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Review Article

Vaccines for Use in Finfish Aquaculture

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Abstract

Aquaculture, the fastest growing animal food-producing agricultural sector in the world which accounts for almost half of the world's food fish production, has been constrained by several infectious viral, bacterial and parasitic diseases. Successful development and expansion of aquaculture sector largely depends upon the control and prevention of emerging and re-emerging infectious diseases which can result in economic loss, food safety hazards and environmental hazards. This review was conducted to investigate the currently available fish vaccines for use in finfish aquaculture against different infectious diseases and the limitations in effective vaccine development. Information was collected from different secondary sources, then compiled systematically and arranged chronologically. The Review reveals that vaccination strategies have become highly effective and economical in protecting the health of fish and other aquaculture organisms from various infectious disease-causing agents. Recent developments in vaccines and vaccinology offer valuable opportunities to discover new vaccine candidates to combat fish pathogens, including mycotic and parasitic agents. This study shows that currently a lot of commercial fish vaccines are available to use against infectious bacterial and viral diseases of fish, but no vaccine is available to control infectious parasitic disease and fungal disease. An immobilized adjuvant heat shock protein (Hsp70C) vaccine has been reported to confer high protection of fish against parasitic disease, Cryptocaryonosis which can be a great breakthrough in parasitic vaccine development for farmed and ornamental fish. Most of the available fish vaccines are empirically designed vaccines based on inactivated or live attenuated bacterin vaccines. Novel and advances in the field of immunology, biotechnology, and molecular biology have led to the development in designing novel and effective fish vaccines and improving the existing vaccines to provide sufficient immune protection against diseases.

Keywords: Aquaculture, Bacterial Disease, Parasitic Disease, Live Vaccines, Adjuvant Vaccine, Hsp70C.

Abbreviations

ERM= Enteric Red Mouth Disease, MAS= Motile Aeromonas Septicemia, IPNV= Infectious Pancreatic Necrosis Virus, IHNV= Infectious Hematopoietic Necrosis Virus, EHNV= Epizootic Hematopoietic Necrosis Virus, ISAV= Infectious Salmon Anemia Virus, SVCV= Spring Viremia of Carp Virus, GCHD= Grass Carp Hemorrhage Disease, VNNV= Viral Nervous Necrosis Virus, VHSV= Viral Hemorrhagic Septicemia Virus, CCVD= Channel Catfish Virus Disease, FW= Freshwater Species, MW= Marine Water Species, KHVD= Koi Herpes Virus Disease, DNA= Deoxyribonucleic Acid, NASS= National Agricultural Statistics Service, BKD= Bacterial Kidney Disease, PKD= Proliferative Kidney Disease, Hsp70C= Heat Shock Protein, and RTF= Rainbow Trout Fry.

Introduction

Aquaculture is currently the fastest growing human food producing agricultural sector in the world [1-2]. It provides a great contribution to food security and socio-economic development in many countries. The World aquaculture practice has shifted from extensive to semi-intensive and intensive culture system where high-value fish species are reared at higher stocking density using commercial feeds [2-4]. But there are many constraints against the sustainable development of this aquaculture sector. Among these, the disease is the most devastating threats to semi-intensive and intensive aquaculture system which results in economic

Bacterial infectious diseases are the most prevalent disease challenges in fish farming while viral diseases are more difficult to control due to the lack of anti-viral therapeutics, challenges in developing effective viral vaccines and lack of information on the mechanisms of viral pathogenesis and disease resistance in fish [6]. The unavailability of efficient treatment modules to control viral and bacterial diseases posed a vital demand for developing and implementing effective approaches for prevention and control of these diseases [1]. Besides, the adverse effects of infectious diseases has also demanded the strategic development of vaccine design because indiscriminate use of antibiotics in aquaculture can make rise in problems of developing bacterial resistance, food safety hazards and environmental problems [5,6]. Treatment of many bacterial infections in fish using only antimicrobials is impossible [1].

In this situation, fish vaccination has become the most important, easy and effective approaches to prevent and control infectious diseases in fish. Vaccination is a process by which protective immune response is induced in animals administering preparation of antigens derived from pathogens and made non-pathogenic by means of heat or other ways. Vaccines stimulates fish immune response and increase protection against diseases. Several significant progress have been made for developing effective fish vaccines. But until now, only a few vaccines are commercially available against infectious viral and bacterial diseases for fish farmers [1]. Currently, vaccines are available for some economically important fish species for treating bacterial and viral diseases. This review aimed to investigate the currently available commercial vaccines against infectious bacterial and viral diseases of fish and their efficiency. This study also focuses on those diseases for which still now there is no vaccine is available.

Methodology

This Review was conducted using the information available in different scientific research papers and the literatures published in different journals either in peer reviewed journals or not, periodicals, proceedings, annual reports, relevant books and other sources. Electronic media was also an important source for information. Information was also collected visiting the websites related to fish health management and fisheries research institutes. All the information collected from the secondary sources have been compiled systematically and chronologically.

Review Findings

Vaccines are preparation of antigens derived from pathogens and made non-pathogenic through various ways which stimulates immune response in fish and increase disease resistance. Fish vaccination was started in 1942 against *Aeromonas salmonicida* infection [3,4,8]. Advancing vaccination is the most important and the prior approaches for prevention and control of infectious diseases of fish [1]. Protection at stock level can be achieved through vaccination. Besides, the licensing and registration of new vaccine is much easier than antibiotics [4].

Currently, there are many commercial vaccines available against infectious bacterial and viral diseases of fish for using in aquaculture. The first commercialized fish vaccines were bacterial vaccine, introduced in the USA in late 1970s [1,3,8]. These vaccines were inactivated whole-cell immersion vaccines and proved efficient in preventing many bacterial diseases [8]. Advances in biotechnology and immunology has led to development and commercialization of many other fish vaccines like DNA vaccines, Nano vaccines, subunit vaccines, genetically modified vaccines and Polyvalent vaccines [1,2]. Modified live *Edwardsiella ictaluri* vaccine, produced in 2000 is the first licensed bacterial live vaccine in aquaculture [1,7].

Inactivated bacterin vaccines and live attenuated vaccines have been proved efficient by immersion of fish [8]. Simple inactivated bacterin vaccines works well against vibriosis but other bacteria are more difficult to control [4]. Polyvalent vaccines, for Salmonids incorporating different Vibrio species and *Aeromonas salmonicida* as an antigen, are also available. DNA vaccines also were employed experimentally as safe live vaccines with a high level of success against Furunculosis but their approval for use in the field has not yet been forthcoming [7,8].

Viral diseases are more difficult than bacterial infectious diseases to control due to the lack of anti-viral therapeutics and effective viral vaccines [1,7]. The World Organization for Animal Health has listed certain viral diseases as catastrophe for large scale aquaculture industry such as Epizootic Hematopoietic Necrosis (EHN), Koi Herpes Virus Disease (KHVD), Infectious Hematopoietic Necrosis Virus (IHNV), Spring Viremia of Carp (SVC) and Viral Hemorrhagic Septicemia (VHS) [1,10]. Large number of research trials have been conducted but only a few viral vaccines are licensed [8]. Currently available commercial viral vaccines for aquaculture are inactivated virus vaccines or recombinant protein vaccines. No live attenuated vaccines are currently licensed for using in aquaculture, only one DNA vaccine against IHN (Infectious hematopoietic necrosis) disease is available [7]. Inactivated viral vaccines are effective at high dose if delivered by injection, but cost-effective inactivated viral vaccines are difficult to develop where live viral vaccines showed good results in fish. The lack of effective viral vaccines is one of the main problems facing fish vaccinology [8,21,22].

Currently, vaccines are available for some economically important bacterial and viral diseases, like there is a Salmon pancreas disease vaccine available under a PMA [1,8]. Economically important fish species such as Atlantic salmon, rainbow trout, seabass, sea bream (*Sparus aurata*), barramundi (*Lates calcarifer*), tilapia, turbot (*Scophthalmus maximus* L.), yellowtail (Seriola quinqueradiata) and gold-striped amberjack (*Seriola dumerili*), striped jack (*Pseudocaranx dentex*) and channel catfish (*Ictalurus punctatus*) [11,13,21,22]. But unlike all the other Salmon vaccines designed for administration in a single injection this has to be given separately from any other injectable vaccine. To date there is not yet any vaccine available for trout. There are also some other bacterial and viral diseases of fish against which no vaccines have been developed yet [8]. Novel advances in Biotechnology and Immunology can lead to effective vaccine design against this disease [1].

Development of fish vaccines is a challenging task, due to a variety of pathogens, hosts, and the uniqueness of host-susceptibility to each pathogen [7]. Major limitations in fish vaccine developments are less understanding of fish immunology, many vaccines unlicensed, not cost effective (expensive) and stressful on administration [8]. It is hoped that, in near future vaccine developments may promote from the increased knowledge of the fish immune system and knowledge of pathogen and virulence mechanisms which helps in development of live vaccines, improved DNA vaccines, sub unit vaccines, polyvalent and monovalent vaccines, improved adjuvants and Oral delivery systems. New vaccination strategies, aquaculture expansion and disease investigation center should be initiated [1,7,20].

SL. No.	Name of Vaccine	Species vaccinated	Diseases prevented
1	Arthrobacter Vaccine	Salmonids	Columnaris disease
2	*Vibrio anguillarum*-Ordalii	Salmonids, Rainbow trout	Vibriosis
3	*Aeromonas salmonicida* Bacterin	Salmonids	Furunculosis
4	*Yersinia ruckeri* Bacterin	Salmonids	Yersiniosis
5	*Edwardsiella Ictalurii* Vaccine	Catfish	Edwardsiellosis
6	*Flavobacterium Columnare* Vaccine	Channel Catfish, Salmonids, FW species	Columnaris disease
7	*Listonella anguillarum* Vaccine	Salmonids, seabass, yellowtail	Vibriosis
8	*Vibrio salmonicida* Bacterin	Salmonids	Coldwater Vibriosis
9	*Vibrio anguillarum-salmonicida* Bacterin	Salmonids	Vibriosis
10	*Edwardsiella ictaluri* Bacterin	Channel Catfish, Japanese flounder	Enteric septicemia
11	*Moritella viscosa* Vaccine	Salmonids	Wound Disease
12	Free-cell *Aeromonas hydrophila* Vaccine	Indian Major Carps	Dropsy
13	*Streptococcus agalactiae* Vaccine	Tilapia	Streptococcosis
14	*Streptococcus iniae* Vaccine	Tilapia	Streptococciosis
15	Enteric Red Mouth (ERM) Vaccine	Salmonids	Enteric red mouth disease
16	Pasteurella Vaccine	Salmonids	Pasteurellosis
17	*Photobacterium damsela* Vaccine	Seabass, yellowtail	Pasteurellosis
18	*Aeromonas hydrophila* Vaccine	Salmonids	Motile Aeromonas Septicemia
19	Carp Erythrodermatitis	Carp species	Erythrodermatitis
20	Piscirickettsia salmonis Vaccine	Salmonids	piscirickettsiosis
21	aemiaGa Vaccine	Lobsters	aemiaGa
22	*Flavobacterium psychrophilum* Vaccine	Salmonids, FW species	Flavobacteriosis
23	*Renibacterium salmoninarum* Vaccine	Salmonids	Bacterial Kidney Disease
24	*Lactococcus garvieae* Vaccine	Rainbow trout, yellowtail	Lactococcosis
25	Infectious Hematopoietic Necrosis Virus Vaccine	Salmonids	Infectious hematopoietic necrosis
26	Infectious Pancreatic Necrosis Virus Vaccine	Salmonids	Infectious pancreatic necrosis
27	Infectious Salmon Anemia Vaccine	Salmonids	Infectious Salmon Anemia
28	*Iridoviral disease Vaccine*	Red sea bream	Iridoviral disease
29	Spring Viremia of Carp Vaccine	Common carp	Spring viremia of carp
30	Koi Herpes Virus (KHV) Vaccine	Koi carp	Koi herpes virus disease
31	Betanodavirus	Grouper	Betanoda virus disease
32	Carp Erythrodermatitis	Carp	Erythrodermatitis
33	Grass Carp Hemorrhage Disease Vaccine	Grass Carp	Grass carp hemorrhage disease
34	aemiaGa vaccine	Lobsters	aemiaGa
35	Nodavirus vaccine	Seabass	Viral Nervous Necrosis
36	Pancreas disease Virus Vaccine	Salmonids	Pancreas Disease

Table 1: Commercial vaccines available against major infectious bacterial and viral diseases of fish [4,7,8,9].

Besides, there is a wide range of infectious parasites in both wild and intensive aquaculture fish stocks. Several parasitic infestation create dangerous problems in fish farming such as Amoebic Gill Disease, Whirling Disease, White Spot Disease, PKD and Salmon lice disease, but no parasite vaccines are commercially available [7]. Parasitic infection in fish results in losses and a decreased immune response in infected fish. These pathogens have been controlled by chemicals that cause limitation for human consumption so vaccines are needed for these parasites. There have been several attempt to produce vaccines against some fish parasites but no commercial vaccine is available [8].

Type of Disease	Causative Agents	Fish Species Affected	Disease
Viral Diseases	Viral Hemorrhagic Septicemia Virus	Trout, turbot, Japanese flounder	VHS Disease
	Viral Nervous Necrosis Virus	Marine fish species	VNN Disease
	Other betanodavirus	Groupers, Seabass, halibut	Betanodavirus Disease
	Channel catfish virus	Channel catfish	CCV Disease
Bacterial Disease	*Flavobacterium branchiophilum*	Salmonids, Carps, FW species	Bacterial gill disease
	Mycobacterium marinum	FW and MW fish species	*Mycobacteriosis*
	Flavobacterium psychrophilum	Salmonids, FW	Rainbow trout fry syndrome
	Edwardsiella tarda	Channel catfish	Edwardsiella septicaemia
	Streptococcus phocae	Asian sea bass, Salmonids	Streptococcosis

Table 2: Major infectious Viral and Bacterial diseases of fish against which vaccines are not available [3,7,8,9].

Limitations and Future Prospects

Fish vaccines have become an established, proved and cost-effective method of controlling infectious diseases in aquaculture. Vaccination can significantly reduce specific disease-related losses resulting in reduction of antibiotics use. The existing vaccines can induce protection after a single administration until the fish are harvested, but actual protection mechanisms has not been investigated properly [8]. Cost effectiveness is an essential limitation to commercial fish vaccine development. The effective viral vaccines for aquaculture in preventing mortality are expensive to produce and license [7].

Some commercial vaccines for fish are consisted of mixtures of two, three, four even five vaccine products. But all the antigens do not stimulate protective immune response. It has become difficult to formulate these complex mixtures into safe and effective commercial products [13]. Many fish species are highly vulnerable to handling stress during vaccination and post vaccination side effects [14]. Most of the research on fish vaccines has been performed by pharmaceutical companies and sufficient scientific information is not available [8]. In some species, the major disease problems occur in the larval or fry stage, when the animal is large enough to be vaccinated. Lack of knowledge on maternal immunity in fish also limits the possibilities to protect offspring by parental vaccination [7,15].

In addition, no vaccine is available for parasitic infectious diseases and fungal diseases of fish. It is more difficult to cultivate parasites for the preparation potential inactivated, killed or live vaccine, even it is more expensive than virus cultivation because a host population is usually required for culture rather than only cell cultures. Along with the high costs, using natural host animal for cultivation of parasites has high possibility to create major problems with respect to safety documentation [7,8]. So it is very important to identify safe host species and production of protective antigens is probably the most feasible strategy towards for low cost commercial parasite vaccines development.

Advances in genome sequencing of pathogens can accelerate the opening of opportunities to investigate new generation vaccines such as subunit vaccine, DNA vaccine, virus-like particle and vector-vehicle vaccine. Recently, the genome of salmon and several other fish species has been fully sequenced. These findings can lead to novel vaccine development strategies in near future [1]. Improvement in oral immunization with biodegradable micro particle based vaccines can facilitate booster vaccination, development of new non-mineral oil adjuvants, development of polyvalent vaccines and standardization of a vaccination calendar with molecular biology and modern technologies can make possible to development novel approaches vaccination [16]. Plant based edible fish vaccines can also contribute a lot in the field of fish vaccination.

Conclusion

Vaccination is now widely used in almost all food-producing animals. In case of aquaculture, vaccination reduces the use of antibiotics and protects fish from infectious diseases avoiding the risk of drug resistance [1]. Most of the fish vaccines have been developed and commercially available are for high-value fresh water and marine fish species to prevent bacterial and viral diseases of fish [11]. But Vaccines for protection against parasitic and fungal diseases have not yet been developed [7]. Currently available vaccines are based on simple empirically developed inactivated pathogens. A few recombinant subunit vaccines and DNA vaccines are also available. Limited knowledge on immune systems of fish limits the

development of vaccines based on non-empirical strategies [1,7,8]. Vaccines against intracellular bacterial and viral pathogens is one of the big challenges for the coming years. DNA vaccine can also play an important role in such cases. New vaccination strategies, aquaculture expansion and disease investigation center should be initiated [7,8]. Strong coordination should be created between pharmaceutical companies and academic research for a better development of live fish vaccines.

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Volume 2 Issue 11 November 2018