

Immuno-Nutrition Strategies in Aquaculture for Enhanced Disease Resistance

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Abstract

Aquaculture intensification has significantly increased the incidence of infectious diseases, leading to substantial economic losses and heightened dependence on antibiotics and chemotherapeutics. In this context, immuno-nutrition—defined as the strategic manipulation of dietary components to modulate and enhance the immune system of cultured aquatic organisms—has emerged as a sustainable and preventive health management approach. This review critically examines the mechanistic basis of immuno-nutrition and synthesizes current evidence on functional feeds, probiotics, prebiotics, synbiotics, β -glucans, nucleotides, phyto-genic additives, and functional lipids in aquaculture. Emphasis is placed on their roles in strengthening innate immune responses, improving gut health, enhancing disease resistance, and reducing mortality under pathogenic stress. Furthermore, this paper highlights experimental frameworks for evaluating immuno-nutritional efficacy under both controlled and farm-scale conditions, along with economic and practical considerations for adoption. By integrating immuno-nutrition with good husbandry practices, biosecurity, and environmental management, aquaculture systems can reduce reliance on antibiotics and move towards more resilient and sustainable production models.

Keywords: Immuno-nutrition; functional feeds; probiotics; β -glucans; disease resistance; sustainable aquaculture.

Introduction

Aquaculture represents one of the fastest-growing sectors of global food production and plays a crucial role in ensuring nutritional security for a rapidly increasing human population. However, intensification of aquaculture practices—characterized by high stocking densities, artificial feeding, and environmental fluctuations—has markedly increased the prevalence of infectious diseases in cultured fish and shellfish (FAO, 2020; Dawood & Koshio, 2016). Disease outbreaks not only cause severe economic losses but also promote excessive use of antibiotics and chemotherapeutics, raising concerns regarding antimicrobial resistance, environmental contamination, and food safety.

Traditional disease management strategies, including vaccines, antibiotics, and chemical treatments, have shown varying degrees of success but are often limited by high costs, pathogen specificity, environmental side effects, and reduced efficacy in early life stages of aquatic organisms (Hoseinifar *et al.*,

2018). Consequently, there is growing interest in preventive and nutrition-based approaches that enhance the host's natural defense mechanisms rather than targeting pathogens directly.

Immuno-nutrition is based on the principle that nutrition and immune function are intrinsically linked. Adequate and balanced intake of specific nutrients and functional feed additives can modulate immune responses, improve disease resistance, and enhance overall health status of aquatic animals (Dawood *et al.*, 2019; Tocher, 2015). Unlike therapeutic interventions, immuno-nutrition aims to prime the immune system, particularly innate immunity, which plays a dominant role in fish and crustaceans due to their comparatively slower adaptive immune responses (Meena *et al.*, 2013).

Recent advances in aquaculture nutrition have demonstrated that dietary supplementation with probiotics, prebiotics, β -glucans, nucleotides, phyto-genics, and functional lipids can significantly improve immune parameters such as lysozyme activity,

phagocytic capacity, respiratory burst, and antioxidant status, ultimately leading to reduced mortality during disease challenges (Kuebutornye *et al.*, 2019; Dawood *et al.*, 2018). However, the efficacy of these interventions is highly species-specific and influenced by life stage, dosage, environmental conditions, and farming practices.

The present review critically evaluates current immuno-nutritional strategies used in aquaculture, with an emphasis on mechanistic understanding, experimental evidence, and practical applicability. Additionally, existing knowledge gaps and future research priorities are discussed to facilitate effective integration of immuno-nutrition into sustainable aquaculture health management programs.

1. Nutrition, Immunity and Aquaculture Species

1.1. Link between Nutrition and Immune Function

Immune competence in aquatic organisms is strongly influenced by nutritional status, as immune responses are metabolically demanding and require a continuous supply of specific nutrients. Proteins and essential amino acids are required for the synthesis of immune cells, enzymes, antibodies, and signaling molecules, while deficiencies can compromise lymphocyte proliferation and phagocytic activity (Li & Gatlin, 2006; Dawood *et al.*, 2019).

Lipids, particularly long-chain polyunsaturated fatty acids (LC-PUFAs), play a crucial role in regulating inflammatory responses and maintaining cellular membrane integrity. Omega-3 fatty acids such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) have been shown to modulate immune signaling pathways and reduce excessive inflammatory damage during infection (Tocher, 2015).

Micronutrients including vitamins (A, C, D, and E) and minerals (zinc, selenium, iron, and copper) act as cofactors in antioxidant defense systems and immune signaling cascades. Inadequate intake of these nutrients increases susceptibility to oxidative stress and infectious diseases in aquaculture species (Gupta *et al.*, 2021; Onuoha *et al.*, 2024).

1.2. Innate and Adaptive Immunity in Aquatic Organisms

Fish and crustaceans rely predominantly on innate immune mechanisms as their first line of defense. These include physical barriers, antimicrobial peptides, lysozyme, complement proteins, phagocytic cells, and pattern recognition receptors that detect

pathogen-associated molecular patterns (PAMPs) (Meena *et al.*, 2013; Sahoo *et al.*, 2018).

Although adaptive immunity is present in teleost fish, its development is relatively slow compared to mammals, particularly during larval and juvenile stages. Consequently, immuno-nutritional strategies that enhance innate immunity are considered more effective and practical for disease prevention in aquaculture systems (Rodrigues *et al.*, 2020; Dawood & Koshio, 2016).

1.3. Species- and Life-Stage-Specific Considerations

The effectiveness of immuno-nutritional interventions varies considerably among species and developmental stages. Nutrient requirements and immune ontogeny differ between finfish and crustaceans, as well as between larvae, juveniles, broodstock, and grow-out stages. A dietary additive that improves immunity in one species may have limited or inconsistent effects in another, highlighting the importance of tailored, species-specific feed formulations (Kumar & Menon, 2022; Dawood *et al.*, 2018).

2. Immuno-Nutritional Strategies in Aquaculture

2.1. Functional Feeds and Essential Nutrients

Functional feeds enriched with high-quality protein and specific amino acids such as arginine and glutamine have been shown to support immune cell proliferation, nitric oxide production, and tissue repair processes (Li & Gatlin, 2006). Balanced lipid profiles, particularly optimal omega-3 to omega-6 ratios, help regulate inflammatory responses and enhance resistance to pathogenic stress (Tocher, 2015).

However, excessive supplementation of fat-soluble vitamins or trace minerals may result in toxicity or metabolic imbalance, emphasizing the need for dose optimization based on species and production stage (FAO, 2020).

2.2. Probiotics

Probiotics are among the most extensively studied immuno-nutritional tools in aquaculture. Their beneficial effects are attributed to competitive exclusion of pathogens, enhancement of gut barrier function, modulation of host immune gene expression, and stimulation of innate immune responses (Hoseinifar *et al.*, 2018; Kuebutornye *et al.*, 2019).

Commonly used probiotic genera include *Lactobacillus*, *Bacillus*, *Enterococcus*, and *Pseudomonas*. Nevertheless, probiotic efficacy is highly strain-specific and influenced by factors such as feed processing, storage conditions, and the ability of

the strain to colonize the host gut (Ringø *et al.*, 2020; Mohammed *et al.*, 2025).

2.3. Prebiotics and Synbiotics

Prebiotics such as mannan oligosaccharides (MOS), fructo-oligosaccharides, and β -glucans selectively stimulate beneficial gut microbiota and enhance immune responsiveness. Synbiotics, which combine probiotics and prebiotics, often produce synergistic effects by improving microbial stability and immune modulation simultaneously (Dawood *et al.*, 2018; Srengaraj *et al.*, 2023).

Despite promising results, variability in gut microbiome composition across species and environments contributes to inconsistent outcomes, warranting further research on optimized formulations.

2.4. β -Glucans and Immunostimulants

β -Glucans derived from yeast and fungi are well-established immunostimulants in aquaculture. They function by activating macrophages and other immune cells through pattern recognition receptors, thereby enhancing phagocytosis, respiratory burst activity, and cytokine production (Meena *et al.*, 2013; Rodrigues *et al.*, 2020).

Although β -glucans have demonstrated consistent improvements in disease resistance, prolonged or excessive stimulation may impose energetic costs, underscore the importance of controlled dosing and feed schedules (Sahoo *et al.*, 2018).

2.5. Phytogetic Feed Additives

Phytogetic additives derived from herbs, spices, and plant extracts—including garlic, turmeric, oregano, neem, and seaweed—have gained attention due to their antimicrobial, antioxidant, and immunomodulatory properties. These compounds often act through multiple mechanisms but exhibit variable efficacy depending on extraction methods, dosage, and species (Caipang, 2020; Appuhami *et al.*, 2025).

Standardization of active ingredients remains a major challenge for their widespread commercial adoption.

Discussion

The present review highlights immuno-nutrition as a preventive and sustainable strategy for enhancing disease resistance in aquaculture systems. Accumulating evidence indicates that functional feeds supplemented with probiotics, prebiotics, synbiotics, β -glucans, nucleotides, phytogetics, and functional lipids can significantly modulate innate immune responses, improve gut health, and reduce mortality during pathogenic challenges (Dawood *et al.*, 2019;

Hoseinifar *et al.*, 2018). These benefits are particularly relevant in intensive farming systems, where chronic stress and high pathogen load compromise host immunity.

Among the various approaches, β -glucans and probiotics have demonstrated relatively consistent immunostimulatory effects across multiple species by enhancing phagocytic activity, lysozyme levels, and antioxidant defenses (Meena *et al.*, 2013; Kuebutornye *et al.*, 2019). However, responses to phytogetic additives and prebiotics remain variable, largely due to differences in formulation, dosage, extraction methods, and host-specific gut microbiota composition (Caipang, 2020; Appuhami *et al.*, 2025). This variability underscores the importance of species- and life-stage-specific feed design rather than generalized application.

A critical issue emerging from the literature is that many studies rely on short-term laboratory challenge tests, which may not fully represent complex farm conditions involving fluctuating water quality, mixed pathogen communities, and management-related stressors (Rodrigues *et al.*, 2022). Consequently, although immuno-nutritional interventions show promise under controlled conditions, their long-term efficacy and economic viability at the farm level require further validation.

Importantly, immuno-nutrition should not be viewed as a standalone solution. Its effectiveness is maximized when integrated with good husbandry practices, biosecurity measures, optimal water quality management, and, where applicable, vaccination programs (FAO, 2020). Such integrated health management approaches align with the One Health concept by reducing antibiotic use and minimizing environmental and public health risks associated with antimicrobial resistance.

Limitations and Challenges

Despite encouraging outcomes, several limitations constrain the widespread application of immuno-nutrition in aquaculture. First, the immunological responses to dietary supplements are highly species-specific and influenced by genetic background, environmental conditions, and nutritional history, limiting the generalization of findings across production systems (Kumar & Menon, 2022).

Second, stability and bioavailability of functional additives during feed processing and storage remain technical challenges, particularly for probiotics and heat-sensitive vitamins. Inadequate quality control

may result in reduced efficacy or inconsistent results at the farm level (Ringø *et al.*, 2020).

Third, excessive or prolonged immune stimulation may impose metabolic costs, diverting energy away from growth and reproduction. Therefore, inappropriate dosing strategies could negate potential benefits (Sahoo *et al.*, 2018). Finally, regulatory frameworks governing the use of live microbial products and novel feed additives differ across regions, posing additional barriers to commercialization.

Future Research Directions

Future research should prioritize long-term, farm-scale trials to validate laboratory findings under realistic production conditions. Integrating immuno-nutrition studies with advanced molecular tools, such as transcriptomics and microbiome profiling, will improve understanding of host–diet–microbiota interactions and enable precision nutrition approaches (Rodrigues *et al.*, 2022; Rajonhson *et al.*, 2024).

Additionally, dose-response studies and cost–benefit analyses are essential to determine economically optimal inclusion levels for different farming systems. Greater emphasis should also be placed on broodstock and early life-stage nutrition, where immune programming can have lasting effects on performance and disease resistance (Kumar & Menon, 2022).

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