

Sustainable Management of Tilapia Lake Virus (TiLV): Seaweed-Based Functional Nutrition and Emerging Vaccine Strategies

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ABSTRACT

Tilapia Lake Virus (TiLV) is recognized as one of the most important viral threats to the global tilapia aquaculture industry, especially to Nile tilapia (*Oreochromis niloticus*). TiLV is a negative-sense RNA virus classified as a member of the family Amnoonviridae. This virus targets vital organs such as the liver and brain, leading to syncytial hepatitis, hepatocellular necrosis, systemic infection, and a short incubation period. Fry and juvenile tilapia are highly susceptible to TiLV, making hatchery and nursery systems highly vulnerable to devastating outbreaks. At present, there are limited control strategies to combat this devastating tilapia disease, and although antibiotics are of no use in combating this viral infection, the use of vaccine is still under evaluation. Recent scientific findings suggest that seaweed bioactive compounds are a new class of natural antiviral substances that are effective in controlling TiLV. In this context, the antiviral effect of marine macroalgal extracts has been proven to show a positive effect in vitro and in vivo. Seaweed supplements are known to show a positive effect in tilapia, and dietary seaweed supplements are known to show a positive effect in tilapia, which helps to improve hematological parameters, innate immunity, antioxidant enzyme activities, and antiviral gene expression.

INTRODUCTION

Tilapia, especially Nile tilapia (*Oreochromis niloticus*), is one of the most widely farmed freshwater fish species and is of immense importance in the context of food security and economic development worldwide. Its fast growth rate, adaptability to different environments, and high demand have contributed to its widespread cultivation in Asia and other developing nations (Arumugam *et al.*, 2023). However, the intensified rearing practices have made them more vulnerable to infectious diseases, which pose a threat to sustainable aquaculture practices.

Among the various emerging pathogens, Tilapia Lake Virus (TiLV) is a serious threat. First reported during mass deaths and classified as a new orthomyxo-like virus (Bacharach *et al.*, 2016), TiLV has now been reported to have spread to various nations, including Thailand and India, resulting in substantial fish deaths (Behera *et al.*, 2018). The virus, a single-stranded RNA virus belonging to the family Amnoonviridae, targets vital organs such as the liver and brain, resulting in syncytial hepatitis, systemic pathologies, and high mortality rates, especially among young fish (Islam *et al.*, 2022). Genomic analysis has revealed its rapid spread and evolution, underlining the need for enhanced surveillance (Thawornwattana *et al.*, 2021).

However, the current control methods are still limited. Although inactivated vaccines have shown experimental potential (Zeng *et al.*, 2021), commercial products are still in the process of being developed. Therefore, other approaches are needed. Seaweed-derived bioactive molecules have been shown to have antiviral and immunostimulatory properties, enhancing survival and immune responses in TiLV-challenged tilapia (Periyannan *et al.*, 2025). Moreover, immunoinformatics-based

multi-epitope vaccine design for conserved viral proteins such as PB1 has been proposed as a promising precision medicine strategy (Islam *et al.*, 2022).

Thus, integrated approaches that incorporate functional nutrition and cutting-edge vaccine development are critical for sustainable TiLV control in contemporary aquaculture.

The Emergence of Tilapia Lake Virus (TiLV)

Tilapia Lake Virus (TiLV) has been recognized as one of the most serious viral threats to tilapia aquaculture worldwide over the last decade. First recognized as a novel orthomyxo-like virus associated with mass mortalities, TiLV rapidly drew international notice after outbreaks in Thailand during 2015-2016 (Bacharach *et al.*, 2016). The virus has since been reported in a number of regions, including India, where it caused substantial mortality in farmed Nile tilapia (*Oreochromis niloticus*) (Behera *et al.*, 2018). Genome analysis indicates a high degree of genetic homology among strains worldwide, suggesting rapid transmission and evolutionary conservation (Thawornwattana *et al.*, 2021).

TiLV is a negative-sense, single-stranded RNA virus belonging to the family Amnoonviridae, which is horizontally and vertically transmitted (Islam *et al.*, 2022). It mainly targets critical organs such as the liver and brain, leading to syncytial hepatitis, generalized tissue lesions, and a high mortality rate, especially in young fish (Islam *et al.*, 2022; Behera *et al.*, 2018). Increased production systems, fish trade, and the lack of early diagnosis have contributed to its spread. While inactivated vaccines have shown promising results in experimental studies, there is no large-scale control strategy yet (Zeng *et al.*, 2021).

Clinical Signs and Pathogenesis

Tilapia Lake Virus (TiLV) is a highly contagious single-stranded RNA virus that belongs to the family Amnoonviridae and causes severe systemic infections in Nile tilapia (*Oreochromis niloticus*) (Islam *et al.*, 2022). The virus shows multi-organ tropism and high pathogenicity, mainly targeting the liver, brain, and eyes. Histopathological lesions include syncytial hepatitis, hepatocellular necrosis, and karyolytic nuclei, reflecting severe tissue destruction (Islam *et al.*, 2022). Genome sequencing studies show high nucleotide similarity among different strains worldwide, reflecting the conservation of crucial pathogenic elements (Thawornwattana *et al.*, 2021).

Clinically, the fish show signs of lethargy, anorexia, erratic swimming, anemia, abdominal distention, and ocular disease, with a very high mortality rate among the fry and juvenile stages (Behera *et al.*, 2018; Islam *et al.*, 2022). The initial outbreak cases showed a rapid and massive mortality rate among the farmed fish (Bacharach *et al.*, 2016).

Although the TiLV infection triggers the innate immune response and regulates the expression of antiviral genes, the immune system is not always capable of resisting systemic infection (Periyannan *et al.*, 2025). The TiLV virus is transmitted both horizontally and vertically, which makes it very easily transmissible in intensive fish farming (Islam *et al.*, 2022). In summary, the high infectivity, multi-organ involvement, and lack of effective treatment make TiLV a serious threat to the global tilapia industry.

Limitations of Conventional Control Measures

The control of Tilapia Lake Virus (TiLV) is still a challenge owing to the absence of effective treatments and established commercial vaccines. Being a viral disease,

TiLV cannot be treated with antibiotics, thus requiring other preventive and immunological measures. Although inactivated vaccines have shown high protective efficacy in experimental studies (Zeng *et al.*, 2021), they are still in the early stages of development. Immunoinformatics tools applied for conserved viral proteins such as PB1 have made it possible to design multi-epitope vaccine constructs with enhanced specificity and safety, which still require validation before commercialization (Islam *et al.*, 2022).

However, despite advances in diagnostic capabilities, TiLV continues to spread rapidly through horizontal and vertical transmission and transboundary fish movement (Islam *et al.*, 2022; Thawornwattana *et al.*, 2021). High mortality rates, especially among fry and juvenile fish, have been shown to affect hatchery productivity (Behera *et al.*, 2018), as has been noted in initial outbreak descriptions (Bacharach *et al.*, 2016).

Conventional biosecurity and experimental vaccine approaches are clearly inadequate, underlining the importance of integrated approaches that combine advances in surveillance, nutrition, and precision vaccine technology for long-term TiLV management.

Seaweed as a Natural Antiviral Resource

Marine macroalgae (seaweeds) are known to be rich sources of bioactive compounds with antiviral, antioxidant, and immunomodulatory activities, thus being promising sustainable alternatives to chemotherapeutic agents in aquaculture (Apostolova *et al.*, 2020). Sulfated polysaccharides like fucoidan have been particularly well recognized for their antiviral and anti-inflammatory properties.

Regarding Tilapia Lake Virus (TiLV), recent research has shown that hot water extracts of *Sargassum ilicifolium*, *Ulva fasciata*, and *Enteromorpha compressa* were able to inhibit viral cytopathic effects in vitro without

cytotoxicity (Periyannan *et al.*, 2025). Dietary supplementation was found to cause a significant improvement in survival rates of Nile tilapia challenged with TiLV, with *S. ilicifolium* having the highest relative percent survival (58.34%), followed by *U. fasciata* (50%), and *E. compressa* (41.67%).

Immune system activation was also improved by seaweed supplements, involving leukocyte function, antioxidant enzyme activity, and antiviral gene expression like TLR-7 and IFN- β (Periyannan *et al.*, 2025). This can be ascribed to biologically active compounds that inhibit viral binding and replication (Apostolova *et al.*, 2020).

In summary, compounds from seaweed are a promising natural approach to sustainable TiLV control, which simultaneously targets antiviral and immune-activating properties in tilapia aquaculture.

Mechanisms of Antiviral Action

Seaweed-derived bioactive compounds have antiviral properties, which can be attributed to both direct inhibition of viruses and modulation of the host immune system. The mechanism of action of these compounds is primarily due to sulfated polysaccharides, fucoidans, phlorotannins, and other secondary metabolites that target various steps of viral infection.

Sulfated polysaccharides have the ability to inhibit viral attachment and entry by binding to either the viral particles or the host cell receptors (Apostolova *et al.*, 2020). In TiLV infection models, seaweed extracts inhibited the cytopathic effect in SSN1 cells without cytotoxicity, indicating the potential of these compounds to target early stages of infection (Periyannan *et al.*, 2025). Marine polysaccharides also have the potential to inhibit viral replication by affecting RNA synthesis and polymerase activity, which is a

crucial step for TiLV genome replication (Islam *et al.*, 2022; Periyannan *et al.*, 2025).

Besides the antiviral properties, the supplementation of seaweed increases the innate immunity of Nile tilapia by promoting the count of leukocytes, respiratory burst, and the activities of antioxidant enzymes such as SOD and catalase (Periyannan *et al.*, 2025). The induction of antiviral genes such as TLR-7, IFN- β , and IPS-1 further improves the immune response (Periyannan *et al.*, 2025). Their antioxidant properties also help in the reduction of oxidative stress and tissue damage caused by the infection.

In conclusion, the antiviral properties of seaweed extracts against TiLV infection are multi-faceted, with a combination of inhibition of viral replication, immune stimulation, and antioxidant activities that result in improved survival rates of the challenged fish (Periyannan *et al.*, 2025).

Experimental Evidence from Recent Studies

Recent findings have validated both nutritional and immunological approaches for the control of Tilapia Lake Virus (TiLV) in Nile tilapia (*Oreochromis niloticus*). In vitro experiments conducted on SSN1 cell lines revealed that hot water extracts of *Sargassum ilicifolium*, *Ulva fasciata*, and *Enteromorpha compressa* possessed significant antiviral activity against TiLV-induced cytopathic effects without cytotoxicity, suggesting antiviral properties (Periyannan *et al.*, 2025).

In vivo fish feeding experiments further validated these findings. Fish fed *S. ilicifolium* (500 mg/kg) exhibited the highest relative percent survival (58.34%), followed by *U. fasciata* (50%) and *E. compressa* (41.67%) when challenged with TiLV (Periyannan *et al.*, 2025). Seaweed supplementation also stimulated the immune system by increasing the levels of leukocytes, respiratory burst activity, antioxidant enzymes (SOD and

catalase), and the expression of antiviral genes such as TLR-7, IFN- β , and IPS-1 (Periyannan *et al.*, 2025).

Concurrent vaccine development has also yielded promising results. Inactivated TiLV vaccines were shown to decrease mortality in experimental settings (Zeng *et al.*, 2021), while immunoinformatics-based multi-epitope vaccines designed against the PB1 domain of TiLV showed high predicted antigenicity (Islam *et al.*, 2022).

Functional immunostimulation by seaweed and precise vaccine development, therefore, offer complementary and sustainable approaches for the improvement of TiLV resistance in tilapia.

Advances in Epitope-Based Vaccine Design

The emergence of Tilapia Lake Virus (TiLV) has accelerated the process of developing efficient vaccines. Although inactivated vaccines have demonstrated encouraging protective efficacy under laboratory conditions (Zeng *et al.*, 2021), immunoinformatics has facilitated the development of epitope-based subunit vaccines against conserved viral proteins.

TiLV is a negative-sense, single-stranded RNA virus belonging to the family Amnoonviridae, with a segmented genome (Islam *et al.*, 2022). The polymerase basic 1 (PB1) segment is very conserved and thus represents an ideal target for broad-spectrum vaccine development (Islam *et al.*, 2022). B- and T-cell epitopes predicted from the PB1 segment using computational approaches were filtered for antigenicity, toxicity, and immunogenicity before being fused into a multi-epitope construct. Structural modeling and immune simulation analyses revealed efficient receptor binding and the ability to stimulate both humoral and cellular immune responses (Islam *et al.*, 2022).

These vaccines are still in the computational phase and need experimental validation *in vivo*. However, they possess several advantages over conventional whole-virus vaccines, including enhanced safety, specificity, and scalability. When supplemented with nutritional immunostimulants like seaweed-derived bioactive molecules (Periyannan *et al.*, 2025), epitope-based vaccines appear to be a bright future prospect for sustainable TiLV control in tilapia aquaculture.

Toward Integrated Disease Management

The need for a comprehensive and sustainable management plan is required due to the global distribution and high pathogenicity of the Tilapia Lake Virus (TiLV). Due to its horizontal and vertical transmission, as well as rapid transboundary spread (Islam *et al.*, 2022; Thawornwattana *et al.*, 2021), a single management strategy is insufficient.

Biosecurity, nutritional immunostimulation, and vaccination must be combined in a comprehensive management plan. Biosecurity strategies such as screening of broodstock, movement restrictions, and regular molecular testing are essential to control its spread (Islam *et al.*, 2022). The genomic analysis has shown the importance of global fish trade in the spread of the virus, emphasizing the need for enhanced surveillance (Thawornwattana *et al.*, 2021).

Functional nutrition is a useful preventive tool. Supplementing diets with seaweed extracts (*Sargassum ilicifolium*, *Ulva fasciata*, and *Enteromorpha compressa*) led to a significant improvement in survival rates, immune function, antioxidant capacity, and antiviral gene expression (TLR-7, IFN- β) in Nile tilapia (*Oreochromis niloticus*) challenged with TiLV (Periyannan *et al.*, 2025).

Vaccination is a key preventive tool for long-term protection. Inactivated vaccines have

proven highly effective in experimental studies (Zeng *et al.*, 2021), while immunoinformatics-assisted multi-epitope vaccines designed for conserved proteins such as PB1 have emerged as promising precision medicine tools (Islam *et al.*, 2022), although these must still be tested in field settings.

In conclusion, a comprehensive strategy combining rigorous biosecurity, rapid diagnostics, functional nutrition with seaweed extracts, and innovative vaccines holds the key to a sustainable and effective TiLV disease management program for tilapia aquaculture.

Future Perspectives

The continuous spread and economic effects of Tilapia Lake Virus (TiLV) emphasize the importance of continued research and innovative measures for its control. Although significant progress has been achieved in understanding its molecular characteristics, pathogenesis, and epidemiology (Islam *et al.*, 2022; Thawornwattana *et al.*, 2021), there are still significant knowledge gaps.

Future research should focus on enhancing genomic surveillance to track the evolution of the virus, emerging strains, and prevent cross-border transmission (Islam *et al.*, 2022; Thawornwattana *et al.*, 2021).

Functional feeds formulated with seaweed have demonstrated substantial efficacy, enhancing immunity and survival in TiLV-challenged Nile tilapia (*Oreochromis niloticus*) (Periyannan *et al.*, 2025). However, additional studies are required to isolate the active antiviral agents, standardize inclusion rates, confirm efficacy under field conditions, and explore economic viability (Apostolova *et al.*, 2020).

Vaccine development, too, needs to be pushed forward. Although inactivated vaccines have demonstrated promising laboratory protection (Zeng *et al.*, 2021), extensive validation under

field conditions is necessary. Immunoinformatics-based multi-epitope vaccines designed against conserved proteins like PB1 represent a promising next-generation alternative (Islam *et al.*, 2022).

Thus, for effective and sustainable TiLV management, there is a pressing need to integrate genomics, functional nutrition, vaccination strategies, and enhanced biosecurity into a comprehensive aquaculture health management strategy.

CONCLUSION

Tilapia Lake Virus (TiLV) poses a significant threat to the global tilapia aquaculture industry with high mortality rates and significant economic losses, especially in fry and juvenile Nile tilapia (*Oreochromis niloticus*) (Bacharach *et al.*, 2016; Behera *et al.*, 2018). Being a negative-sense RNA virus belonging to the Amnoonviridae family, it leads to systemic infection and hepatic necrosis, and its geographical distribution is facilitated by the movement of fish across borders (Islam *et al.*, 2022; Thawornwattana *et al.*, 2021).

Effective control measures are not yet available. Inactivated vaccines have demonstrated promising laboratory protection (Zeng *et al.*, 2021), and immunoinformatics-based multi-epitope vaccines designed against conserved proteins like PB1 have provided accurate next-generation approaches, although these require further confirmation (Islam *et al.*, 2022).

Bioactive compounds from seaweed offer a sustainable complementary strategy. Dietary supplementation has been demonstrated to boost innate immunity, activate antiviral genes, and increase survival rates in TiLV-infected fish (Periyannan *et al.*, 2025), validated by the antiviral activity of sulfated polysaccharides from marine seaweed.

In conclusion, the most promising strategy for sustainable TiLV control in aquaculture is the combination of biosecurity, functional nutrition based on seaweed, and precision vaccine development.

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