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Review Article

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Impact of *Aeromonas veronii* Infection in Freshwater Fishes and Its Threat to Mankind: A Review

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ABSTRACT:
The emerging pathogen *Aeromonas veronii* is extensively dispersed and can infect fishes, humans and animals. It is a broadly distributed gram-negative, facultatively anaerobic bacterium. It causes Epizootic Ulcerative Syndrome (EUS) and fish sepsis in several freshwater fishes such as tilapia, catfish, carp, and loach etc. The high mortality rates among commercial fish species leads to huge financial losses to the aquaculture sector. Antibiotics were once a successful preventative measure in this regard. However, the widespread use of antibiotics in recent years has resulted in antibiotic resistance. Probiotics, vaccines, and phytochemicals are some of the control measures that can be used in place of antibiotics. The present review will provide information about overview of *A. veronii* infection in fishes, its effect on both human and animal wellbeing, virulence, and its management approaches in aquaculture.

Keywords:
Bacterial infection, *Aeromonas veroni,* Aquaculture fishes, Host-pathogen interaction.

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1. INTRODUCTION

Aquaculture is one of the swiftly expanding food-producing industries, accounting for over 40% of global fish food production. It is spreading, expanding, and intensifying in nearly every region of this world. Aquaculture is more diversified than other agricultural sectors in terms of species, feeds, production methods, illnesses, products, and organisational structures (Yue & Shen, 2022). With the growing world population, consumer interest in aquaculture is expected to exceed 62% of total global production by 2030 (Ahmad *et al.,* 2021). However, the production of aquaculture is being hampered by a number of developing diseases caused by bacteria, viruses, fungus, amoebas, oomycetes, and other ectoparasites. Bacteria can survive in any aquatic ecosystem in the absence of their host, so bacterial disease has become an important obstacle to aquaculture (Klesius & Pridgeon, 2011).

Aeromonas which is a member of family Aeromonadaceae, is one such developing bacterial pathogen in aquaculture, inflicting harm to the health of freshwater species through acute or chronic illnesses (Thakur *et al,*. 2022). The *Aeromonas* causes mass mortality in fishes that cause financial losses in aquaculture sector

(Kaur *et al.,* 2020; Yu *et al.,* 2010). *Aeromonas* has a wide dispersion and had been obtained from various sources, including fresh water, vegetables, soil, fruits, processed food and sewage (Barger *et al.,* 2021). This genus of bacteria is recognized to naturally exist in aquatic habitats and commonly known as opportunistic pathogens (Lü *et al.,* 2016; Barger *et al.,* 2021). The *Aeromonas* lateral flagella are crucial for boosting cell attachment, biofilm formation, and invasion which help the bacteria to survive in harsh environments and develop pathogenicity (Gavin *et al.,* 2003). There are 36 species in the *Aeromonas* genus, including *A. veronii, A. sobria, A. caviae,* and *A. hydrophila* which are regarded as emerging pathogens, not only to fishes, amphibians, and reptiles, but also humans (Wahli *et al.,* 2005; Yu & Park., 2008; Fernández-Bravo & Figueras, 2020).

2. OVERVIEW OF *AEROMONAS VERONII* IN FRESHWATER FISHES

Oreochromis niloticus, also referred to as the aquatic chicken or the Nile tilapia, is one of the world's fastest-growing aquaculture species. Global tilapia production was projected to be 4.5 million tonnes in 2014, and by 2030, it is expected to reach 7.3 million tonnes, providing the majority of developing nations with an affordable source of protein (Bacharach *et al.,* 2016). In Egyptian fish farms, *Aeromonas veronii* appears to be the primary cause of mass mortality among *Oreochromis niloticus* (Latif *et al.,* 2019). Red tilapia also showed acute mortality due to *A. veronii* (Dong *et al.,* 2015). It was found that TiLV and *A. veronii* spontaneously co-infect a Malaysian red hybrid tilapia (*O. niloticus* × *O. mossambicus*). However, the issue might become worse if TiLV and other bacteria co-infected synergistically (Amal *et al.,* 2018). In juvenile *O. niloticus, A. veronii sobria* causes anorexia, abdominal bloating, skin pigmentation, bleeding spots, rotting of the tail and erosion of the caudal fin with a prevalence of 99.80% (Li & Cai, 2011).

Yellow catfish (*Pelteobagrus fulvidraco*) and channel catfish (*Ictalurus punctatus*) are commercially important freshwater-farmed species with a production rate of over 834 thousand tons in 2019 (Yu *et al.,* 2020). These species of catfish experienced widespread fatalities and epidemics of ulcerative conditions showing symptoms such as ulcerations in the skin, ascites, bleeding, hemorrhagic septicemia due to *A. veronii* (Zhai *et al.,* 2023). *Aeromonas veronii* has been found to be the cause of channel catfish mortality in Vietnam (Hoai *et al.,* 2019). In China and the Indo-Pakistan region, *A. veronii* was isolated from diseased catfish (Cai *et al.,* 2012). The primary signs of disease in farmed channel catfish have been recorded as skin ulcers and bleeding (Gui *et al.,* 2018). When ulcers develop on the skin of the fish due to *A. veronii*, some external bacteria, such as Kurthia, (*Kurthia gibsonii)* have also been isolated from infected mucosa in both diseased yellow and channel catfish (Preena *et al.,* 2019; Zhai *et al.,* 2023).

The common carp (*Cyprinus carpio*) is regarded as an important aquaculture species in many European and Asian countries because of its high adaptive capability to both environment and food (Parkos & Wahl, 2014; Choudhary *et al*. 2023; Thakur *et al*., 2025). In some European countries, common carp accounts for more than 80% of total fish farming (Rahman, 2015). *Aeromonas veronii* has been identified as the causative agent of disease outbreaks and mass mortality in *Cyprinus carpio* in Korea (Yu *et al.,* 2010). Chen et al (2019) also discovered *A. veronii* in diseased crucian carp in a Chinese fish farm (Chen *et al.,* 2019). A variety of clinical signs, such as gill congestion, hyphema, cutaneous hemorrhage, hemorrhages in the fins and operculum, abdominal swelling, abdominal congestion, hepatic portal redness, skin lesions (erythrodermatitis), intestinal swelling, dropsy symptoms are frequently present in *A. veronii* infected crucian carp (Yu *et al.,* 2010; Chen *et al.,* 2019). In addition to crucian carp, grass carp, and cyprinid fish also exhibit these symptoms when infected with *A. veronii* (Ran *et al.,* 2018).

Numerous studies have documented the tragic deaths and huge financial losses of ornamental fish from bacterial infections (Sahoo *et al.,* 2016; Lewbart, 2001). The most popular ornamental fish species worldwide are goldfish (*Carassius auratus*), zebra danio (*Danio rerio*), neon tetra (*Paracheirodon innesi*), angelfish (*Pterophyllum* spp.), discus (*Symphysodon* spp.) and guppy

(*Poecilia reticulata*). Over 14% of the traded fish is made up of guppy and zebra danio. Additionally, koi fish (*Carassius auratus*), which are primarily exported from Japan, make up 10% of world trade. *Aeromonas veronii* is a significant bacterial pathogen and also a symbiont in the digestive tract of zebrafish (Bates *et al.,* 2006; Silver *et al.,* 2011). In ornamental fish farms, the prevalence of skin ulcerative illness caused by *A. veronii*, which is characterised by internal and external bleeding is increasing (Sun *et al.,* 2016). Strongly virulent to ornamental fish, *A. veronii* causes glomerulus hemorrhage, necrosis of the hepatic cell, leukocyte infiltration of gill filaments, and skin ulcerative syndrome (Song *et al.,* 2017). Goldfish farms in India suffered significant losses due to *A. veronii* infection. These infected goldfish displayed symptoms such as anorexia, a swollen abdomen, tail rot, and cutaneous haemorrhage (Shameena *et al.,* 2020).

Table 1: Different species of freshwater fishes infected by *A. veronii*

S. No.	Affected Species	Common name	Diseased caused	symptoms	Reference
1	*Oreochromis niloticus*	Nile tilapia	Hemorrhagic septicemia	Anorexia, lethargy, detached scales, abdominal bloating, skin pigmentation, bleeding spots, rotting of the tail and erosion of the caudal fin	Li and Cai, 2011
2	*Pelteobagrus fulvidraco*	Yellow catfish	Epizootic ulcerative syndrome	Abdominal enlargement and body surface ulcers	Fu *et al.,* 2021
3	*Ictalurus punctatus*	Channel catfish	Hemorrhagic septicemia	Skin ulcers and bleeding	Yang *et al.,* 2017; Gui *et al.,* 2018
4	*Ctenopharyngodon idella*	Grass carp	Bacterial septicemia	Abdominal ascites, bleeding from the skin and internal organs	Wu *et al.,* 2021
5	*Cyprinus carpio*	Common carp	Motile Aeromonad Septicemia (MAS)	Abdominal congestion, hepatic portal redness, abdominal distention, skin lesions and abdominal swelling	Ran *et al.,* 2018
6	*Carrasius auratus gibelio*	Crucian carp	Haemorrahgic septicemia	Gill congestion, hyphema, cutaneous hemorrhage,	Chen *et al.,* 2019

				intestinal swelling, dropsy symptoms	
7	*Carrasius auratus*	Goldfish	Epizootic ulcerative syndrome	Skin lesions, anorexia, swollen abdomen, exophthalmia, fin and tail rot, and cutaneous haemorrhages	Song *et al.*, 2017; Shameena *et al.*, 2020
8	*Odontobutis potamophila*	River snakehead	Epizootic ulcerative syndrome	Hemorrhage on fins, ulceration on the abdomen	(Liu *et al.*, 2022)
9	*Astronotus ocellatus*	Oscar	Motile Aeromonad Septicemia (MAS)	Infectious abdominal dropsy, anorexia, lethargy, scale protrusion and petechial haemorrhage	Sreedharan *et al.*, 2011
10	*Myxocyprinus asiaticus*	Chinese Sailfin Sucker	Motile Aeromonad Septicemia (MAS)	Rotting fins, red ascitic fluid, liver and kidney swelling, hyperaemia, a black swollen spleen, pale gills, cloacal pore swell- ing and intestinal inflammation.	Li *et al.*, 2019
11	*Ophiocephalus argus*	Snakehead fish	Enteritis Epizootic ulcerative syndrome(EUS)	Enteritis- Loss of appetite, red blotches on abdomen, congested fins, swollen anus, and ascites. EUS- Ulcers on skin, fins, and abdomen, lethargy, swollen abdomen and bleeding.	Wang *et al., 2020;* Zheng *et al.*, 2012
12	*Anabas testudineus*	Climbing perch	Epizootic ulcerative syndrome(EUS)	Swollen abdomen, ulcers on skin, skin pigmentation,	Ehsan *et al.*, 2023

				bleeding spots, rotting of the tail	
13	*Micropterus salmoides*	Largemouth bass	Epizootic ulcerative syndrome(EUS)	Gill hemorrhage, fin hemorrhage, dorsal and abdomen ulcers , and rotting fins	Pei *et al.,* 2021
14	*Labeo rohita*	Rohu	Motile Aeromonad Septicemia (MAS)	Haemorrhage, rotting fins and gross lesions.	Tyagi *et al.,* 2022
15	*Paramisgurnus dabryanus*	Loach	Hemorrhagic septicemia	Ulcers on the body surface, hemorrhages under the skin, darkening of liver, necrosis of liver, l lesions in the liver, spleen, kidney and muscle	Du *et al.,* 2020
16	*Procambarus clarkii*	Crayfish	Motile Aeromonad Septicemia (MAS)	Weakness of limbs, slow movements, lethargy, gill rot, and weak stress ability	Yang *et al.,* 2022

3. *A. VERONII* AS A PUBLIC HEALTH ISSUE

Zoonotic disease are those infectious disease which are transmitted from an animal host to a human host (Han *et al.,* 2016). The majority of fish-related zoonotic diseases spread to humans by eating raw or improperly cooked fish and drinking water contaminated with sick fish (Ziarati *et al.,* 2022). This pathogen can still invade through bruises, which can occur while handling fish aquaria, or while dealing with diseased fish (Gauthier, 2015). The fish pathogen *A. veronii* can also infect humans with weak immunity causing gastroenteritis, wound infections, and septicemia (Fernández-Bravo & Figueras, 2020). These patients may also experience some other symptoms like nausea, abdominal pain, diarrhoea, and vomiting (Vila *et al.,* 2003). Potential health risk arises from the abundance of *Aeromonas* in foods and drinking water. In warm weather, humans are most likely to contract stomach illnesses from *A. veronii* (Yuwono *et al.,* 2021). *Aeromonas veronii* prevalence varies geographically and is associated with poor sanitation practices in less developed areas (Tsai *et al.,* 2015). Mohan et al. (2017) evaluated 50 samples of diarrheal stools from 1,595 patients to identify *Aeromonas;* the biochemical analysis of 35 strains revealed that *A. biovar sobria* and *A. veronii biovar veronii* were the most prevalent species (Mohan *et al.,* 2017). *Aeromonas veronii* was found in abundance in 193 of the 4,529 diarrheal patient samples collected from 16 institutions in Shanghai, China (Li *et al.,* 2015). According to a study conducted in Taiwan, 76 cases per million individuals occurred between 2008 and 2010 (Wu *et al.,* 2014). At Galdakao-Usansolo Hospital in Spain from January 2015 to December 2017, 98 patients were enumerated who had positive stool cultures for *A. veronii*, giving an estimated incidence of 32 cases for every 105 individuals annually (Elorza *et al.,* 2020). According to a study of 109 clinical isolates of *Aeromonas* from patients with diarrhoea, *A. veronii* was the most common species in both Mexico and Spain

(Aguilera-Arreola *et al.,* 2007). Both healthy individuals and individuals on immunosuppressive medications have had genitourinary tract infections brought on by *A. veronii* (Chao *et al.,* 2012). Although a majority of patients recover without medical intervention, those who have severe symptoms and persistent illnesses frequently need hospitalization and antibiotic therapy (Chen *et al.,* 2015).

4. ANIMAL HEALTH CONCERNS RELATED TO *A. VERONII*

Aeromonads can frequently be retrieved from vertebrates as well as other hosts like insects. Pigs, poultry, cattle, sheep, buffalo, and fish are just a few of the food animals and products that have been shown to have *A. veronii* (Gowda *et al.,* 2015). A number of aquatic fauna can be infected by *A. veronii* which mainly causes organ bleeding, skin ulcers, and severe ascites. Various *M. nipponensis* farms, experienced fatalities from June to October of the year 2019 in Xinghua county, Jiangsu province, China. These sick *M. nipponensis* had red gills, weakness, and a poor appetite as symptoms of their illness. Results showed that *A. veronii* was the pathogen responsible for *M. nipponensis's* high mortality rate (Gao *et al.,* 2020). *Macrobrachium rosenbergii* could die in large numbers as a result of the *A. veronii* (Sung *et al.,* 2000). In the Al-Ahsaa area, marsh frogs have experienced outbreaks of Ulcerative Syndrome brought on by *A. veronii bv. veronii*, which is especially harmful to *P. ridibundus* larvae (Khalifa *et al.,* 2021). *Aeromonas veronii* caused outbreaks of respiratory disease in a sheep breeding farm in Shaanxi, China, showed 2.53% (15/594) of sheep with respiratory (clinical) symptoms like dyspnea, nasal discharge, wet cough, fever, and progressive emaciation disease (Miao *et al.,* 2023).

5. PATHOGENICITY

Aeromonas veronii is known to cause Epizootic Ulcerative Syndrome (EUS) or Motile Aeromonad Septicemia (MAS) characterized by glomerulus hemorrhage, swollen abdomen, skin pigmentation, fin and tail rot, dropsy symptoms, necrosis of the hepatic cell, leukocyte infiltration of gill filaments, and skin ulceration (Li & Cai, 2011; Song *et al.,* 2017; Fu *et al.,* 2021). Previous research have shown that a number of connected variables help to make *A. veronii* pathogenic. There are recognized virulence characters, including hemolytic and cytotoxic activity, toxins, iron ion acquisition systems, proteases, outer membrane proteins, secretion systems, quorum, and motility-related factors (Qin *et al.,* 2022). Another link between pathogenicity and virulence is the presence of the cytotonic enterotoxins, aerolysin, glycerophospholipid: cholesterol acyltransferase, serine, lipase, and protease genes which were identified in an infected crucian carp (Hossain *et al.,* 2018; Chen *et al.,* 2019). The most frequent virulence genes identified in an infected tilapia are lipase (lip), elastase (ahp), hemolysin (hyl), and aerolysin (aer) (Gohary *et al.,* 2020). These virulent genes contribute to the pathogenicity of *A. veronii* by encoding proteins and toxins (Zhu *et al.,* 2022). The enterotoxin-producing genes act and alt, aerA, as well as hemolytic toxin-producing genes hlyA, all have an important role to play in the virulence of *A. veronii* (Sreedharan *et al.,* 2013). The aer gene is a crucial gene linked to aerolysin while the fla gene is crucial for the ability of motility and cell adhesion (Abrami *et al.,* 2003; Sen and Rodgers, 2004). The gene hly is important for the cytotoxic effects including erythrocyte lysis whereas the vipB gene plays an important role in virulence, adhesion ability, motility, and resistance to oxidative stress (Gao *et al.,* 2013; Song *et al.,* 2023).

6. HOST-PATHOGEN INTERACTION

Various innate immune system tissues and functions have been studied in *M. salmoides*, a fish species with an adaptive immune system that can generate a targeted antibody response against infections (Zhu *et al.,* 2022). Specifically, hemolysin produced by *A. veronii* caused injury to the host spleen. Several immune-related signalling pathways are favoured in the host during infection, including Toll-Like Receptor Signaling Pathway, T Cell Receptor Signaling Pathway, and Cytokine-Cytokine Receptor Interaction (Qin *et al.,* 2023). Figure 1 show the various pathways involved in the host's response towards infection. Toll like receptor pathway with the Tumor necrosis factor (TNF), Retinoic acid-inducible gene (RIG)-like receptor (RLR) and nuclear factor kappa B (NF-κB) are involved in inflammatory response generated from the host. To begin innate immune responses, TLRs are very essential and are the first Pattern recognition receptor (PRRs) to be described. It consists of three components: a transmembrane region, a C-terminal cytoplasmic TIR domain that contacts adaptor molecules, and an N-terminal ectodomain with LRR (Leucine-rich repeat) that is necessary for PAMP (Pathogen-associated molecular pattern) recognition (Li *et al.,* 2019). IL15 is a key molecule that regulates the growth of dendritic cells, NK cells, and T-cells as well as taking part in some immune-related signal transmission pathways, which plays a significant role in innate and adaptive immunity (Bae *et al*., 2013).

In addition to being the main antibody in the primary reaction, IgM plays a crucial role in the fish's adaptive immune response (Defoirdt *et al.,* 2011). TNF-α and IL-1β can be released during apoptosis, which is induced by the hypoxia-inducible factor (HIF) (Zhang *et al.,* 2021). After infection with *A. veronii*, Zhu et al. (2022) discovered that there was a significantly higher level of IgM expression in the liver and spleen as well as higher levels of HIF-1 expression. Caspase-3 is a vital executory enzyme and apoptosis's last effector (Zhu *et al.,* 2022). The host immunological defence system was activated and these immune-related genes were impacted by *A. veronii*, providing a plausible basis for host-pathogen interactions (Zhang *et al.,* 2019).

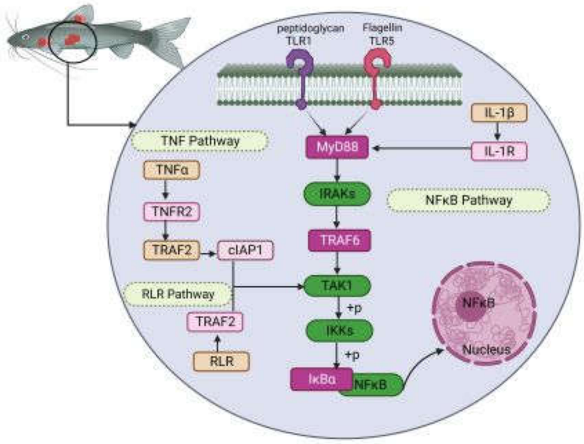

Figure 1: TLR pathway that induces the inflammatory response in the host.

TLR1 and TLR5 are located on the cell surface. TLR1 receives peptidoglycan while TLR5 receives flagellin produced by A. veronii. MyD88 is an adaptor molecule that interacts with IRAK-4, which has active IRAK-1 and IRAK-2. The IRAKs then separate from MyD88 and engage with TRAF6, TRAF6 will respond to TAK1 and IKK, after the deduction of immune signals from MyD88 to TRAF6. Activated IKK phosphorylates IκBa which is degraded via ubiquitin mediation, causing dissociation of NF-κB, which activates the NF-κB pathway. The activated NF-κB binds to target genes, proinflammatory cytokines genes (TNF-a, IL-1β), and IκBa after it translocated to the nucleus. TNFa and IL-1β production are both strengthened by NF-κB activation, and both of them in turn activate NF-κB via TNFRs and IL-1R. (Modified Li et al., 2019)

7. CONTROL AND MANAGEMENT

Fish grown in ponds with recirculation are commonly affected by infections caused by *A. veronii* bacteria, are managed using antibiotics (Saavedra *et al.,* 2004). As a result, antibiotic tolerance and antimicrobial residues could consequently emerge in aquaculture (Vivekanandhan *et al.,* 2002). Apart from being chemical pollutants, antibiotics also impose a selection pressure that promotes the spread of various antibiotic resistance genes (ARG), endangering human health (Kemper, 2008). Tekedar et al (2020) reported resistance genes in *A. veronii* including chloramphenicol and florfenicol resistance gene (*floR*), beta-lactamase resistance genes (*imiS* and *ampS*), macrolide resistance genes (*mcr-3* and *mcr-7.1*), acetyltransferase genes, tetracycline resistance genes [*tet(34), tet(35),* and *tet(E)*], and streptogramin B resistance *vat(F)*. These genes help *A. veronii* to be resistant towards a number of antibiotic drugs such as phenicol, tetracyclines, sulfamethoxazole, beta-lactam class and macrolides etc. (Tekedar *et al.,* 2020). *Aeromonas veronii* strains exhibit resistance to drugs that were often used in aquaculture, including penicillin G, chloramphenicol, levofloxacin, trimethoprim, oxacillin, tetracycline, norfloxacin, sulfonamide, ofloxacin, cefazolin, and ciprofloxacin but found to be susceptible to cefoperazone, cephradine, cefuroxime, cefoxitin, chloramphenicol, cefepime, cefotaxime, clarithromycin, gentamycin, streptomycin, tobramycin (Sun *et al.,* 2016). Tetracycline resistance is shown by *A. veronii* isolated from catfish (Nawaz *et al.,* 2006). Penicillin resistance is shown by an extract of *A. veronii* from moribund freshwater ornamental fish (Sreedharan *et al.,* 2013). Therefore, antibiotics are no longer a good option to treat bacterial diseases in aquaculture system because of the emergence of antibiotic resistance of pathogens. Probiotics, vaccines, and phytochemicals are a few non-antibiotic strategies that can be used in response to the rising antibiotic resistance among *A. veronii* strains.

8. PROBIOTICS

It is generally recognized that probiotics have the ability to influence aquatic animals' innate immune systems (Figure 2). Probiotics are living bacteria that, when taken in the right quantities, can improve the immune and digestive systems, increase viability, promote development, and benefit the host (Munir *et al.,* 2016). To reach the intestinal tract undamaged and continue to be alive, the optimal probiotic should be resistant to acid and bile salts and nonpathogenic (Boyle *et al.,* 2006). Many endogenic bacteria, including *Lactobacillus*, *Bacillus* (*B. subtilis* and *B. velezensis*), and yeast have gained attention as prospective probiotic contenders in the aquaculture industries in recent years due to their high level of antagonistic activity, availability, and exo-enzyme synthesis (Banerjee & Ray, 2017). As feed additives, *Lactobacillus, Bacillus* and yeast can colonise the digestive tract and maintain the microenvironmental balance in aquatic animals, stimulate development, enhance immunity, and increase resistance towards diseases (Zhang *et al.,* 2022; Brar *et al,* 2023). *Bacillus velezensis* is a heterotypic synonym of *B. amyloliquefaciens*. *B. velezensis* combats *A. veronii* by secreting compounds like surfactins, bacillomycin, amylocyclicin and fengicins (Fan *et al.,* 2017). In a study by Yang et al. (2022), *B. subtilis* CK3 was found to be able to inhibit the growth of *A. veronii* in crayfish (Yang *et al.,* 2022). Fish are benefited from the probiotic effects of LAB like *Pediococcus pentosaceus, Lactobacillus paraplantarum, Lactococcus lactis, and Enterococcus faecalis* (Martinez *et al.,* 2017; Meidong *et al.,* 2021; Heo *et al.,* 2013; Banos *et al.,* 2019). In order to increase probiotics' effectiveness in various animals (species and sizes) and environmental conditions, additional research should be conducted to identify the most suitable procedures and dosage levels (Di *et al.,* 2019). In order to avoid partially suppressing the immune responses, Farias et al.(2016) cautioned against feeding too many probiotics (Farias *et al.,* 2016). There are still gaps in our understanding of the fundamental mechanisms underlying the probiotics' beneficial and potentially harmful effects (Amenyogbe *et al.,* 2020). It is important to consider the dangers associated with probiotics producing antibiotics and transmission of antibiotic resistance genes to pathogenic bacteria (Martínez Cruz *et al.,* 2012).

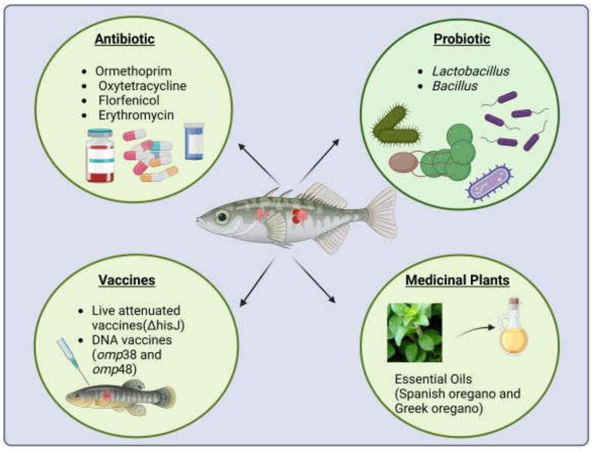

Figure 2: **Different types of control measures used in aquaculture against *A. veronii***

Control strategies for bacterial infections caused by Aeromonas cover antibiotics, probiotics, vaccines and Herbal extracts.

9. VACCINES

It is generally known that vaccinations reduce the need for antibiotics and other antimicrobials and are a sustainable method of preventing serious fish infections. Currently, a variety of vaccinations, including subunit vaccines, DNA vaccines, live attenuated vaccines (LAVs), and formalin-killed vaccines are frequently used to prevent *A. veronii* infections (Huang *et al.*, 2014; Kong *et al.*, 2019). Vaccines have several benefits, including improved immunity, lower costs, reduced toxicity and drug side effects (Wu *et al.*, 2012). The effectiveness of commercial inactivated vaccines against MAS for some freshwater fish species depends entirely on the particular strain of the pathogenic bacteria (Ma *et al.*, 2019). Despite being approved in North America and Chile, live attenuated vaccines for catfish and salmonids are currently not commercially viable in other nations due to a lack of regulations governing their secure use in aquaculture (Adams, 2019). Zhang et al (2020) found a live attenuated vaccine called " ΔhisJ " which is ideal for use in the development of a safe and effective immunisation against *A. veronii* infection in loach aquaculture (Zhang *et al.*, 2020). OMPs, or outer membrane proteins, (OmpF,OmpC, OmpR, OmpTS, Omp38, OmpA1, Omp48, OmpW, Tdr, 46 kDa maltoporin, and S-layer protein) are highly immunogenic bacterial components. These OMPs are targeted by subunit vaccines for MAS because they have exposed cell epitopes, found at the host-bacterial interface and provide cross-protection due to their conserved antigenic determinants (Abdelhamed *et al.*, 2016). Iron-related protein A0KIY3, ATPase protein, fimbrial proteins Fim and FimMrfG, G-protein coupled receptor—GPR18, proaerolysin and hemolysin co-regulated protein—Hcp are additional antigenic proteins that could be used as recombinant protein vaccines (Pridgeon & Klesius, 2013; Zhang *et al.*, 2013; Guo *et al.*, 2018). Because subunit vaccines lack the components necessary to stimulate the immune system as effectively as a whole-cell vaccine, their capacity to elicit a potent immune response is constrained. Subunit vaccines are additionally expensive and unaffordable to scale up in developing nations due to the production and purification process (Dien *et al.*, 2023). By simulating the natural route of infection, DNA vaccination can produce protection against intracellular pathogens. DNA vaccination is a type of genetic immunisation that uses a gene or genes encoding protective antigens (Dien *et al.*, 2023). DNA vaccines using *Omp*38 and *Omp*48 genes show increased immune response in spotted sandbase (Vazquez-Juarez *et al.*, 2005). *OmpAI* and lactic acid bacteria can combine to create a dietary vaccine for carp against *A.*

veronii infection (Zhang *et al.,* 2018). The oral administration of the recombinant *L. casei* vaccine can successfully generate fish to establish cellular and humoral immunity that can colonize the intestine (Chen *et al.,* 2022). Furthermore, using DNA vaccine raises the additional safety concern of the link between intramuscular DNA vaccine administration and the onset of myositis, which needs to be clarified in further research (Dien *et al.,* 2023).

10. PHYTOCHEMICALS

To combat serious infections brought on by *Aeromonas* spp., botanicals and essential oils have also been utilised. More and more people are becoming interested in the antibacterial properties of natural materials and products, like the essential oils (EOs) obtained from medicinal aromatic plants (MAPs) (Cunha *et al.,* 2018). Because of their strong insecticidal, antiviral, antibacterial, and antifungal properties along with significant antioxidant activity, EOs stick out as effective alternative natural agents in fish aquaculture and animal husbandry for the prevention or treatment of a variety of infectious disorders (Elabd *et al.,* 2017). To reduce bacterial infections during fish rearing, EOs have been added to fish feed with encouraging results (Awad & Awaad, 2017). Few studies have examined the effectiveness of EOs and each of its separate elements against *A. veronii* to date (Anastasiou *et al.,* 2019). The EOs with the highest phenolic/carvacrol content are the most potent ones against *A. veronii*. More specifically, the EOs from savoury, Greek, and Spanish oregano are the most effective growth inhibitors of this particular fish illness (Mandalakis *et al.,* 2021). These pure EOs' increased effectiveness is most likely brought on by their higher concentrations of powerful chemicals including carvacrol (32.8% to 72.0%), y-terpinene (5.3 to 34.0%), and p-cymene (6.5 to 11.9%). The most lethal EO is pure Spain oregano, which has a carvacrol content of 42.0%, not Greek oregano, which has a carvacrol content of 72.0%. So, it is evident that these EOs' ability to kill bacteria may be significantly influenced by other minor components and how they interact with the major components (Anastasiou *et al.,* 2019). It has been demonstrated that the Lamiaceae family members, especially MAPs rich in carvacrol, have beneficial antibacterial properties (Cunha *et al.,* 2018). By affecting bacterial cell shape and deforming organelles, EOs primarily penetrate and operate on bacterial membrane and cytoplasm to impede their action mechanisms (Calo *et al.,* 2015). A variety of additional common vegetables, beans, and conventional herbs have been investigated for use in aquaculture as immunostimulants and antipathogens to manage *Aeromonas* infections in aquaculture including *Ocimun basilicum, Ocimum sanctum*, *Moringa oleifera*, *Mucuna pruriens*, *Aegle marmelos*, *Cynodon dactylon*, *Urtica dioica* and *Adrographis paniculata* (Kaleeswaran *et al.,* 2011; Das *et al.,* 2015). Combinations of various plant-based ingredients have demonstrated the potential to treat MAS in addition to the use of a single phytobiotic. In comparison to the group not given any medicinal herbs, the combination of huangqi root extract (*Astragalus membranaceus*) and Japanese honeysuckle flower extract (*Lonicera japonica*) reduced the mortality rate of Nile tilapia by 55% when administered orally (Ardó *et al.,* 2008) New phytochemical plants and novel combinations of probiotic- and plant-based products should be discovered through further research, which will also aim to improve the extraction process and standardise feed formulation, dose, and duration.

11. CONCLUSION

Globally widespread pathogen *Aeromonas veronii* has been one of the most significant bacteria influencing aquaculture and infects both humans and animals, causing heavy economic losses. The threat of an *A. veronii* infection in freshwater fish is constant to a number of fishes because they are surrounded by an *Aeromonas* environment. *Aeromonas veronii* may be hazardous to public health, particularly for individuals with weak immunity and those who are frequently exposed to infected fish. The control of *A. veronii* infection relies heavily on antibiotics. The improper use of antibiotics leads to the development of antibiotic-resistant genes in *A. veronii*. As a result, this pathogen is no longer susceptible to a number of antibiotics. Therefore, we ought to choose non-antibiotic tactics like probiotics, vaccinations, and phytochemicals. However, these techniques still need to be studied further to increase their effectiveness and to get rid of any potential side effects. This review also omits some non-antibiotic strategies based on bacteriophage, omics, and nanobubble.

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