



Bacterial Virulence: How Invisible Microbes Outsmart Fish Defenses

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INTRODUCTION

Bacterial virulence factors play a central role in the initiation and progression of infectious diseases, exerting devastating effects on the aquaculture industry worldwide (Praveen Kumar et al., 2020; Rasmussen-Ivey et al., 2016). Disease outbreaks caused by bacterial pathogens not only result in mass mortalities but also lead to chronic infections, reduced productivity, and significant economic losses. Virulence factors are extracellular, surface-associated, or secreted molecules produced by pathogenic microbes that enable them to induce disease, establish themselves within the host, and weaken host defense mechanisms depending on their pathogenic nature (Duport et al., 2019). The virulence of bacteria is influenced by multiple factors, including the number of infecting microorganisms, the route of entry into the host, environmental stressors, and the efficiency of the host's immune response (Praveen Kumar et al., 2020).

Bacterial virulence factors (BVF) are specialized molecules that allow pathogens to colonize host tissues, invade cells, evade immune responses, and damage host organs at the cellular and systemic levels (Rasmussen-Ivey et al., 2016). These virulence factors can be broadly categorized into (i) **surface-associated structures**, (ii) **secreted products**, and (iii) **nutrient acquisition systems (Figure 1)**. Surface membrane proteins, such as adhesins including pili (fimbriae) and non-fimbrial adhesins, facilitate the initial attachment of bacteria to host epithelial cells, a critical step for successful colonization and invasion (Jozwick et al., 2019). Capsules, composed primarily of polysaccharides, surround the bacterial cell and confer anti-phagocytic properties that protect pathogens from host immune defenses (Zhang et al., 2019).

Secreted virulence products mainly include toxins—exotoxins and endotoxins—that alter the host cellular environment, disrupt physiological processes, and mediate host–pathogen interactions (Duport et al., 2019). Additional virulence components include invasion factors that promote tissue penetration and dissemination, often resulting from bacterial growth by-products, tissue-degrading enzymes, and immune-mediated pathogenesis (Rasmussen-Ivey et al., 2016). Many pathogenic bacteria also possess anti-phagocytic factors and specialized mechanisms for intracellular survival, allowing them to persist within host cells and evade immune clearance.

Antigenic heterogeneity, achieved through antigenic and phase variation, further enables bacteria to modify surface antigens and escape immune recognition (Rasmussen-Ivey et al., 2016). Iron acquisition represents another critical virulence strategy, as bacteria secrete siderophores or express specific receptors to capture iron from host molecules, ensuring survival and proliferation in iron-limited host environments (Lange et al., 2020). Moreover, the increasing ability of bacterial pathogens to resist antibiotics and tolerate host immune responses has emerged as a major challenge in aquaculture disease management.

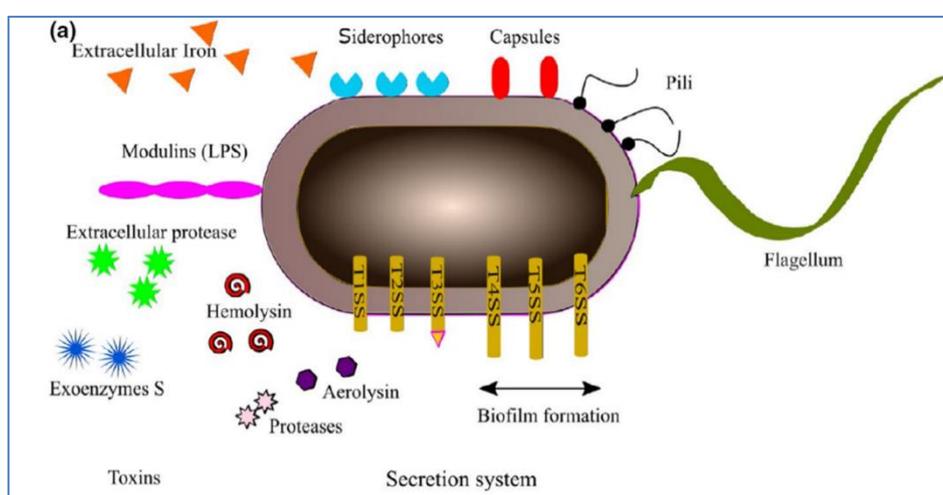


Figure 1. Major bacterial virulence factors involved in fish infections, including adhesion, immune evasion, toxin production, nutrient acquisition, and host tissue invasion.

1. Sticking to the Host: Adhesins and Motility

The first step in infection is attachment. Bacteria use adhesins, which are surface molecules made of proteins or polysaccharides, to firmly bind to fish tissues such as gills, skin, or the intestinal lining. These adhesins may be present as fimbriae (pili), capsules, or surface proteins and often interact with **host epithelial receptors and mucus glycoproteins**. Many fish pathogens are also equipped with flagella, whip-like structures that enable movement through water and mucus layers. Beyond motility, flagella play a role in immune activation and virulence. In pathogens like *Aeromonas* spp., *Listonella anguillarum*, and *Yersinia ruckeri*, flagella help bacteria reach

target tissues and establish infection (Jozwick et al., 2019).

2. Biofilms: A Safe House for Bacteria

Once attached, bacteria often form biofilms—complex communities enclosed within a protective extracellular matrix. Biofilms allow pathogens to survive harsh environmental conditions, resist antibiotics, and escape immune responses. In aquaculture systems, biofilms formed by *Aeromonas* and *Edwardsiella* species are particularly problematic, as they persist on tank surfaces and fish tissues, contributing to chronic infections and treatment failure (Jahid & Ha, 2014; Arunasri & Mohan, 2018).

3. Capsules and Cell Wall Components: Hiding from Immunity

Many bacterial pathogens are surrounded by capsular polysaccharides (CPS) that act as invisible shields. Capsules prevent recognition by immune cells and reduce phagocytosis. In fish pathogens like *Streptococcus agalactiae* and *Aeromonas* spp., capsules significantly enhance survival within the host (Zhang et al., 2019; Rasmussen-Ivey et al., 2016). Another powerful component is lipopolysaccharide (LPS), found in Gram-negative bacteria. LPS acts as an endotoxin that triggers inflammation and immune activation. In fish, LPS stimulates cytokine production and alters physiological processes, contributing to disease symptoms (Rebl et al., 2010). Recent studies have shown that fish can recognize LPS not only through classical receptors but also via NOD-like receptors, which activate inflammatory signaling pathways such as NF- κ B (Bi et al., 2018). This alternative recognition pathway reflects evolutionary adaptations in fish innate immunity compared to mammals.

4. Toxins: The Bacterial Weapons

Exotoxins include pore-forming toxins like aerolysin (*Aeromonas hydrophila*), neurotoxins, enterotoxins, and tissue-degrading enzymes. These toxins disrupt cell membranes, interfere with metabolism, and suppress immune responses, leading to tissue damage, septicemia, and mortality in fish. Bacterial pathogens produce both endotoxins and exotoxins, which contribute to disease either by directly damaging host tissues or by triggering excessive inflammation. Exotoxins are soluble proteins actively secreted by bacteria that enter host cells and disrupt normal cellular functions. They include A-B toxins, proteolytic toxins, pore-forming toxins, and other functional types. A-B toxins bind host receptors and enzymatically alter intracellular targets, proteolytic toxins degrade host proteins, and pore-forming toxins damage cell membranes, leading to cell death (Duport et al., 2019). These toxins are often responsible for ulcerative lesions and systemic infections in aquaculture species.

5. Secretion Systems: Molecular Syringes

Pathogenic bacteria use specialized secretion systems to deliver toxins and enzymes. Systems

such as Type III and Type VI secretion systems function like molecular syringes, injecting bacterial effector proteins directly into host cells. These effectors manipulate host signaling pathways, suppress immune responses, and promote intracellular survival. These systems are crucial for diseases caused by *Edwardsiella*, *Aeromonas*, and *Vibrio* species in aquaculture (Rivas et al., 2015).

6. Stealing Iron: Siderophores

Iron is essential for bacterial growth but is tightly controlled in fish bodies as part of host defense. To overcome this limitation, bacteria release siderophores—small molecules that bind iron with high affinity. Fish pathogens such as *Vibrio anguillarum* and *Edwardsiella tarda* use siderophores to survive and multiply within the host, particularly during stress conditions that weaken host immunity (Lange et al., 2020).

7. Plasmids

Virulence plasmid (pPHDD1) of *P. damsela* encodes three types of haemolysin, namely Dly, HlyApI and HlyAch, in which HlyApI and HlyAch are a pore-forming toxin and haemolysin damselysin is a phospholipid D cytotoxin (Rebl et al., 2010).

Host–Pathogen Battle in Fish

Fish are not defenseless. Their skin and mucus form the first line of defense, containing antimicrobial peptides, enzymes, complement proteins, and immune molecules. Pattern recognition receptors (PRRs), especially Toll-like receptors (TLRs), detect bacterial components and activate immune responses. Species such as tilapia, salmon, and catfish possess diverse TLRs that recognize bacterial invaders and trigger protective inflammation (Rebl et al., 2010). In addition to innate immunity, adaptive immune responses involving antibodies and immune memory play a critical role in long-term protection, forming the basis for vaccine development against bacterial diseases.

CONCLUSION

Understanding bacterial virulence is more than academic knowledge—it is essential for sustainable aquaculture. By identifying key

virulence factors, scientists can design better diagnostics, vaccines, and targeted therapies. This approach is especially important as antibiotic resistance continues to rise. Future disease control strategies will increasingly focus on antivirulence approaches, molecular diagnostics, and omics-based technologies to reduce pathogen fitness without promoting resistance, thereby protecting aquatic ecosystems.

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