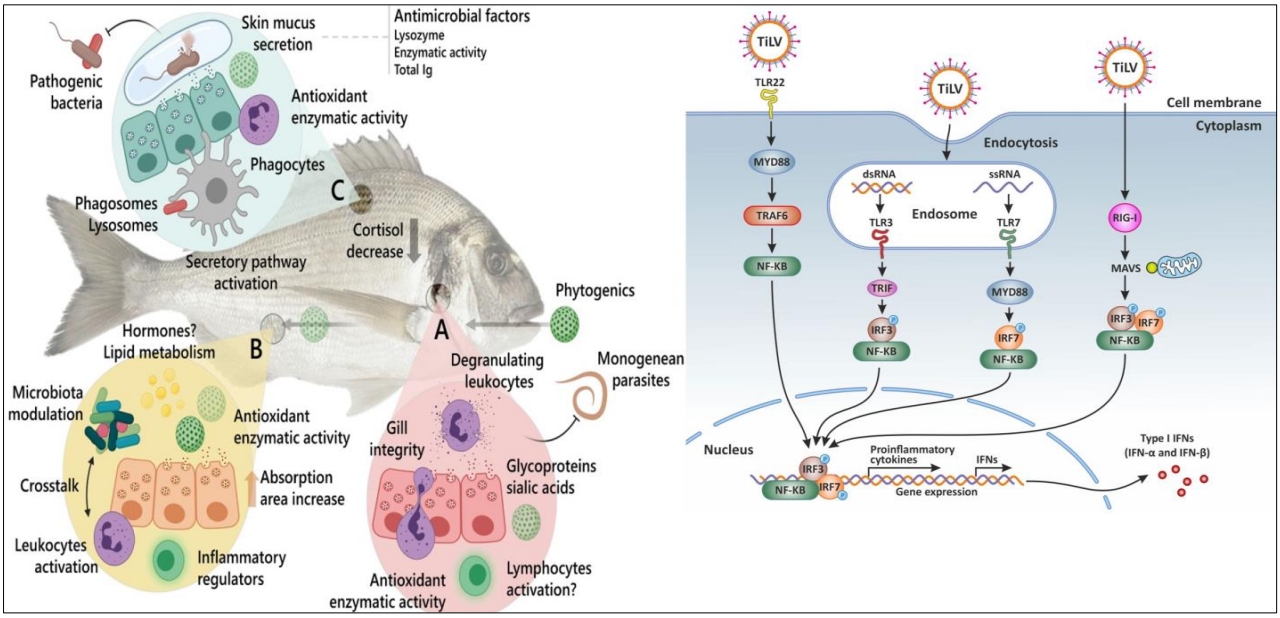

Figure 1: A simple overview of tilapia immune system against bacterial pathogens in improving health and aquaculture production

The innate immunological responses exhibited by tilapia consist of several cellular and humoral components (Van Doan *et al.*, 2019), as well as physical barriers that includes the fish's skin, scales, gastrointestinal tract epithelial layers, and gills help keep pathogens out of the body. Along with serving as a physical barrier to keep infections out, the mucus coating these surfaces also includes lectins, lysozymes, complement proteins, and antimicrobial peptides (AMPs), which are chemicals that may neutralize and kill bacteria (Gomez *et al.*, 2013). If the pathogen is able to penetrate the host's physical defenses and enter the body, cellular and humoral components of the innate immune system respond to try and stop the infection from spreading (Wangkahart *et al.*, 2019). The humoral response employs a wide variety of antimicrobial substances (such as AMPs, lysozyme, complement proteins, and acute phase proteins) to either eliminate the pathogen directly or to encourage inflammation and phagocytosis by the cellular components of the innate immune response (Rakers *et al.*, 2013).

The innate immune response in tilapia is composed of granulocytes, or neutrophils and eosinophilic granule cells, and monocytes/macropages. The cellular response is triggered by pattern recognition receptors (PRRs) on these cells binding to either danger-associated molecular patterns (DAMPs) on proteins or other molecules released from stressed or injured cells, or pathogen-associated molecular patterns (PAMPs) on a variety of microbial pathogens, including viruses, bacteria, fungi, and parasites (Smith *et al.*, 2019). If a pathogen persists in the host, the host's adaptive immune system is activated. Comparable to other teleosts, tilapia possess both humoral and cell-mediated immune responses (Uribe *et al.*, 2011), with B and T lymphocytes cells being in charge of supplying cellular immunity.

Dendritic cells, monocyte/macrophages, B cells, and other antigen-presenting cells (APCs) of the innate response deliver processed phagocytosed materials to T cells in a process known as antigen presentation, which links the innate and adaptive immune responses. Tilapia have been shown to possess genes linked to pathogen identification, antigen presentation, and adaptive response activation using transcriptome analysis (Zhu *et al.*, 2018). An essential immune response against intracellular pathogens (viruses and bacteria) or tumor cells is provided by T cells, often known as cytotoxic T lymphocytes or CTLs. T helper cells, also known as CD4+ T cells, are important for the initiation and control of adaptive immune responses (Secombes and Belmonte, 2016).

B cells, via producing high-affinity immunoglobulins (Ig) specific for their target antigen, are the carriers of the humoral adaptive immune response. IgA, IgT, and IgD are three main types of Ig found in teleosts; tilapia have been shown to express all three of these classes of Ig (Velázquez *et al.*, 2018). Major immunoglobulin M (IgM) is present in all immunological organs and is detected in serum and the tilapia's systemic response. The mucosal-associated lymphoid tissues (MALTs), which are linked to the skin (skin-associated lymphoid tissue [SALT]), gut (gut-associated lymphoid tissue [GALT]), gills (gill-associated lymphoid tissues [GIALT]), and nares (nasopharynx-associated lymphoid tissue [NALT]), are crucial in preventing pathogen invasion into the fish during the early stages of infection (Rombout *et al.*, 2014). Although the exact role of MALTs in tilapia immunity is still unknown, it has been demonstrated that vaccinating tilapia's mucosa with an immersion-delivered nanoparticle vaccine against F. columnar causes an increase in IgT, IgM, TNF α, IL1-β, and MHC-1 in the fish's gills (the mucosal response) and blood (the systemic response) (Kitiyodom *et al.*, 2021).

Since the vaccines included in this study are often administered intraperitoneally to fish, we need to learn more about how they affect the GALT and other MALT responses. Knowing how these vaccinations affect various aspects of the tilapia's immune system might help with their use against particular pathogen types, such as bacteria, viruses, or parasites. The effectiveness of autogenous vaccines on fish immune responses has been documented in a number of studies fish (Ramírez-Paredes *et al.*, 2019; Shahin *et al.*, 2019; Mai *et al.*, 2021). But these reactions rely on the kind, dosage, and mode of administration (route and duration) of the vaccination.

Development of Autogenous Vaccines

Autogenous vaccines, commonly referred to as autogenous or autologous vaccines, are tailored vaccinations made from pathogens that are directly isolated from the afflicted farm(s), and then administered under a limited or minor use authorization (Arsenakis *et al.*, 2018). These vaccinations are specially designed to target specific disease pathogens that are present in a certain farm or animal population. Aquaculture commonly uses auto-vaccines, which have been shown to be effective against a typical Aeromonas infection(Gudmundsdottir *et al.*, 1997), novel biotypes of Yersinia ruckeri infections in salmonids (Barnes *et al.*, 2016), Streptococcal pathogens in barramundi and stingrays (Kawasaki *et al.*, 2018), and autogenous vaccines against the intracellular pathogen *Francisella noatuensis* in tilapia (Ramírez-Paredes *et al.*, 2019).

Autogenous vaccines have a quicker development route than approved commercial vaccines, but they also work better against local serotypes of changeable diseases and can be produced or reformulated more quickly. Besides, it might not be possible to produce commercial generic vaccinations that are effective against diseases with quickly developing, highly variable antigens without the need for re-formulation (Ramírez-Paredes *et al.*, 2019). The creation of novel serotypes persists even after the introduction of multi-serotype vaccinations in humans, but it is not as concerning as the evolution of antibiotic resistance (Kennedy and Read, 2018).

Notably, it is clear that pathogen evolution in freshwater environments occurs more quickly than in both terrestrial and marine areas (Johnson and Paull, 2011). Therefore, in the absence of an autogenous vaccine regulatory system, disease outbreaks in vaccinated populations (vaccine escapes) resulting from new serotypes are inevitable and their integration into an approved commercial formulation may take years (Nikoskelainen *et al.*, 2007). Moreover, the production of cross-serotype approved vaccines by antigen mixing may decrease effectiveness due to the reduction of protection against the attacking strain caused by antigenic competition. Therefore, this issue is solved with autogenous vaccinations that can be more precisely targeted for each crop.

Moreover, the main epidemiological importance of autogenous vaccines' high specific effectiveness and quick deployment in the face of danger is that they may stop or limit the spread of pathogen serotypes that are developing locally to a larger region. Auto-vaccines' superior efficacy in compared to fully licensed alternatives is largely due to their formulation, which is based on evidence. For accurate field and laboratory diagnosis and the collection of a suitable range of samples, the necessary information must be acquired. Only then one can be confident that the detected microorganism is the true cause of the sickness that is manifesting. During field sampling, it is quite simple to culture and identify the incorrect microorganism (Kawasaki *et al.*, 2018). Histopathology, microbiology, and occasionally molecular biology are among the several laboratory diagnostic modalities needed to support and integrate the field diagnosis. The

interaction of the pathogen, host, and environment results in any disease. In order to determine the co-contributory risk factors and provide suitable mitigations, a qualified aquatic field veterinarian is essential.

Autogenous vaccines require the right antigens combined with an adjuvant suitable for the species and farming conditions, after an accurate causal diagnosis suggesting that immunization would be a helpful prophylactic measure. Pathogen typing has become significantly less expensive and more accurate because of recent advancements in genomics. The formalin-killed vaccines for gram-positive and gram-negative bacteria, respectively, provide serotype-specific protection by the quick detection of critical antigenic variations in the capsular and lipopolysaccharide O-antigens (Gulla *et al.*, 2018). One major breakthrough in adjuvant technology during the 1990s was the routine formulation of vaccines as water-in-oil emulsions. This technique not only significantly increased the potency of the vaccine but also extended its duration of immunity to the entire farm lifecycle, from nursery to harvest (approximately 4 years for salmon in water ranging from 8 to 17°C) (Lillehaug, 2014). For tropical and sub-tropical farming conditions and cycles (6–12 months, 20–34°C), adjuvants may need to be optimized. On the other hand, via adjusting emulsion droplet size and oil biodegradability, it is possible to precisely tailor antigen delivery and particular antibody response for the circumstances. Off-the-shelf solutions are accessible with verified safety profiles (Jansen *et al.*, 2005; Schijns *et al.*, 2014).

These are some common methods used for the development of autogenous vaccines: By following these steps, veterinarians and researchers can develop autogenous vaccines tailored to address specific infectious diseases in a particular group of animals, helping to improve overall health and productivity. These vaccines are specifically designed to address specific infectious agents present within a given farm or group of animals. The development of more effective and tailored autogenous vaccines has been made possible by innovations in molecular biology and vaccination delivery technologies.

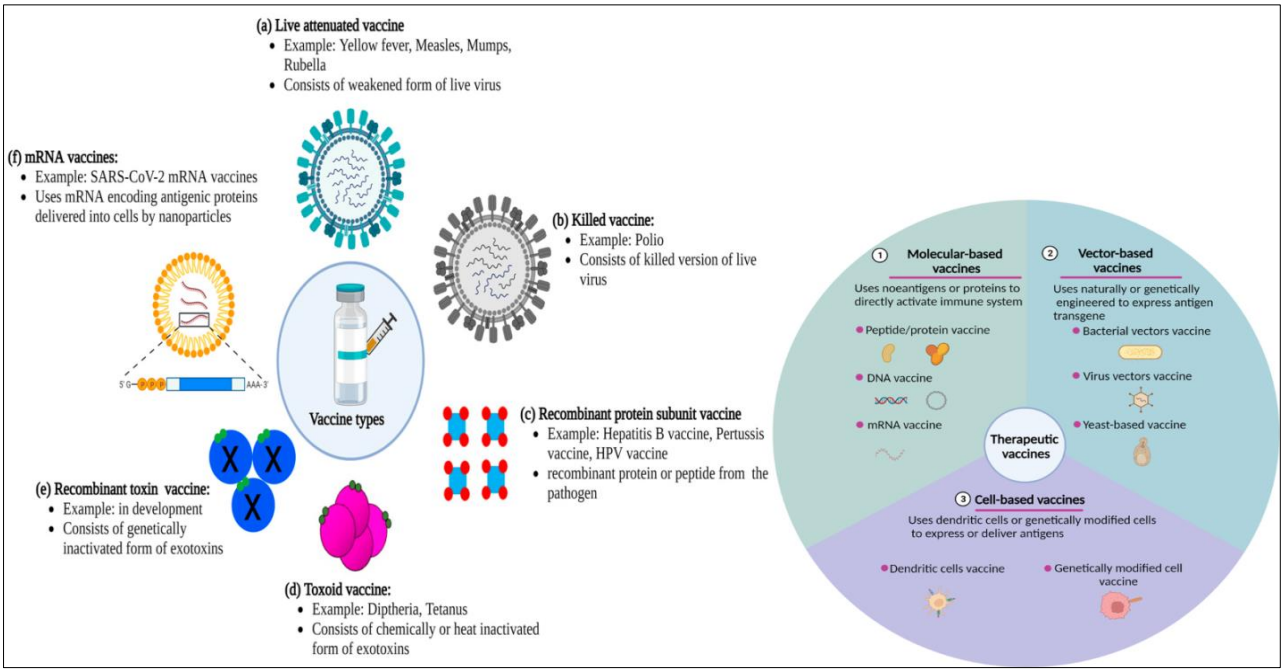

Figure 2: Different steps are involved in the production of autogenous for health management in tilapia aquaculture

Autogenous Vaccine Delivery Methods

An effective vaccine route is essential for the efficient execution of the vaccination process. It symbolizes the process by which a vaccination interacts with the immune system (Ji *et al.*, 2015). The vaccination's safety and efficacy are closely related to how it is administered. The five most common methods of administering fish vaccinations are via immersion, intraperitoneal injection, intramuscular injection, oral, and anal routes. Furthermore, the method of delivery is contingent upon the vaccine type, fish species, size, dosage of introduced immunogen, and adjuvant utilized in vaccine formulation. Some vaccines require a booster shot for optimal protection; hence, the same vaccination may be administered in two different ways, such as an oral or injectable primer and a submersion second shot (Villumsen *et al.*, 2014).

Oral Vaccination

The oral vaccination method is one of the approaches to immunize fish, where the vaccine is mixed into the feed before the fish are fed it. Oral immunization is not a cost-effective procedure, similar to the immersion method, especially for bigger fish. An oral vaccination has lower effectiveness as compared to injection and immersion procedures. Due to the

gastrointestinal tract's destruction, degradation, and absorption of antigens as well as the fish's limited rate of antigen transfer from the intestinal lumen to the immune reactive cells, (Brudeseth *et al.*, 2013) reported a lower intensity and somewhat shorter duration of defense.

Antigens require specific consideration in order to be included in the feed. Vaccines must be top-dressed on the feed to stop the antigen from draining out of the pellet. According to (Plant and LaPatra, 2011), antigen delivery in fish feed has several advantages, including minimal stress, safe administration at all phases to fish of all sizes, simplicity, and cost effectiveness. Different techniques of micro-encapsulation are investigated and assessed for sensitive antigens. In order to strengthen immunity against specific chronic endemic illnesses, oral vaccinations can also be given as a booster shot after an initial immunization. This immunity is mostly attributed to humoral immune responses rather than cellular and innate immunological responses (Newaj-Fyzul and Austin, 2015).

Immersion Vaccination

Fish may be immunized for infection protection using this kind of immunization, which is both easy and effective. According to (Dadar *et al.*, 2017), live suspensions of attenuated bacteria or vector vaccines, or live bacterial vaccines, are used as immersion type immunization vaccines. The commercially marketed immersion type of vaccinations consists of both live and formalin-inactivated microorganisms. After briefly immersing themselves in a diluted vaccination solution, fish are released into the culture unit, which is usually ponds or net cages.

Dip vaccination is swift because the fish are immersed in water containing a relatively high dosage of vaccine antigen(s) for one or several minutes, whereas bath vaccination involves the fish receiving a more diluted vaccine antigen preparation over a longer period of time. Fish can be booster vaccinated by dip or wash to strengthen their immunity (Bøgwald and Dalmo, 2019). Through the gills, their skin, or their food, immersed fish come into close touch with the antigen. Vaccinating fish in large quantities using immersion is a less stressful, labor-intensive, and risk-free method that works for fish of all sizes. The long period of immunity, limited degree of protection, and high dose necessary for vaccination are the main drawbacks. (Huising *et al.*, 2003) employed a hyperosmotic atmosphere to boost the effectiveness of the immersion vaccination. When positively charged chitosan with mucoadhesive qualities was coated on inactivated flavobacterium antigens, increased adherence and absorption of the antigens were observed (Bøgwald and Dalmo, 2019).

Injection Vaccination

In fish, injectable vaccination is the most widely used technique of vaccine administration due to its great efficacy in stimulating humoral and cellular responses. But small fish cannot use this procedure since it needs a special injection equipment, causes a lot of handling stress, and increases the risk of fungal infections after immunization (Thim *et al.*, 2014). Before being injected, the fish must be fasted and given anesthesia for their protection. Although a number of immunization devices have been created, human intervention is still required to assess the health of the fish both before and after injection. Additionally, the needle length selection needs to be done with extreme caution in order to coincide with the size of the fish.

A single strain of a single antigen may be included in a monovalent injected vaccination, or it may be multivalent and contain a variety of bacterins, killed virus, or viral proteins in addition to bacterins. While intramuscular (IM) injections are the most effective method for administering autogenous vaccines, intraperitoneal (IP) vaccinations against the VHS and IHN viruses are very new and should be delivered by this route (Corbeil *et al.*, 2000). In his comparative investigation against *Vibrio anguillarum*, he used injection, immersion, and oral vaccine delivery. He found that all three vaccination types provided equivalent protection and that protection associated favorably with serum antibody levels following boosting, but not before to it. Although injection makes it possible to employ lower, precisely calculated antigen concentrations, the process necessitates more fish handling and the use of anesthesia, which puts the fish under stress and increases their risk of injury in addition to being expensive for the producer (Rivas-Aravena *et al.*, 2013).

Efficacy of Autogenous Vaccines

Autogenous vaccinations have been shown in several trials to be effective in managing disease outbreaks and lowering death rates in tilapia populations. Following immunization, field tests and experimental investigations have demonstrated notable improvements in immune response and disease resistance. Many nations have utilized commercially approved and registered vaccinations for farmed fish. Nevertheless, there is currently a dearth of systematic research on the effectiveness of these vaccinations against the variety of regional strains seen in the field.

However, because of the variations between the commercial vaccination and local strains, several studies showed that the protection provided by these vaccines were insufficient when used in the field. These include *Streptococcus iniae* serotype I and *S. iniae* serotype II in a rainbow trout farm in Israel (Bachrach *et al.*, 2001) and Red Sea Bream Iridovirus (RSIV) vs. Infectious Spleen and Kidney Necrosis Virus (ISKNV) in an Asian seabass farm in Vietnam (Dong *et al.*, 2017).

Serological diversity has in fact also led to vaccine escape outbreaks of Streptococcosis caused by *S. iniae* in Australia, where fish received commercial

autogenous vaccines. This underscores the significance of including the appropriate antigens and the crucial role polysaccharide antigens play in vaccine protection (Rudenko *et al*., 2020). In both Gram-positive and Gram-negative bacteria, where capsular polysaccharide and LPS O-antigen are the protective components in many killed bacterins, such as *Listonella anguillarum* (Sadovskaya *et al*., 1998), *Vibrio ordalii* (Velji *et al*., 1992) and *S. agalactiae* (Chen *et al*., 2012), the significance of polysaccharide antigens to the protective efficacy of fish vaccines is critical.

Mutations and recombinations in the intricate machinery of LPS O-antigen and capsular polysaccharide production have the potential to result in a rather high level of serologically significant variation (Rudenko *et al*., 2020). In scientific fish vaccination studies, serological diversity is seldom taken into account (with a few noteworthy exceptions), as the vaccine strain is used for the vast majority of challenges. Low cross-serotype protection has often been shown in laboratory trials utilizing multiserotype models (Jiménez *et al*., 2019). Auto-vaccines made from local strains should, in this sense, have a significant edge commercially licensed vaccine.

Table 1: Autogenous/Bacterin vaccines experimentally tested in various species of Tilapia.

Pathogen	Type of vaccine	Vaccine delivery	Vaccine efficiency	References
Aeromonas hydrophila	Formalin killed bacteria with ascogen feeding	Intramuscular (IM) injection/Direct immersion (DI)	Moderate to high protection in IM injected fish; whereas low to moderate protection in DI vaccinated fish	(Ramadan *et al*., 1994) 1994
Streptococcus agalacitae	Formalin killed bacteria	Intraperitoneal (IP)injection/ bath immersion	High protective ability in vaccinated fish (>30g) following challenge, reduction in fish protective ability in fish through immersion	(Evans *et al*., 2004) 2004
Aeromonas hydrophila	Formalin killed bacteria ARS-98-60 vaccine	Intraperitoneal (IP)injection	100% protection in Nile tilapia vaccinated with the mutant strain following challenge with the parental strain; increase agglutination titers	(Pridgeon and Klesius, 2011) 2011
Streptococcus iniae and *Vibrio vulnificus*	Bivalent Formalin killed cells vaccine	Intraperitoneal (IP)injection	Relative percent survival values ranged from 79 to 89% for *V. vulnificus* and 69 to 100% for *S. iniae* following challenge of bivalent vaccinated fish.	(Shoemaker *et al*., 2012) 2012
Streptococcus agalacitae	Combined formalin killed cell (FKC) vaccine	Intraperitoneal (IP)injection	Relative percentage survival (RPS) of ≥86 % in vaccinated fish; immunize the vaccinated tilapia against infections of homologous isolates	(Jantrakjorn, 2016) 2016
Lactococcus garvieae	whole-cell inactivated vaccine (bacterin)/ oil-adjuvanted bacterin	Intraperitoneal (IP)injection/ bath immersion	Relative percentage survival value of 81.7% in vaccinated fish/increased the immunogenicity, greater agglutination titres	(Fukushima *et al*., 2017) 2017
Lactococcus garvieae	oil-adjuvanted, inactivated whole cell autovaccine	Intraperitoneal (IP)injection	significantly high amount ($p<0.001$) of anti-*L. garvieae* specific antibodies; reduced clinical signs and lack of pathology.	(Bwalya *et al*., 2020) 2020
Streptococcus iniae & Aeromonas hydrophila	feed-based bivalent vaccine	Oral administration/ Intraperitoneal (IP)injection	Relative percentage survival value of 77.78 ± 3.85% in vaccinated fish/ increased the immunogenicity.	(Monir *et al*., 2021) 2021
Francisella orientalis	inactivated whole-cell vaccine	Immersion administration/ Intraperitoneal (IP)injection	Relative percentage survival value of 63% in vaccinated fish/ reduced the mortality rate in Nile tilapia against francisellosis.	(Oliveira *et al*., 2022) 2022
Streptococcus agalactiae	Heat-killed cell vaccine with Ozone	Direct Immersion/Oral administration	Relative percentage survival value of 50% in vaccinated fish	(Vinh *et al*., 2023) 2023

Pathogen	Type of vaccine	Vaccine delivery	Vaccine efficiency	References
	nanobubble pre-treatment		/Alternative of expensive injection-based vaccination	
Aeromonas veronii	formalin-killed vaccine (FKV), with chitosan polymer-based nanovaccine (CS-NV)	Immersion vaccination	Relative percentage survival value of % / Increase IgM antibody and bactericidal activity against A. veronii in vaccinated fish	(Sukkarun *et al.*, 2024) 2024

Challenges and Limitations

In actual implementation, autogenous vaccines encounter several obstacles and limits, notwithstanding their potential advantages. These include the necessity for specific knowledge in vaccine development, quality control standards, and regulatory requirements. Additionally, developing effective autogenous vaccines for broad usage is hampered by the diversity of antigens and the heterogeneity of pathogen strains. Moreover, there is ongoing discussion on the relative cost-effectiveness of autogenous vaccines vs commercial alternatives, especially in small-scale tilapia farming operations. The present state of aquatic disease prevention and control must give way to a more proactive, evidence-based future, requiring the unmistakable improvements in knowledge, infrastructure, and bureaucracy. For reform to be successful, farmer confidence and trust must be increased. In each location, the function of the veterinarian, aquatic health specialist, and service extension worker will be crucial in this regard.

In order to be honest and share outbreak metadata without fear of damaging effects on their company or reputation, farmers need to use safe and reliable systems for data collection and storage. When knowledge is provided to stakeholders in the form of self-implemented techniques, rather than through top-down approaches, trust among farmers is more readily established. This is known as a bottom-up self-help paradigm (Jiménez *et al.*, 2019). For effective illness care and diagnosis, equitable access to qualified personnel for sample collection using established methods is essential. Finding early outbreak reports and accurate field/laboratory diagnosis will continue to be challenging, and this will make achieving high auto-vaccination success rates challenging. There will still be a chance that vaccinations will be developed against opportunistic pathogens—organisms that prey on animals weakened by malnourishment or unfavorable environmental conditions—rather than against the agents that cause the disease to manifest (Derome *et al.*, 2016). Standardized and high-resolution pathogen identification and typing are required for evidence-based therapies. It should be possible to establish a documented process from sample collection to a locally owned biobank of pure bacterial isolates. This process should include regular antimicrobial sensitivity testing (AST) conducted by local, regional, or national laboratories in accordance with international standards. For farmers to decide on the appropriate course of action for biosecurity precautions, feed and water management, guided antibiotic usage, or emergency harvesting during an epidemic, this knowledge is essential.

Typing at high resolution is easier to handle. Sequencing may now be used for diagnosis and documentation because to developments in sequencing technology and cost savings. As an illustration, Nanopore instruments are portable and suitable for field use (Quick *et al.*, 2016). They have proven to be able to produce high-resolution typing data from bacterial infections almost instantly and with accuracy. (Wu *et al.*, 2021). While serotype is necessary for the manufacturing of autogenous vaccines, sequence type information may influence local biosecurity protocols. lengthy read Additionally, antimicrobial resistance genes can be found using nanopore sequencing. If "ground-truthing" against phenotype is strong enough, targeted prophylaxis may be able to be informed in real-time by sequence readings (Tamma *et al.*, 2019). In many countries, there will need to be some consolidation and transition before vaccination programs can be distributed to farmers. This is because vaccination programs work best when they are conducted in hatcheries or nurseries. With the implementation of specific pathogen free (SPF) seed production in the local shrimp business, methods are gradually changing. However, other less value locally eaten species like tilapia, carp, and catfish have not yet benefited from this transformation.

The production and sale of auto-vaccines to hatcheries that supply farms impacted by the same strains should be permitted within a clear regulatory framework that supports these pathways and permits flexibility in autogenous format. There are a few aspects of effective vaccination programs that must be addressed in the specific farming environment. While they are not a panacea for illness prevention, vaccines can contribute to the reaction. The necessary skill set is possessed by aquatic veterinarians and health professionals to help address each of the co-contributory environmental factors that drive the manifestation of illness. To ensure optimal outcomes in a One Health framework for sustainable aquaculture, a vaccination program should incorporate various strategies, such as enhanced parasite surveillance and control, improved diagnostic capacity, improved biosecurity to reduce the risk of pathogen introduction and spread, reduced pollutant exposure via water and diets combined with improved water quality monitoring and response to aberrant changes, improved nutrition, improved handling and farming practices, and

use of genetic improvement programs towards disease resilient stock.(Wernli *et al.*, 2020). An antibiotic use restriction framework based on regulations and compliance is equally crucial. With-holding times after treatment would be prolonged, for instance, if the permissible MRL was reduced. When combined with routine compliance sampling of the product, this might alter farmers' decision-making on the care of giant fish approaching market size, prioritizing early intervention measures like as vaccination and husbandry.

CONCLUSION AND FUTURE DIRECTIONS

To overcome the obstacles posed by autogenous vaccines and realize their full potential in tilapia aquaculture, further research and creativity are required. Technological developments in genomics and bioinformatics can speed up the detection and characterization of harmful strains, leading to more accurate vaccine development. Standardized procedures for the manufacture, assessment, and control of autogenous vaccines must also be established via cooperative efforts between academic institutions, business, and regulatory bodies. Moreover, integrated methods that incorporate disease surveillance, better husbandry techniques, biosecurity precautions, and immunization might strengthen tilapia farming's overall health management plans.

Mass mortalities in tilapia production have been caused by recent epidemics brought on by novel bacteria and viruses. This has had major ramifications for nations that depend on tilapia aquaculture for food security and socioeconomic advantages. The risks associated with illnesses that might harm aquatic populations can be addressed through a variety of techniques. Good health management, responsible aquaculture practices (including the movement of live aquatic animals responsibly), and effective biosecurity governance (at the farm, sectoral, industry, and legislation/policy levels) are a few examples. Other examples include effective preventive technologies (such as the use of clean seed through specific pathogen-free stocks, vaccination), which are supported by timely and sensitive diagnostics, surveillance, emergency preparedness, and contingency plans.

Good aquaculture and biosecurity methods are combined with the crucial "control point thinking" and "risk mindset" to manage risk at each stage of the chain and to comprehend and detect threats (MacKinnon *et al.*, 2023). It is necessary to raise awareness and keep developing capacity, especially for small-scale producers. Aquatic species may be sustainably farmed for food and livelihood if robust hosts are produced by a combination of adequate diet, good health, and good genetics.

(Department, 2018). Establishing a strong disease prevention program, utilizing state-of-the-art immunization technologies, and sound management practices may all help limit disease outbreaks and perhaps increase tilapia output (Pandiyan *et al.*, 2013). However, the choice to employ products to improve tilapia health will be based on a number of variables, including as farming methods, farmer attitudes, and the overall cost-benefit analysis of doing so. Crucially, proper husbandry management may reduce stress in fish environments by preserving high water quality, sufficient feed, and strong biosecurity. Limiting the harm caused by these illnesses requires both quick responses to epidemic episodes and the availability of swift and accurate diagnostics techniques. As we can see from the tilapia aquaculture business, vaccination is one of the most important and effective health strategies used to combat infectious diseases.

In conclusion, there is a lot of potential for improving tilapia aquaculture health issues through the use of autogenous vaccines. Autogenous vaccines provide unique problems, but they also provide individualized solutions based on the unique disease profiles that aquaculture operations confront. With continued research and development, autogenous vaccinations have the potential to significantly improve tilapia farming's sustainability and production while reducing the need for antibiotics and lowering the danger of disease outbreaks. To lessen the detrimental effects of infectious illnesses in tilapia farms, more research and development of potent vaccinations is nonetheless required. In order to improve fish survival when exposed to severe infections, novel methods will be employed to select strains of disease- resistant tilapia utilizing marker-assisted selection (MAS) and next-generation sequencing (Adamek *et al.*, 2022).

Improvements in sensor-based technology to keep an eye on water quality, regulate feed properly, and keep an eye out for pathogens in rearing conditions will help boost tilapia health management effectiveness and stop diseases from spreading across the farms. The health of tilapia, fish survival, and the usage of antibiotics will all be significantly enhanced by the integration of these technologies with the tactics outlined in the current study.

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