Vaccines for infectious bacterial and viral diseases of fish: a review.

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Abstract

Infectious disease is still now one of the key threats to the sustainable development of aquaculture and fisheries in the world. The recent expansion of aquaculture system has increased the chances of the infectious disease outbreak. This review was conducted to investigate the available vaccines for infectious bacterial and viral diseases of fish in aquaculture to cope with the emerging and re-emerging diseases. Information was collected from different secondary sources related to this topic. This investigation reveals that vaccination has become the most accepted disease control approach over the world and the vaccine production strategy has been turned into a large pharmaceutical industry with the expansion of aquaculture. Currently, available fish vaccines are empirically designed live attenuated and inactivated whole cell vaccines. Novel advances in fish immunology, biotechnology, and molecular biology have led to the development of effective new generation vaccines like DNA Vaccines, subunit vaccines, Nano-vaccines, edible plant vaccines and many others. Bacterial vaccines have gained considerable success compared to viral vaccines in recent years because bacteria vaccines are more effective than viral vaccines.

Keywords: Aquaculture, infectious disease, vaccines, polyvalent vaccines, nano-vaccines

Abbreviations: IPN: Infectious Pancreatic Necrosis; IHN: Infectious Hematopoietic Necrosis; VHS: Viral Hemorrhagic Septicemia; VNN: Viral Nervous Necrosis; EHN: Epizootic Hematopoietic Necrosis; SVC: Spring Viremia of Carp; KHV: Koi Herpes Virus; ISA: Infectious Salmon Anemia; DNA: Deoxyribonucleic Acid; RNA: Ribonucleic Acid; FW: Freshwater Species; MW: Marine Water Species; NASS: National Agricultural Statistics Service; ERM: Enteric Red mouth.

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Introduction

Aquaculture is the fastest growing animal food producing sector that provides almost half of the total fish production of the world and contributes to the food security and socio-economic development in many countries [1]. Aquaculture practice has been shifted to semi-intensive and intensive culture system from extensive culture system where high valued fish species are reared at higher stocking density using commercial feeds [2,3]. The rapid expansion of aquaculture has increased the chances of several pathogens outbreak infecting different fish species. The disease is probably the most devastating threats to the intensive fish culture that can result in economic loss causing high mortality of cultured animals. The National Agricultural Statistics Service (NASS) has reported that 90% production loss in rainbow (Oncorhynchus mykiss) trout in 2009 was caused by disease [2]. Among the fish diseases, infectious bacterial and viral diseases are the most dangerous constraint to the sustainable expansion of aquaculture through the world. The major causative agents of infectious diseases in aquaculture include bacteria, viruses, parasites, and fungus (Figure 1).

Bacterial infectious diseases are the most prevalent disease challenges in fish farming, viral diseases are more difficult to control due to the lack of anti-viral therapeutics and effective viral vaccines. The unavailability of efficient treatment modules to control viral and bacterial diseases posed a vital demand for developing and implementing effective approaches to the prevention and control of these diseases [4-6]. Besides, the adverse effects of infectious diseases have also demanded the strategic development of vaccine design because indiscriminate use of antibiotics in aquaculture can make a rise in problems of developing bacterial resistance, food safety hazards and environmental problems [7,8]. Treatment of many bacterial infections in fish using only antimicrobials is impossible [1]. So fish vaccination has become the most important, easy and effective approaches to prevent and control infectious diseases in fish [4]. Several significant progresses 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]. This paper reviewed the currently available commercial fish vaccines for infectious bacterial and viral diseases, to isolate the bacterial and viral

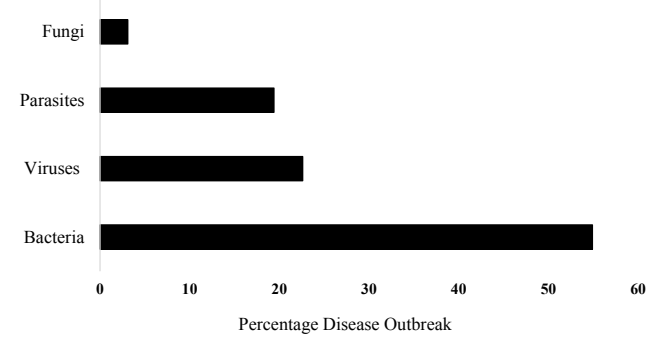

Figure 1. *Percentage of infectious disease outbreaks caused by major causative agents in aquaculture [5].*

diseases for which vaccines are not available with the limitations in effective vaccine development.

Materials and Method

This review was conducted using the information available in different forms either in scientific research reports, literature published in different peer-reviewed journals, open access journals, proceedings, periodicals, relevant books, annual reports, and other sources. Electronic media was also an important source of 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 has been compiled systematically and chronologically.

Review of Findings

Vaccines are the preparation of antigens derived from pathogens and made non-pathogenic through various ways which stimulate the immune response in fish and increase disease resistance. Fish vaccination was started in 1942 by vaccinating Cutthroat against Aeromonas salmonicida infection [3,9,10]. Advancing vaccination is the most important and probably the prior approaches for prevention and control of infectious diseases of fish [1]. There are improvements in fish vaccination recently. Some of the improvements include immunization of large stock at a time and the development of multivalent vaccines [2]. Protection at stock level can be achieved through vaccination. Besides, the licensing and registration of new vaccine are much easier than antibiotics [3].

Currently, there are many commercial vaccines available against infectious bacterial and viral diseases of fish for use in aquaculture. The first commercialized fish vaccines were the bacterial vaccine, introduced in the USA in the late 1970s against enteric Redmouth disease and vibriosis [1,9,10]. These vaccines were inactivated whole-cell immersion vaccines which have been proved effective in preventing many bacterial diseases [9]. Advances in biotechnology and immunology have led to development and commercialization of many other fish vaccines like DNA vaccines, Nano vaccines, subunit vaccines, genetically modified vaccines and polyvalent vaccines [1].

Modified live Edwardsiella ictaluri vaccine has been produced since 2000, by Intervet Inc., under the trade name AQUAVAC-ESCO, and constitutes the first licensed bacterial live vaccine in aquaculture formulated with an attenuated pathogenic strain [9]. Among those, some inactivated bacterin vaccines and live attenuated vaccines have been proved efficient by immersion of fish and some others are of relatively lower efficiency [9]. Simple inactivated bacterin vaccines work well against a bacterial disease vibriosis but other bacteria are more difficult to control by means of vaccination [3].

Polyvalent vaccines, for Salmonids incorporating different Vibrio species and Aeromonas salmonicida as antigens, 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 [9,11]. Different polyvalent oil-adjuvanted vaccines, including combinations of Vibrio anguillarum with other pathogens, such as Vibrio ordalii, Vibrio salmonicida, Aeromonas salmonicida, Moritella viscose and infectious pancreatic necrosis virus, are also available on the market to be used for Salmonids by the intraperitoneal route (Table 1)[1,9].

Viral diseases are more difficult than bacterial infectious diseases 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 disease resistance in fish [1,11]. The World Organization for Animal Health has listed certain viral diseases as catastrophe for large-scale

Table 1. *Vaccines available for major infectious bacterial diseases of fish [3,9,11,23,24,26].*

Sl. No.	Name of Vaccine	Species vaccinated	Diseases prevented
1	*Yersinia* Ruckeri Bacterin	Salmonids	Yersiniosis
2	*Vibrio Anguillarum*-Ordalii	Salmonids, Rainbow trout	Vibriosis
3	*Edwardsiella Ictalurii* Vaccine	Catfish	Edwardsiellosis
4	Arthrobacter Vaccine	Salmonids	Columnaris disease
5	*Flavobacterium Columnare* Vaccine	Channel Catfish, Salmonids, FW species	Columnaris disease
6	*Vibrio anguillarum-salmonicida* Bacterin	Salmonids	Vibriosis
7	*Listonella anguillarum* Vaccine	Salmonids, seabass, yellowtail	Vibriosis
8	*Vibrio salmonicida* Bacterin	Salmonids	Coldwater Vibriosis
9	*Edwardsiella ictaluri* Bacterin	Channel Catfish, Japanese flounder	Enteric septicemia
10	*Aeromonas salmonicida* Bacterin	Salmonids	Furunculosis
11	*Moritella viscosa* Vaccine	Salmonids	Wound Disease
12	*Streptococcus agalactiae* Vaccine	Tilapia	Streptococcosis
13	Free-cell *Aeromonas hydrophila Vaccine*	Indian Major Carps	Dropsy
14	*Streptococcus iniae* Vaccine	Tilapia	Streptococciosis
15	*Photobacterium damsela* Vaccine	Seabass, yellowtail	Pasteurellosis
16	ERM Vaccine	Salmonids	ERM Disease
17	Pasteurella Vaccine	Salmonids	Pasteurellosis
18	*Flavobacterium psychrophilum Vaccine*	Salmonids, FW species	Flavobacteriosis
19	Aeromonas hydrophila Vaccine	Salmonids	MAS Disease
20	Carp Erythrodermatitis	Carp species	Erythrodermatitis
21	*Renibacterium salmoninarum Vaccine*	Salmonids	Bacterial Kidney Disease
22	Piscirickettsia salmonis vaccine	Salmonids	piscirickettsiosis
23	aemiaGa Vaccine	Lobsters	aemiaGa
24	*Lactococcus garvieae Vaccine*	Rainbow trout, yellowtail	Lactococcosis

aquaculture industry including DNA and RNA virus diseases such as Epizootic Hematopoietic Necrosis (EHN), Koi Herpes Virus Disease (KHVD), Infectious Hematopoietic Necrosis Virus, Spring Viremia of Carp (SVC) and Viral Hemorrhagic Septicemia (VHS) [1,12].

A large number of research trials have been conducted for developing effective viral vaccines by companies and academic organizations, but only a few viral vaccines are licensed [9]. Currently available commercial viral vaccines for aquaculture are inactivated virus vaccines or recombinant protein vaccines. No live attenuated vaccines are currently licensed for use in aquaculture, only one DNA vaccine against IHN (Infectious hematopoietic necrosis) disease is available (Table 2) [11,20]. 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 [9].

Challenges and Prospects

Fish vaccines have become established, proved and cost-effective method of controlling infectious diseases in aquaculture. Vaccination can significantly reduce specific disease-related losses resulting in the reduction of antibiotics use. The existing vaccines can induce protection after a single administration until the fish are harvested, but actual protection mechanisms have not been investigated properly (Table 3) [9]. 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 [11]. Some commercial vaccines for fish consist of mixtures of two, three, four even five vaccine products. But all the antigens do not stimulate a 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 [9]. 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 of maternal immunity in fish also limits the possibilities to protect offspring by parental vaccination [11,15]. Advances in genome sequencing of pathogens can accelerate the opening of opportunities to investigate new generation vaccines such as subunit vaccine, DNA vaccine, the virus-like particle, and vector-vehicle vaccine. Recently, the genome of salmon and several other fish species have been fully sequenced [18]. These findings can lead to novel vaccine development strategies in near future [1,20]. Improvement in oral immunization with biodegradable microparticle-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 develop 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

Table 2. *Major infectious diseases of fish for which vaccines are not available [3,9,11,19,21-26].*

SL. No.	Name of Vaccine	Species vaccinated	Diseases prevented
1	IHN Virus Vaccine	Salmonids	IHN Disease
2	IPN Virus vaccine	Salmonids	IPN Disease
3	ISA Vaccine	Salmonids	ISA Disease
4	*Iridoviral disease Vaccine*	Red sea bream	Iridoviral disease
5	SVC Vaccine	Common carp	SVC Disease
6	KHV Vaccine	Koi carp	KHV Disease
7	Betanodavirus	Grouper	Betanoda virus disease
8	Carp Erythrodermatitis	Carp	Erythrodermatitis
9	Grass Carp Hemorrhage Disease Vaccine	Grass Carp	Grass carp hemorrhage disease
10	aemiaGa vaccine	Lobsters	aemiaGa
11	Nodavirus vaccine	Seabass	Viral Nervous Necrosis
12	Pancreas disease virus vaccine	Salmonids	Pancreas Disease

Table 3. *Commercially available vaccines against major infectious viral diseases of fish [3,9,11,19,21,22,25].*

Disease	Causative Agents	Fish Species Affected	Disease
Viral Disease	VHS Virus	Trout and flounder	VHS Disease
	VNN 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

animals. In the 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 freshwater and marine fish species to prevent bacterial and viral diseases of fish [17]. But Vaccines for protection against parasitic and fungal diseases have not yet been developed [11,18]. Currently available vaccines are based on simple empirically developed inactivated pathogens. A few recombinant subunit vaccines and DNA vaccines are also available. Limited knowledge of the immune systems of fish limits the development of vaccines based on non-empirical strategies [1,9]. Vaccines against intracellular bacterial and viral pathogens are one of the big challenges for the coming years. DNA vaccine can also play an important role in such cases [20-26]. New vaccination strategies, aquaculture expansion, and disease investigation center should be initiated [9]. Strong coordination should be created between pharmaceutical companies and academic research for a better development of live fish vaccines.

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