

# Functional Feeds for Future Aquaculture: A Review of Nutritional Strategies for Fish Health

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## Abstract

Functional nutrition plays a pivotal role in aquaculture by promoting fish growth, enhancing immune responses, and mitigating the impact of environmental and pathogenic stressors. With the intensification of fish farming and growing concerns over antibiotic resistance, the use of functional feeds including nutraceuticals, prebiotics, probiotics, antioxidants, and immunostimulants has emerged as a sustainable alternative to conventional practices. This review critically examines the nutritional requirements of fish, explores the bio efficacy of various feed additives, and evaluates their roles in gut health modulation, disease resistance, and stress mitigation. We also discuss proactive health management strategies and the integration of vaccination and feed-based interventions. The review highlights current advancements, identifies research gaps, and emphasizes the need for precision in formulating functional feeds tailored to species-specific requirements. This integrated nutritional approach supports healthier fish stocks, improves aquaculture productivity, and reduces the industry's ecological footprint.

**Keywords:** Nutraceuticals, Functional feeds, Prebiotics, Probiotics, Fish Health Managements.

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## 1. INTRODUCTION

Proper nutrition in animal husbandry is indispensable for inexpensive and efficient assembly of high-quality, healthy products. In aquaculture, nutrition plays a critical role, as feed typically accounts for almost half of the flexible production costs. Recent advancements in fish nutrition have led to the development of well-adjusted profitable diets that promote the optimal growth and health of fish. Complete diets provide every element protein, carbohydrates, lipids, vitamins, and minerals necessary for optimal growth and health of fish. Complete meals are used in most fish farms, including lipids (10–25%), carbohydrates (15–20%), proteins (18–50%), ash (<8.5%, <1.5%, <10%), and trace levels of vitamins and minerals. The nutritional value of feed depends on the type of fish being raised and their developmental stage. Whether raised in high density indoor settings or housed in cages where they cannot forage for food on naturally occurring substrates, such as algae, aquatic plants, and aquatic invertebrates, fish require a complete diet. Conversely, partial or incomplete supplemental meals are designed to supplement the natural food sources that fish normally have access to in ponds or outside raceways. These diets often consist of extra protein,

carbohydrates, and/or lipids, in addition to the naturally occurring diet; nevertheless, they do not contain all the recommended vitamins and minerals. (Craig and Helfrich, 2017).

## 2. Major Nutrient Groups

### 2.1. Carbohydrates

Starch is used in fish feed as the least expensive energy source to improve the physical quality and promote protein sparing activity. The capacity of fish to use starch differs among species, and it is typically difficult to metabolize, digest, or absorb it (Kamalam *et al.*, 2017). Because they are the least expensive energy source, fish feed contains a limited amount of carbohydrates to improve the physical qualities of fish. Carbohydrates are essential nutrients that provide ribose, a hydrogen donor, and a carbon skeleton (Zhang *et al.*, 2019). In aqua feed, they are also a comparatively less expensive energy source when compared to proteins and lipids. The main source of carbohydrates in feedstuff is starch, which is a polysaccharide composed of several monosaccharides joined by glycosidic linkages. Carbohydrates are composed of monosaccharides, disaccharides, and other polysaccharides (Romano and Kumar 2019).

The health of the intestine is essential for absorbing nutrients, particularly carbohydrates. Dietary carbohydrates have been found to have an impact on microbial composition and intestinal histology in recent research (Huang *et al.*, 2021). High dietary starch levels have been associated with an increase in pathogenic bacteria, including *Vibrio*, *Photobacterium*, and *Mycoplasma*, in the golden pompano (*Trachinotus ovatus*) (Zhao *et al.*, 2020). However, when largemouth bass (*Micropterus salmoides*) were fed a 15% starch diet, their midgut villus height and width decreased, the amount of intestinal probiotics decreased, and the number of harmful bacteria increased. This led to an imbalance in the microbial community and a decrease in the production of short-chain fatty acids, which in turn prevented *Micropterus salmoides* from growing (Zhou *et al.*, 2021).

## 2.2. Protein

Protein is a crucial component of fish feed, and it is vital to precisely determine the protein requirements for each species and life period. Each Protein is composed of individual amino acids (AA). Although more than 200 amino acids are present in nature and only 20 of them are common, Ten of these 20 amino acids cannot be synthesized, including methionine, histidine, arginine, tryptophan, isoleucine, threonine, valine, lysine, phenylalanine, and leucine. The first amino acids to become limited were methionine and lysine. Fish diets produced using bacterial or yeast proteins frequently lack both methionine and lysine, whereas feeds created with plant protein sources, such as soybean meal, are typically low in methionine. Therefore, when these protein bases are substituted for fishmeal, these amino acids must be added to the diet (Craig and Helfrich, 2017).

The price of fishmeal has been steadily rising owing to the growing demand for it, while its production remains stable. Plant protein sources are commonly used in the aquaculture industry to meet the protein requirements of farmed fish species. However, the large volume of data produced under various experimental conditions presents a challenge in summarizing and comparing the effects of plant protein sources on carnivorous fish species (Qian *et al.*, 2024).

## 2.3. Lipids

A major barrier to further expansion of the aquaculture industry is the lack of marine oils high in long-chain (LC) n-3 polyunsaturated fatty acids, which are primarily made up of docosahexaenoic acid and eicosapentaenoic acid (Tocher *et al.*, 2019). Over the past 20 years, plant oils, mainly rapeseed oil, have gradually replaced fish oil in salmon feed to reduce the dependency on fixed natural fish sources. This decreases the availability of EPA and DHA in fish (Aas *et al.*, 2019). This substitution has a detrimental impact on the health and wellbeing of farmed salmon, and lowers the health benefits of consuming salmon for humans (Lutfi *et al.*, 2022).

Microalgal biomass and oil are two well-known potential sources of EPA and DHA in aquafeeds, according to several studies (Halten *et al.*, 2022). Fish oil may soon give way to microalgal oil owing to its high n-3 LC-PUFA content and potential for use (Pereira *et al.*, 2020). Other substances could also be employed, although their use is restricted by law in Europe. One such ingredient is transgenic *Camelina sativa* seeds, which have been altered to produce EPA and DHA in amounts comparable to fish oil (West *et al.*, 2021).

Another method of recycling involves the use of by-products from fisheries and aquaculture, such as the incomprehensible section of Atlantic salmon, which makes up approximately 55% of its lipids (Malcorps *et al.*, 2021). Aquaculture accounts for over 60% of the output of fish oil by-products by 2020 (FAO, 2022). Aquafeeds that are both economically viable and nutritionally balanced can be produced using a variety of lipid sources to reduce the adverse effects of using a single ingredient (Zheng *et al.*, 2019). Additionally, because muscle oxidation susceptibility can result in the development of unwanted lipid oxidation products that negatively affect product quality, it is a major concern in the fish industry. This affects the shelf life and nutritional value of the finished product (Wu *et al.*, 2022).

## 2.4. Mineral and Vitamins

Fish are an important source of unsaturated fatty acids (UFA), particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). It has been discovered that EPA and DHA can prevent hypertension and heart disease (Ruyter *et al.*, 2022). Vitamin E (VE), a fat-soluble nutrient containing tocopherols and tocotrienols, considerably increases the PUFA content in both raw and cooked golden pompano (*Trachinotus ovatus*) (Zhang *et al.*, 2021).

Since vitamin E cannot be produced, vitamin E supplementation is thought to be important for the majority of fish species. Dietary VE deficiency in fish typically causes several deficiency symptoms, including immune system depression, internal bleeding, delayed growth, and muscle degeneration (Head *et al.*, 2021). Vitamin E (VE) is essential for controlling the growth and physiological processes of fish vitamin E (VE). Studies have demonstrated that VE deficiency causes muscle atrophy and fin bleeding in the blue tilapia (*O. aureus*). Furthermore, in Black Sea bream and channel catfish fingerlings, lipid peroxidation and growth performance are affected by vitamin E deprivation. By providing lipid free radicals with phenolic hydrogen, VE functions as the main lipid-soluble antioxidant and shields cells from peroxidative lipid damage. (Liu *et al.*, 2020).

Direct interactions between the constituents in structural processes are well known. Examples include the requirement of iron (Fe) and copper (Cu) for the creation of hemoglobin and the involvement of calcium

(Ca), phosphorous (P), and magnesium (Mg) in the synthesis of bone hydroxyapatite. Furthermore, it has been recognized that the interaction between zinc (Zn) and manganese (Mn) shapes the appropriate conformational structure of RNA molecules in the liver.

On the other hand, antagonistic relationships can arise when trace elements such as zinc (Zn) and cadmium (Cd) in metallothioneins compete for binding sites because of their similar electronic configurations

and ionic radii, or when magnesium (Mg) and manganese (Mn) substitutions occur at the active sites of enzymes. Several animal investigations have indicated that the bioavailability of minerals from different feed additives and constituents has a substantial impact on the amount needed. The percentage of dietary intake of an element used for biochemical or physiological processes is referred to as the bioavailability (Lall and Kaushik, 2021).

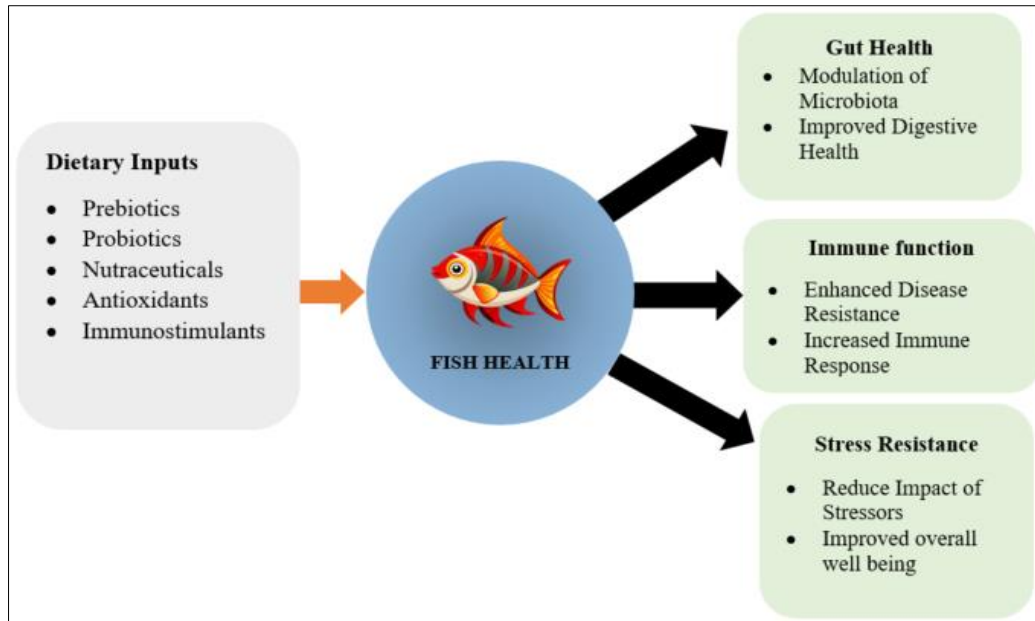
**Table 1.1: Summary of Key Nutrients in Fish Feed**

Nutrient	Key Points	Effects & Considerations	Sources & Alternatives
<b>Carbohydrates</b>	Least expensive energy source. Improves feed physical quality. Protein-sparing effect. Composed of monosaccharides, disaccharides, polysaccharides (e.g., starch).	Digestibility varies by fish species. High starch levels may increase pathogenic bacteria (e.g., <i>Vibrio</i> , <i>Mycoplasma</i> ). Can alter gut microbiota and reduce short-chain fatty acid production.	Starch (main source). Plant-based ingredients.
<b>Protein</b>	Essential for growth, varies by species and life stage. Composed of amino acids (AAs). 10 essential AAs (e.g., methionine, lysine often limiting).	Fishmeal is costly; plant proteins (e.g., soybean meal) are alternatives but may lack methionine. Carnivorous fish may struggle with plant-based proteins.	Fishmeal (traditional). Plant proteins (soybean meal). Microbial proteins (yeast, bacteria).
<b>Lipids</b>	Provide energy and essential fatty acids (EPA, DHA). Key for fish and human health.	Fish oil replacement with plant oils (e.g., rapeseed) reduces EPA/DHA. Oxidation affects shelf life and nutritional quality.	Fish oil (traditional). Plant oils (rapeseed). Microalgae (rich in EPA/DHA). Transgenic crops (e.g., <i>Camelina sativa</i> ). Fishery by-products.
<b>Minerals &amp; Vitamins</b>	Essential for metabolic functions, bone formation, and antioxidant defense. Vitamin E prevents lipid peroxidation. Minerals (Fe, Cu, Ca, P, Mg, Zn, Mn) have structural and enzymatic roles.	Deficiency causes muscle atrophy, fin bleeding, poor growth. Antagonism between minerals (e.g., Zn vs. Cd, Mg vs. Mn). Bioavailability varies by source.	Synthetic supplements. Natural sources in feed. Vitamin E from plant oils, microalgae.

### 3. Functional feeds

Functional feeds are specially formulated diets that contain natural additives such as essential nutrients or nutraceuticals, which provide various health benefits. These feeds can improve fish health, reduce the severity of infectious diseases, enhance immunocompetence, and counteract suppression of the immune system caused by

stress or contaminants. Functional feed additives include probiotics, antioxidants, prebiotics, enzymes, vitamins, immunostimulants, organic acids, and plant extracts. These functional feeds can also be combined with different medications, with specific feed schedules and details (Wagboo and Remo 2022) [Fig 1].



**Fig. 1: Role of functional feed additive in Fish Health**

Antibiotics have been commonly used in aquafeeds to reduce the effects of infectious diseases and increase growth performance. Therefore, there is growing interest in finding alternative ways to enhance fish health and growth without relying on antibiotics (Dawood *et al.*, 2017). Astaxanthin is a pigment that is often supplemented in fish feeds to enhance skin coloration; however, it also has numerous physiological and health benefits. Selenium is another trace element essential for maintaining the antioxidant defense system, hormone production, and synthesis of selenoproteins (Khan *et al.*, 2017). Microalgae are also being explored as nutritional supplements in fish diets, with promising results in reducing infection and bacterial populations in fish tanks. However, there are drawbacks to using microalgae, yeast, and other alternative feed sources, and

more research is needed to fully understand their potential benefits and limitations (Gamboa-Delgado and Márquez-Reyes, 2018).

Macroalgae, also known as seaweeds, can be categorized into three primary types: *Rhodophyta* (red), *Chlorophyta* (green), and *Phaeophyta* (brown). These types have varying nutritional values, which can be influenced by factors such as season and location. Research has evaluated the use of macroalgae in fish feed, focusing on their nutritional value and the content of functional compounds that are important for fish health. The suitability of macroalgae for fish feed depends on both the type of macroalgae used and fish species (Wan *et al.*, 2018).

**Table 2.1: Summarizes major classes of functional feed additives, their roles in aquaculture, mechanisms of action, and current limitations**

Additive Type	Examples	Primary Function	Mechanisms of Action	Challenges/Limitations
<b>Nutraceuticals</b>	L-tryptophan, selenium, β-glucans	Anti-stress, antioxidant, immune booster	Modulate cytokine expression, reduce ROS	Efficacy varies by species and dose
<b>Prebiotics</b>	FOS, MOS, inulin, GOS, XOS	Gut microbiota modulation	Promote beneficial microbes, suppress pathogens	Limited data on long-term effects
<b>Probiotics</b>	Bacillus spp., Lactobacillus, Yeast	Improve digestion, immunity	Enhance barrier function, enzyme production	Survivability in feed and gut stability
<b>Synbiotics</b>	Prebiotics + Probiotics combos	Synergistic gut health benefits	Combined probiotic survival and microbiome support	Requires precise formulation and dosing
<b>Antioxidants</b>	Vitamin E, seaweed polyphenols, astaxanthin	Oxidative stress reduction	Scavenge free radicals, inhibit lipid peroxidation	Stability during feed processing
<b>Immunostimulants</b>	Spirulina, β-glucans, yeast extracts	Immune enhancement	Stimulate leukocytes, increase resistance to pathogens	Overstimulation risk, species-dependent

#### 4. Role of prebiotics and probiotics in fish functional feed

Probiotics are live microorganisms that are utilized in fish feed at low concentrations (0.1%–2% of the feed) to promote health, control bacterial diseases, enhance feed intake, and improve feed conversion and growth. Several microbial species have been studied as potential probiotic candidates for use in farmed fish. Probiotic bacteria have been found to have various biological effects, including improved digestion, enhanced epithelial barrier function, modulation of host immune responses, and antimicrobial mechanisms (Banerjee and Ray, 2017)

In addition to probiotics, prebiotics are also used in fish feed to improve gut health and modulate the microflora balance. Prebiotics are unconceivable carbohydrates derived from yeast cell walls, and are classified based on their molecular size or degree of polymerization into monosaccharides, oligosaccharides, or polysaccharides. Examples of prebiotic compounds include inulin and isomaltooligosaccharides (IMO), short-chain fructooligosaccharides (scFOS), galactooligosaccharides (GOS), mannooligosaccharides (MOS), xylooligosaccharides (XOS), arabinoxylooligosaccharides (AXOS), and fructooligosaccharides (FOS), as well as commercial products and mixtures. Prebiotics are often combined with probiotics or other prebiotics, and the term synbiotics refers to the supplementation of both probiotics and prebiotics in the diet. This combination improves the survival of beneficial microorganisms in the gut, leading to improved host welfare (Ringo and Song, 2016).

The primary objective of this study was to investigate the use of combination supplements, including plant products and immune stimulants, such as  $\beta$ -glucans and yeast. These supplements offer several advantages such as increased flexibility in adapting to variable farming conditions and a higher probability of success. The selection of probiotic bacterial species has been confined to *Bacillus sp.* and *Enterococcus sp.*, as well as prebiotics such as MOS AXOS, short-chain FOS, GOS, IMO, FOS chitosan oligosaccharide, and inulin. To provide examples of the application of synbiotics in aquaculture, Ringø and Song (2016) listed various shrimp species and fish, probiotic and prebiotic types and doses, treatment durations, and the resulting biological outcomes (Ringo and Song, 2016).

#### 5. Immunostimulants

Immunostimulants play a crucial role in enhancing the growth of aquatic organisms by improving feed digestion and consumption efficiency. Probiotic supplements, which are live microorganisms such as gram-negative or gram-positive bacteria, algae, and fungi, can improve the nutritional content of feed when added in appropriate quantities. Scientists have used commercial probiotics, including *Bacillus spp.*,

*Streptococcus*, *Lactococcus lactis*, *Pseudomonas fluorescens*, *Saccharomyces cerevisiae*, *Spirulina*, *Debaryomyces hansenii*, and *Vibrio alginolyticus* to enhance the growth performance and immune response of juvenile Nile tilapia (*O. niloticus*). These probiotics offer numerous benefits such as increasing the feed conversion rate, improving growth efficiency by balancing gastrointestinal microbial communities, increasing the production of digestive enzymes, and enhancing immune system responses against pathogenic bacteria by producing inhibitory compounds (Amenyogbe *et al.*, 2020).

Immunostimulants and vaccines are innovative approaches to fish farming and disease prevention. Recently, there has been a growing interest in immunostimulants as a means to avoid infections in aquaculture, in light of the increasing public concern over the use of antibiotics in farmed animals. Nutrition is the process of supplying organisms with the nutrients necessary to support life, growth, and reproduction. These nutrients include carbohydrates, fats, minerals, proteins, dietary fiber, and vitamins, which can be categorized as macronutrients or micronutrients, depending on the quantity required by the organism (Cuesta and Esteban, 2021).

In the context of sustenance, the diet of a living organism comprises the food it consumes, which is primarily determined by the availability and palatability of the food sources. Many herbivorous animals rely on bacterial fermentation to break down indigestible plant cellulose into digestible nutrients, whereas carnivores require diets rich in meats to obtain vital vitamins and nutrients that their bodies cannot produce on their own. Animals generally have higher energy levels than plants (Singh *et al.*, 2021).

#### 6. Antioxidants

Antioxidants act as shields against the negative reactions of oxygen (oxidation) on complex structures such as proteins, lipids, carbohydrates, and DNA in cells. These structures are constantly under attack from both internal (digestive, respiratory, disease, injury, etc.) and external (environmental) factors. Antioxidant defense is mediated by enzymes like catalase (CAT), glutathione peroxidase (GPx), glutathione reductase (GR), and superoxide dismutase (SOD) which is called enzymatic antioxidant defense. On the other hand, non-enzymatic antioxidant defense is expressed through substances like, ascorbic acid (Vitamin C), retinol (Vitamin A) and tocopherol (Vitamin E). Numerous antioxidants have been identified in various natural foods. Antioxidants can be classified in various ways, such as their source, mode of action, activities, and biochemical properties (Kebede and Admessu, 2019).

Despite its potential adverse effects on aquatic life and humans, ethoxyquin has been previously authorized as a feed additive for all animal species and

categories. However, owing to growing evidence of its adverse effects, the EU commission has suspended its authorization (Gunathilake *et al.*, 2022). However, new information has emerged regarding the use of ethoxyquin. Natural plant antioxidant sources that are high in phenolic compounds have been shown to be effective in reducing oxidation in fish fillets as synthetic antioxidants (Vargas- Sanchez *et al.*, 2019).

According to recent studies, seaweed phenolics have gained significant attention as a sustainable source of antioxidants. These compounds possess a range of bio functional properties and may potentially replace the existing aquatic feed additives (Gunathilake *et al.*, 2022). Polyphenolic algae have been found to effectively delay fish oil rancidity by acting as good antioxidants (Mukherjee and Pal, 2021).

### 7. Nutraceutical Approaches

Although it is impossible to completely prevent all consequences of climate change in fish, certain measures can be taken to alleviate the impact of these negative effects. One approach involves the use of nutraceuticals to mitigate various stressors in fish. Studies have shown that nutraceuticals can stimulate the defense systems of fish, even under stressful conditions, and counteract the harmful effects of stress. For instance, diets high in protein have been found to have ameliorative effects against various stressors. Aquaculture production could be enhanced through the use of nutraceuticals as anti-stress agents, as studies have shown that these substances can trigger defense systems in fish, even during stressful situations, and mitigate the harmful effects of stress to some extent. Some promising nutraceuticals for aqua feed include microbial levan, L-tryptophan, vitamin C, pyridoxine, vitamin E, and methyl donors. The use of these nutraceuticals in feed formulations is a relatively recent development, and there is still a need for further research to determine their field efficiency. However, exploring newer feed ingredients and nutraceuticals for immune modulation and stress mitigation in fish is necessary to improve both

the qualitative and quantitative aspects of aquaculture production (Varghese *et al.*, 2021).

### 8. Proactive measurements in Fish Health Management

Fish farming is a multi-billion-dollar industry and one of the fastest-growing sectors in animal food production. In addition to providing a stable source of income for millions of people and contributing to food security, it drives economic development in several regions (Adam *et al.*, 2019). However, environmental factors in the culture environment such as low water quality, high stocking density, and low oxygen levels can cause stress in fish, making them more susceptible to infectious diseases. Although effective management practices and prophylactic treatments can significantly reduce disease susceptibility, the aquaculture industry still faces a significant challenge, with more than 10% of all cultured fish lost annually due to infectious diseases. This results in global losses of over 10 billion USD, highlighting the persistent impact of fish diseases on the aquaculture sector (Wanja *et al.*, 2020).

Disease outbreaks in fish cultures are caused by various agents, including bacterial pathogens (54.9 %), viruses (22.6 %), parasites (19.4 %), and mycotics (3.1 %) (Surachetpong *et al.*, 2020). This poses a significant issue, not only leading to substantial losses in aquaculture production, but also giving rise to economic concerns in the developing world, which accommodates 90% of the aquaculture industry. Therefore, there is a significant emphasis on the development of methods to prevent and control the spread of diseases. In the early stages, antibiotics served as the primary tool to combat infections owing to their accessibility, affordability, and effectiveness in treating bacterial diseases. However, the repeated use of antibiotics has been observed to suppress the immune system of fish and induce antibiotic resistance, thereby posing a threat to consumer health and safety. As an alternative approach, vaccinations have been introduced to decrease reliance on antibiotics (Salam *et al.*, 2023).

**Table 3.1: Challenges and Disease Management in Aquaculture**

Category	Key Facts/Statistics	Impact/Consequences	Current Solutions	References
<b>Industry Overview</b>	Multi-billion-dollar industry Fastest-growing animal food production sector	Provides income for millions Contributes to food security Drives economic development	Effective management practices Prophylactic treatments	Adam <i>et al.</i> , 2019
<b>Environmental Stressors</b>	Low water quality High stocking density Low oxygen levels	Causes fish stress Increases disease susceptibility	Improved farming techniques Water quality monitoring	Wanja <i>et al.</i> , 2020
<b>Disease Losses</b>	>10% annual loss of cultured fish Global losses >10 billion USD	Significant economic impact Threat to food security	Disease prevention research Vaccination development	Wanja <i>et al.</i> , 2020
<b>Pathogen Distribution</b>	Bacterial (54.9%) Viral (22.6%)	Major production losses Economic concerns in	Pathogen-specific control measures	Surachetpong <i>et al.</i> , 2020

Category	Key Facts/Statistics	Impact/Consequences	Current Solutions	References
	Parasitic (19.4%) Mycotic (3.1%)	developing countries (90% industry)		
<b>Antibiotic Use</b>	Initially primary treatment method Accessible and affordable	Immune suppression Antibiotic resistance Consumer health risks	Reduced antibiotic reliance Alternative therapies	Salam <i>et al.</i> , 2023
<b>Vaccination Alternative</b>	Emerging disease control method	Reduces antibiotic dependence Sustainable approach	Development of various vaccine types Improved delivery methods	Salam <i>et al.</i> , 2023

### 8.1. Vaccination

In the context of fish vaccination, it is essential to gain a thorough understanding of the immune system of fish. Vaccination typically involves a trial-and-error approach with respect to pathogen identification, cultivation, and vaccine formulation. Following the vaccination of a fish with a trial vaccine, the duration and intensity of the developed protective immunity were examined to determine whether the antigen was immunogenic and elicited the appropriate type of response, as well as to identify limitations within the vaccine that require attention. Recent studies in fish immunology have revealed the advantages of using cytokines as adjuvants instead of oil adjuvants because they stimulate the expression of co-stimulatory molecules and polarize antigen-presenting cells. Moreover, research has shown that utilizing interferon-

responsive genes (IRGs) provides a form of innate immunity against viral infections (Guo and Li, 2021).

Live attenuated vaccines have been found to be more efficacious as they replicate natural infection conditions and can stimulate both humoral and mucosal immunity to produce a strong antibody response (Swain *et al.*, 2023). Live attenuated vaccines were developed in the 1990s and have been successfully implemented in aquaculture to improve production and reduce the use of antibiotics. Recombinant attenuated *Edwardsiella piscicida* vaccines (RAEVs) have been explored as vaccine delivery platforms for heterologous antigens in aquaculture (Swain *et al.*, 2022). In a study involving carp, an *E. tarda* live attenuated vaccine was found to induce higher levels of cellular immunity and provide greater levels of protection against the wild-type strain than a formalin-killed vaccine (Rathor and Swain 2024).

**Table 4.1: Advances in Fish Vaccination Strategies**

Aspect	Details	Advantages	Examples/Findings	References
Vaccine Development Approach	Trial and error for pathogen ID, cultivation, and formulation	Identifies immunogenic antigens and response types	Testing vaccine efficacy by monitoring duration/intensity of immunity	-
Adjuvants	Cytokines (replacing oil adjuvants)	Stimulate co-stimulatory molecules, polarize APCs	Enhances adaptive immune response	Guo and Li, 2021
Innate Immunity Boost	Interferon-responsive genes (IRGs)	Provides antiviral innate immunity	Protects against viral infections	Guo and Li, 2021
Live Attenuated Vaccines	Weakened pathogens mimicking natural infection	Stimulates humoral + mucosal immunity; strong antibody response	Higher efficacy than killed vaccines	Swain <i>et al.</i> , 2023
Historical Use	Developed in 1990s	Reduces antibiotic use; improves aquaculture production	Widely adopted for bacterial/viral pathogens	Swain <i>et al.</i> , 2023
Recombinant Platforms	Recombinant attenuated <i>Edwardsiella piscicida</i> vaccines (RAEVs)	Delivers heterologous antigens	Versatile for multiple pathogens	Swain <i>et al.</i> , 2022
Comparative Efficacy	Live attenuated vs. killed ( <i>E. tarda</i> in carp)	Induces stronger cellular immunity and protection	Live vaccine outperformed formalin-killed vaccine against wild-type strain	Rathor and Swain, 2024

### 8.2. Pollution and toxic stress impact on Fish Health

Pollution and toxic stress have detrimental impacts on fish health. These environmental factors enter fish systems through various mechanisms, some of

which result in direct toxicity, whereas others cause subtle disruptions to fundamental biological processes. Direct toxicity can harm organs, impair cellular functions, and even cause death. Indirect harm can affect

metabolism, hormonal signaling, and the immune response, diminishing the overall health and resilience of fish (Samuel *et al.*, 2023).

The consequences of pollution-induced stress on fish populations are severe. Fish may experience stunted growth, decreased energy reserves, and a reduced capacity to cope with environmental changes. Contaminants often interfere with the endocrine system, leading to reduced fertility, increased developmental abnormalities in offspring, and long-term population declines (Canosa and Bertucci 2023). Additionally, impaired immune function renders fish vulnerable to disease and infection, further exacerbating the impact of pollution. Pollutants can disrupt the neurological systems of fish, causing behavioral problems such as feeding, predator avoidance, and social interaction, which can affect their survival and alter the complex relationships within their ecosystem. Urgent action is necessary to address this critical issue. A comprehensive approach that includes both proactive and reactive strategies is required. Strict regulations for industries, a shift towards sustainable agriculture, and improved wastewater treatment systems are needed to significantly reduce the flow of pollutants into aquatic environments (Satker *et al.*, 2024).

Despite promising advances in functional feed applications, key challenges persist that require targeted investigation. Foremost is the need for species-specific formulations, as current studies disproportionately focus on salmonids and tilapia while neglecting emerging farmed species. Additionally, while short-term benefits are well-documented, longitudinal studies examining microbiome stability and immune adaptation over production cycles remain scarce. Perhaps most critically, the aquaculture industry lacks cost-benefit analyses comparing functional feed strategies against conventional approaches, particularly for small-scale operations. Addressing these knowledge gaps through carefully designed, application-focused research will be essential for transitioning from experimental success to widespread commercial adoption.

## 9. CONCLUSIONS

Advancements in aquaculture nutrition have highlighted the transformative potential of functional feeds in improving fish health and overall industry sustainability. The strategic inclusion of nutraceuticals, prebiotics, probiotics, antioxidants, and immunostimulants not only enhances nutrient utilization and immune resilience but also offers promising alternatives to conventional antibiotic treatments. These interventions contribute to disease prevention, better growth performance, and improved product quality. However, their efficacy is often influenced by fish species, farming conditions, and feed formulation precision. To support sustainable aquaculture practices, it is imperative to prioritize integrative fish health strategies combining evidence-based dietary

interventions with proactive health management and environmental monitoring. A holistic, nutrition-based approach will be vital in meeting the global demand for safe, high-quality fish while ensuring ecological responsibility and animal welfare.

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### Highlights:

1. Functional feeds enhance fish growth, immunity, and resilience to environmental and pathogenic stressors.
2. Nutraceuticals, probiotics, prebiotics, antioxidants, and immunostimulants offer sustainable alternatives to antibiotics in aquaculture.
3. Feed additives play a critical role in gut health modulation, disease resistance, and stress mitigation.
4. Integration of nutrition-based strategies with vaccination supports proactive fish health management.
5. Precision formulation of species-specific functional feeds is essential to improve productivity and reduce ecological impact.

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