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Bacteriophage Therapy For *Aeromonas Hydrophila* Control In Freshwater Aquaculture

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Abstract

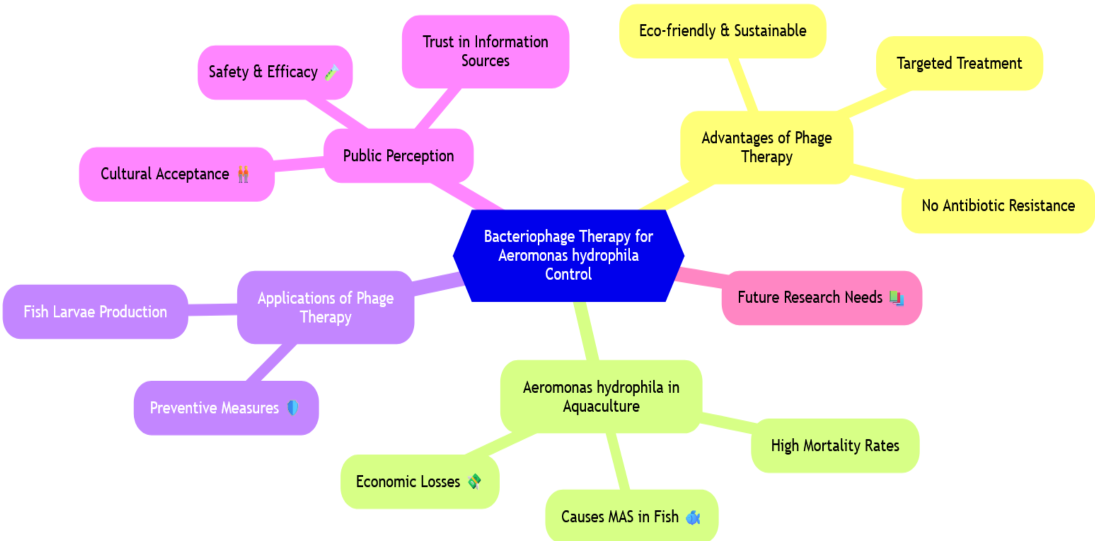
Due to bacterial infections, especially from *Aeromonas hydrophila*, a main pathogen in freshwater aquaculture, global aquaculture suffers significant difficulties. Diseases, including motile aeromonad septicaemia (MAS), which this bacterium produces, have substantial death rates and financial losses. Using antibiotics extensively to fight *A. hydrophila* has resulted in the development of antibiotic-resistant strains, therefore reducing the efficacy of therapy and generating public health issues. Consequently, there is an increasing demand for substitute, environmentally acceptable, sustainable methods to control bacterial diseases. Promising is bacteriophage therapy, in which particular bacteria are targeted and killed using viruses (bacteriophages). Phages have great selectivity, infecting just the intended bacteria, and they could fight strains resistant to many drugs. Phages can also self-replicate at the infection site, therefore reducing ecological disturbance and causing a weak immunological reaction in fish. The promise of phage therapy as a focused substitute for antibiotics in aquaculture in the control of *A. hydrophila* is investigated in this review. It goes over the benefits of phage therapy over conventional antibiotics, summarises present studies, and outlines future research requirements. The application in aquaculture is the public view of bacteriophage treatment, including elements of safety, efficacy, and cultural acceptance.

Keywords: Bacteriophage therapy, *Aeromonas hydrophila*, Antibiotic resistance, Aquaculture, Public perception

Introduction

Global aquaculture, crucial for meeting seafood demand, faces significant challenges, particularly from bacterial diseases. *Aeromonas hydrophila*, a common and harmful bacterial pathogen, is a major threat to freshwater aquaculture. This bacterium causes diseases like motile aeromonad septicaemia (MAS), resulting in high fish mortality and economic losses.Extensive antibiotic use to combat *A. hydrophila* has unfortunately led to a widespread increase in antibiotic-resistant bacteria. This resistance limits treatment effectiveness and poses risks to both animal and human health. Therefore, there's a critical need for new, sustainable, and eco-friendly ways to manage bacterial infections in fish farming.Bacteriophage therapy, using viruses (bacteriophages, or phages) to target and kill bacteria, is a promising alternative. Phages infect and destroy specific bacteria without harming other organisms. This review explores the potential of phage therapy to control *A. hydrophila* in aquaculture. It discusses the benefits of this targeted approach compared to traditional antibiotics, reviews current research, and considers future research needs.*A. hydrophila* is a significant freshwater bacterial pathogen, causing hemorrhagicsepticemia and ulcerative conditions in fish, resulting in economic losses (Prasad & Qureshi, 1994; Qureshi et al., 2000; Parvez & Mudarris, 2014). The bacterium is Gram-negative, motile, rod-shaped, facultative anaerobic, oxidase-positive, and glucose-fermenting (Austin & Austin, 2012). Disease outbreaks caused by *A. hydrophila* can lead to high mortality rates, with reports of over 75% mortality among Indian major carps (Prasad & Qureshi, 1994).

Figure 1: Graphical Abstract: Bacteriophage Therapy for Controlling *Aeromonas hydrophila* in Freshwater Aquaculture



The Problem: Antibiotic Resistance

The widespread use of antibiotics in aquaculture to circumvent these infectious diseases has driven the emergence of antibiotic-resistant *A. hydrophila* (Cabello, 2006; Defoirdt*et al.*, 2007; Zhang *et al.*, 2020), diminishing treatment effectiveness and raising public health concerns regarding the transfer of resistance genes (Ghan*et al.*, 2021). Resistance to antibiotics such as chloramphenicol, erythromycin, kanamycin, tetracycline, rifampicin, and novobiocin has been reported (Vivekanandhan*et al.*, 2002).

Bacteriophage Therapy: A Targeted Alternative

Bacteriophage therapy offers a targeted alternative. Phages are viruses that infect and kill specific bacteria. Lytic phages, of primary interest, replicate within the bacterial host, causing lysis and cell death. During lysis, 20-500 virion particles are released at a time due to the action of enzymes lysine and holin (Carlton *et al.*, 1999).Phages exhibit high host specificity, typically infecting only the targeted bacterial species, thus minimizing disruption to the aquaculture ecosystem (Sulakvelidze*et al.*, 2001). They also self-replicate at the infection site (Gandham, 2015; Morrison & Rainnie, 2004), and new phages can be isolated relatively quickly to target resistant bacteria (Morrison & Rainnie, 2004). Phages are abundant in nature (Irshad *et al.*, 2012), and classified into 13 families based on morphology, type of nucleic acid and presence or absence of an envelope or lipid. About 96% are tailed phages, order Caudovirales with three families *Myoviridae, Siphoviridae,* and *Podoviridae* (Maniloff& Ackermann, 1998). Phage particles are composed of two different types of polypeptide chains, which vary from species to species. Two types of proteins identified in phages are the major protein and minor protein, which are also denoted as B protein and A protein and encoded by gene 8 and gene 3, respectively. The genome of DNA bacteriophage normally contains glucosylated 5, hydroxyl-methyl-cytosine rather than cytosine. The strong confinement of bending of the entire genome inside the viral capsid impose force which is very high 50 PN (Kindt *et al.*, 2001, Smith *et al.*, 2001 and Evilevitch *et al.*, 2003).Furthermore, phages generally elicit a weak immune response in fish (Prasad *et al.*, 2011) and can be used either independently or in conjunction with other antibiotics to help reduce the development of bacterial resistant (Kutter &Sulakvelidze, 2005). The narrow host range of bacteriophages avoids activity against non-targeting bacterial species (Sulakvelidze*et al.*, 2001). Phages are effective against multidrug-resistant pathogenic bacteria and have self-limitation, meaning that the number of phages remain in very low level after killing the targeting bacteria (Nakai and Park, 2002). Phages could be administered through any route (bath, oral, IM, IP under experimental condition) hence very easy in the field of application (Prasad *et al.*, 2010 and 2011).

Potential Applications

Phage therapy can be applied preventively, such as during larvae production, to improve overall fish production and sustainability.

Public Perception

In addition to the direct benefits to aquaculture, public perceptions of novel therapeutic interventions are important. Factors such as perceived safety and efficacy (Betsch *et al.*, 2018), trust in information sources (Freimuth *et al.*, 2001), risk-benefit assessment (Jansen *et al.*, 2007), social and cultural factors (Hauser &Joussaume, 2022), and clear communication (Jacobson *et al.*, 2010) influence acceptance.

Conclusion

In conclusion, phage therapy presents a promising, sustainable, and environmentally friendly approach to controlling *A. hydrophila* infections in freshwater aquaculture. It offers a targeted alternative to antibiotics, addressing the critical issue of antibiotic resistance. Further research is needed to fully explore its potential and facilitate its application in aquaculture.

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