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REVIEW

Nanotechnology in Aquaculture: Food Safety, Human Health Risks, and Regulatory Challenges

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ABSTRACT

The integration of nanotechnology into aquaculture presents transformative opportunities to enhance feed efficiency, disease control, and sustainability. However, the potential for engineered nanoparticles (ENPs) to accumulate in edible tissues raises significant food safety and human health concerns. Recent analyses using single-particle ICP-MS have detected ENPs in seafood at trace but measurable concentrations. For example, titanium dioxide ENPs were identified in tuna and clam samples at levels ranging from 0.5 to 2.5 mg/kg, corresponding to estimated dietary exposures of 0.9–3.2 µg/kg body weight/day. Similarly, experimental exposure studies show that silver ENPs can accumulate in edible fish muscle at concentrations ranging from 10 to 80 µg/kg, depending on particle size and exposure duration. These findings underscore the need for strengthened analytical monitoring and risk assessment frameworks to evaluate potential human health implications. This review focuses on nano-enabled applications that directly affect seafood safety, including nano-feed additives, antimicrobial agents, and nanocarriers for therapeutics. Evidence from bioaccumulation studies, toxicokinetics, and *in vitro* assays is examined to assess potential human exposure and risks via seafood consumption. Regulatory frameworks from the EFSA, FDA, and Codex Alimentarius are compared to highlight gaps in oversight. Risk mitigation strategies, including Safe-by-Design nanomaterials and improved analytical

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detection, are also discussed. The review concludes with research priorities aimed at ensuring the safe and sustainable adoption of nanotechnology in the seafood sector.

Keywords: Nanotechnology; Aquaculture; Food Safety; Human Health; Bioaccumulation; Regulatory Frameworks

1. Introduction

Aquaculture is the controlled farming of aquatic organisms in freshwater or marine water for human consumption. It is the fastest-growing food production sector globally, contributing over 50% of the world's fish supply [1,2]. The growth of the aquaculture sector is primarily driven by its potential to enhance global food security, alleviate poverty, support diversified livelihoods, strengthen the resilience of coastal communities, attract investment, and ease the burden on wild fisheries, thereby aiding the restoration of marine and coastal ecosystems [3]. Projections indicate that aquaculture production will increase to 106 million tonnes by 2030, underscoring its importance in meeting the protein demands of a growing population [2].

Despite its growing contribution to global seafood supply, the sector faces persistent challenges such as disease outbreaks, poor water quality, inefficient feed utilization, and environmental degradation which can limit production efficiency and affect product safety [1,4]. These constraints not only reduce profitability but also threaten environmental integrity and food safety. For instance, disease alone accounts for over USD 10 billion annually and poses significant environmental and public health risks [5]. Conventional strategies such as prophylactic antibiotic use, chemical disinfectants, and intensive water exchange often prove costly and unsustainable, contributing to antimicrobial resistance (AMR), nutrient pollution, and biodiversity loss [6,7]. This confluence of biological, environmental, and economic pressures highlights the urgent need for innovative, more sustainable technologies capable of simultaneously improving system efficiency and reducing health and environmental risks. **Table 1** summarises major challenges in aquaculture. These challenges call for innovative, sustainable solutions to enhance productivity while safeguarding ecosystems and human health.

Table 1. Summary of major challenges in aquaculture: Conventional interventions vs. nano-enabled solutions.

Challenge	Conventional Methods	Limitations	Nano-Enabled Solutions	Advantages
Disease management	Antibiotics, chemical treatments	AMR, environmental pollution	Nanovaccines, nanocarriers	Reduced antibiotic use, targeted
Feed efficiency	Conventional feeds	Nutrient wastage	Nano-feed additives	Enhanced bioavailability
Water quality control	Water exchange, filtration	High water use, incomplete removal	Nanomaterials (TiO_2, AgNPs)	Improved purification, pathogen control
Environmental monitoring	Periodic sampling, lab analysis	Delayed detection	Nanosensors, real-time monitoring	Early warning systems

Nanotechnology, defined as the manipulation of materials at the nanoscale (1–100 nm), offers transformative opportunities for aquaculture due to the unique physicochemical properties of nanomaterials [8,9]. The unique physicochemical properties of engineered nanomaterials, such as high surface area and reactivity, enable enhanced nutrient bioavailability through nano-enabled feed additives and improved disease resistance via nanovaccines and targeted drug delivery [10]. Applications include nano-enabled feed additives for improved nutrient bioavailability and growth performance [11], nanovaccines and nanocarrier-based therapeutics for targeted drug delivery and enhanced immunity [12], and nanomaterials for water purification and nanobubbles for oxygenation, all of which enhance system efficiency and sustainability. In addition, nanomaterials like titanium dioxide (TiO_2 NPs), iron oxide (Fe_3O_4 NPs), and silver nanoparticles (Ag NPs) have been investigated for water purification and pathogen control [13], while nanosensors allow for real-time monitoring of water quality and pathogen presence, advancing precision aquaculture [10].

Despite these advances, unresolved concerns remain regarding the environmental fate of nanoparticles (NPs), their accumulation in aquatic organisms, and long-term human health impacts [14,15]. Regulatory frameworks from agencies such as the European Food Safety Authority (EFSA), Food and Drug Administration (FDA), and Codex Alimentarius remain fragmented and lack harmonization, creating uncertainties that may hinder global trade and commercialization [16,17]. Emerging trends, including biodegradable nanomaterials, CRISPR-based nano-delivery systems, and AI-driven nano-enabled monitoring tools, highlight the sector's innovation trajectory, yet they also amplify the need for robust risk assessment and governance [18,19].

Most existing reviews focus on either the technological applications or toxicological aspects of nanotechnology in aquaculture separately, rarely integrating human health risks, regulatory challenges, and trade implications into a comprehensive analysis. Considering the COVID-19 pandemic, which has underscored vulnerabilities in global food systems and amplified the use of disinfectants and antiviral chemicals, a holistic approach is urgently needed to ensure the safe and sustainable development of nano-enabled aquaculture. This review uniquely bridges this gap by synthesizing recent breakthroughs in nano-aquaculture technologies with an interdisciplinary evaluation of human health impacts, regulatory landscapes, and risk mitigation strategies. A novel conceptual framework, the Sustainability–Risk Nexus, which integrates technological innovation, environmental and human health risk assessment, regulatory compliance, and trade considerations is proposed. This framework aims to guide researchers, policymakers, and industry stakeholders in balancing the benefits of nano-enabled aquaculture with consumer safety and ecosystem preservation in the post-COVID era. As aquaculture products enter global markets, ensuring food safety and consumer protection is imperative.

2. Applications of Nanotechnology in Aquaculture

The integration of nanotechnology into aquaculture addresses key challenges such as disease management, feed efficiency, water quality control, and environmental monitoring. The following subsections critically evaluate recent advancements in these domains, comparing nanotechnology-based interventions with traditional practices to highlight the potential transformative impact of nano-enabled technologies. **Table 2** provides a comparative analysis of conventional and nano-enabled technologies in aquaculture.

Table 2. Comparative Analysis of Conventional vs. Nano-Enabled Technologies in Aquaculture.

Application	Conventional Technology	Nano-Enabled Technology	Key Advantages	Challenges
Feed additives	Mineral/vitamin premixes	Nanoencapsulation of nutrients	Improved bioavailability, lower doses	Potential nanoparticle toxicity, cost
Disease control	Antibiotics, vaccines	Nanovaccines, nano-drug carriers	Enhanced immune response, reduced AMR	Regulatory uncertainty, safety data gaps
Water purification	Mechanical filtration, exchange	Nanoparticle photocatalysis, magnetic adsorption	Efficient pollutant removal, water saving	Nanoparticle environmental persistence
Monitoring	Periodic manual sampling	Nanosensors with AI integration	Real-time data, early warning	Sensor fouling, data management issues

2.1. Nano-Enabled Nutrition and Feed Efficiency

Feed constitutes the largest operational expense in aquaculture, accounting for 50–60% of total production costs [20,21]. To feed the growing global population projected to reach 9.8 billion in 2050, fish is the cheapest source of protein. However, conventional feed formulations, supplemented with bulk minerals, vitamins, and other additives, often exhibit low bioavailability. This inefficiency leads to nutrient wastage, elevated costs, and water quality degradation through nutrient leaching, which contributes to eutrophication and environmental stress [21–23]. Addressing these limitations is critical for improving economic viability and sustainability in intensive aquaculture systems.

Nanotechnology-based feed interventions have emerged as a promising solution to enhance nutrient delivery, absorption, and utilization. Nanoparticles, due to their high surface area and reactivity, enable better nutrient absorption, sustained release, and targeted delivery, contributing to overall improved health and productivity of farmed aquatic species [24]. For instance, Zn NPs incorporated into fish diets have demonstrated superior growth performance and improved immune responses compared to conventional bulk zinc sources, attributed to enhanced bioavailability and cellular interaction [25,26]. Similarly, nano-supplementation with nano-selenium and nano-ZnO has been shown to improve growth rates, antioxidant capacity, and disease resistance in fish and shrimp [27,28].

One of the most promising strategies in aquaculture for enhancing nutrient delivery and fish health is nano-encapsulation. This involves enclosing bioactive compounds such as vitamins, essential fatty acids, probiotics, and essential oils within nanoscale carriers made from biopolymers (e.g., chitosan), lipids, or inorganic materials [29]. This controlled-release mechanism protects sensitive compounds from degradation during feed processing and digestion, improving gut health and feed conversion ratios (FCR) [30–32]. Moreover, by minimizing nutrient leaching into surrounding waters, nano-enabled feed technologies significantly reduce the risk of eutrophication, aligning with sustainability objectives and lowering environmental footprints. In species such as tilapia and beluga sturgeon, nano-encapsulation using chitosan NPs has been shown to significantly enhance growth performance, antioxidant defenses, immune function, and resistance to Aeromonas pathogens [33,34]. Nano-encapsulated essential oils also demonstrated enhanced antimicrobial, antioxidant, and immunostimulatory effects, improving resistance to infections and supporting growth in Nile tilapia (*Oreochromis niloticus*) [35,36]. Collectively, these innovations not only improve growth performance and health outcomes in aquatic species but also reduce production costs and mitigate ecological impacts. As research progresses, integrating nano-enabled feed solutions into aquaculture holds promise for advancing both productivity and environmental stewardship. Nano-supplementation enhances nutrient absorption and fish immunity. However, residual nanoparticles may accumulate in muscle tissues, posing dietary exposure risks. Controlled-release formulations reduce nutrient leaching but require evaluation of bioavailability in humans.

2.2. Disease Management

Disease outbreaks remain a major constraint in aquaculture, causing substantial economic losses and posing serious biosecurity challenges worldwide [37–39]. Conventional control measures, primarily the prophylactic use of antibiotics and chemical therapeutics, have contributed to the emergence of AMR, residual contamination of aquatic environments, and negative impacts on human health [6,7]. Nanocarriers (e.g., chitosan) are used to deliver drugs and vaccines. These systems improve therapeutic efficiency and reduce antibiotic use, mitigating AMR. However, concerns persist regarding the fate of carrier particles in edible tissues and their transformation during digestion. These limitations necessitate the urgent need for alternative, sustainable disease management strategies. Nanotechnology offers transformative solutions for improving disease prevention and treatment through three main approaches:

2.2.1. Nanovaccines

Nanovaccines utilize NPs as carriers or adjuvants to enhance antigen stability, stimulate stronger immune responses, and enable controlled antigen release. Polymeric NPs, such as chitosan-based systems, have demonstrated high efficacy in oral vaccine delivery by promoting mucosal immunity in fish and crustaceans, reducing stress associated with injection-based methods [40,41]. A recent study by Ibrahim et al. [42] demonstrated the therapeutic potential of chitosan-based nano-encapsulated neem (*Azadirachta indica*) extract (CNNC) in managing bacterial infections in Nile tilapia. In both *in vitro* and *in vivo* trials, CNNC exhibited significant antibacterial activity against *Aeromonas sobria*, a common aquaculture pathogen. Fish challenged with *A. sobria* exhibited oxidative stress, immune suppression, and reduced survival (60%). However, treatment with CNNC at 1 mg/L in water restored antioxidant levels (e.g., catalase, glutathione), normalized liver and kidney function markers, and significantly improved survivability. The minimum inhibitory and bactericidal concentrations of CNNC were 6.25 mg/mL and 12.5 mg/mL, respectively. These results support CNNC as a promising, eco-friendly alternative to antibiotics for disease control in aquaculture.

Lipid-based nanocarriers and other biodegradable polymers provide additional benefits by prolonging antigen release and improving bioavailability compared to conventional vaccines [43,44]. These attributes significantly improve protection against pathogens with reduced dosing frequency and minimal side effects. Jonjaroen et al. [45] reviewed the use of nano-encapsulation technologies to enhance the stability and cellular delivery of double-stranded RNA (dsRNA) for antiviral applications in shrimp aquaculture. Due to dsRNA's inherent instability and susceptibility to enzymatic degradation, the study emphasized the importance of nanoparticle carriers such as virus-like particles (VLPs), liposomes, chitosan, and β-glucan. Chitosan- and glucan-based nanocarriers not only protect dsRNA from degradation but also stimulate the immune response in shrimp, improving resistance to viral pathogens. Yeast-derived β-glucan particles were highlighted for their dual role as immunostimulants and delivery systems. The authors also addressed formulation challenges (e.g., pH, solvents, and metal ions), regulatory hurdles, and the need for field-level validation and environmental risk assessment before commercialization. This work positions dsRNA-loaded NPs as a promising, targeted antiviral strategy in sustainable shrimp farming.

2.2.2. Nanocarrier-Based Therapeutics

Nanocarriers have transformed therapeutic delivery in veterinary, and agricultural fields by enabling targeted and controlled release of active compounds, thereby enhancing efficacy and reducing off-target effects. Recent trends indicate a shift from delivering small molecules to the use of nanocarriers for peptides, proteins, and nucleic acids. This change is largely driven by advances in bioengineering and the rise of environmentally friendly, bioinspired nanocarriers. Despite these innovations, several challenges remain. In agriculture, the lack of clear regulatory frameworks continues to hinder the commercial use of nanocarriers. Nonetheless, nanocarriers hold significant potential for precision treatment of diseases and improved productivity across sectors [46]. Nano-encapsulation of drugs and immune-stimulants enhances therapeutic efficiency by enabling targeted delivery, controlled release, and improved bioavailability. Controlled release is a key application of nanotechnology in drug delivery, enabling the accurate and sustained release of therapeutic agents from NPs or other carriers over a prolonged duration [47]. This approach reduces dosage requirements and mitigates risks of toxicity and environmental accumulation, making it a promising strategy for sustainable health management in aquaculture.

Chitosan nanoparticles (CNPs) have shown promise in improving disease resistance and health in Nile tilapia (*O. niloticus*). In a recent feeding trial, fish diets supplemented with up to 5 g/kg of CNPs significantly enhanced immune responses, intestinal morphology, and antioxidant activity compared to both control and conventional chitosan groups. Notably, fish receiving 3 and 5 g/kg CNPs exhibited lower mortality rates following a challenge with *Aeromonas veronii* biovar *sobria*. These effects were supported by upregulated expression of immune-related genes (TLR-2, MUC-2, and IGF-1) and increased phagocytic and respiratory burst activity, without triggering heat shock responses (HSP70). The findings support dietary CNPs, particularly at 5 g/kg, as an effective and safe strategy to enhance disease resistance in aquaculture [33].

2.2.3. Antimicrobial Nanomaterials

Metal-based NPs, including Ag NPs, ZnON Ps, gold (Au NPs), and copper oxide (CuO NPs), have emerged as potent antimicrobial agents in aquaculture. These NPs display broad-spectrum efficacy against various aquatic pathogens such as *Aeromonas hydrophila*, *Edwardsiella tarda, Vibrio spp.*, *Pseudomonas fluorescens,* etc. Though effective against pathogens, these materials can persist in water and be absorbed by aquatic species. Their mechanisms include damaging microbial membranes, generating reactive oxygen species (ROS), and disrupting DNA and protein synthesis [48].

Among these, Ag NPs have shown notable promise. In marine shrimp aquaculture, Ag NPs have been investigated as both prophylactic and therapeutic agents against bacterial and viral pathogens, including *Vibrio spp.* and white spot syndrome virus (WSSV) [49]. These NPs can be administered through feed, injection, or immobilized in water filters. Their broad-spectrum activity and flexibility make them attractive alternatives to antibiotics. However, most toxicity studies have been limited to short-term exposures. Data on chronic effects, bioaccumulation, and stage-specific sensitivities in shrimp are lacking.

Despite these gaps, Ag NPs offer a safer and more environmentally sustainable option compared to antibiotics. Studies report effective antimicrobial action at low concentrations, reducing both toxicity and environmental persistence [50]. This is especially relevant given the misuse of antibiotics in aquaculture. A study in Vietnam found that 91.7% of small-scale freshwater fish farmers used antibiotics, often without diagnostic testing or proper guidance [51]. Alarmingly, 98.2% of them did not perform antibiotic susceptibility testing, and 78.9% treated disease outbreaks based solely on visual symptoms. Some even used antibiotics prohibited in aquaculture or classified as "critically important" in human medicine. These practices raise serious concerns about AMR and food safety. Nanoparticles, by contrast, act via multiple mechanisms and are less likely to drive resistance.

Nanoparticle-based antimicrobials could serve as a safer and more responsible alternative to indiscriminate antibiotic use. They offer targeted, non-specific microbial killing without contributing to resistance. Still, the adoption of antimicrobial NPs in aquaculture depends on proper risk assessments, species-specific safety data, and regulatory approval. There is also a need for cost-effective, scalable production methods tailored for commercial shrimp and fish farming. Overall, these nanotechnology-driven approaches, encompassing nanovaccines, targeted drug delivery, and antimicrobial nanomaterials represent a paradigm shift in aquaculture health management. They offer sustainable and efficient alternatives to conventional practices, improving biosecurity while reducing reliance on antibiotics and chemical treatments.

2.3. Nanomaterials for Water Quality Management and Pathogen Control

Optimal water quality is a cornerstone of sustainable aquaculture, directly influencing animal health, growth performance, and system biosecurity. Traditional methods such as frequent water exchange, mechanical filtration, and chemical disinfection, while effective, are resource-intensive and may contribute to environmental degradation through nutrient loading and chemical residues. In response, nanotechnology presents innovative, eco-friendly solutions for water purification and pathogen control.

2.3.1. Photocatalytic and Antimicrobial Nanomaterials

Recent studies highlight the effectiveness of nanomaterials in treating aquaculture effluents by improving physicochemical parameters and reducing harmful contaminants. Nanoparticles have been shown to remove heavy metals like lead, and degrade persistent organic pollutants such as polychlorinated biphenyls, polycyclic aromatic hydrocarbons, and pesticides. Additionally, they exhibit antimicrobial properties, significantly reducing microbial loads of pathogens such as *Salmonella, Escherichia coli, Campylobacter,* and *Vibrio spp*. [52]. Engineered NPs such as TiO_2 NPs, Ag NPs, and ZnO NPs exhibit strong photocatalytic and antimicrobial properties. A study by Ozkaleli and Erdem [53] demonstrated the antibacterial efficacy of TiO_2 NPs against *Staphylococcus aureus* and *Bacillus subtilis*, two gram-positive bacteria commonly found in contaminated water. TiO_2 NPs were tested under varying concentrations (10–1000 mg/L) and water chemistries (pH 6.5; ionic strength 10–100 mM). Results showed significant bacterial inactivation even in the absence of light, with enhanced photocatalytic activity under visible light. *B. subtilis* exhibited higher resistance than *S. aureus*, as reflected by lower specific die-off rates (k′). These findings support the potential of TiO_2 NPs as effective agents for waterborne pathogen control in aquaculture environments.

A comparative study by Şimşek et al. [54] evaluated the effectiveness of graphene oxide (GO), Ag NPs, and GO–Ag nanocomposites in drinking water purification against a conventional treatment method. GO-based filtration significantly improved water quality parameters, including color, total inorganic carbon (TIC), total organic carbon (TOC), and hardness, with up to 86.8% enhancement in TOC removal. The GO–Ag nanocomposite also achieved substantial microbial reduction, effectively inhibiting pathogens such as *E. coli*, *Salmonella typhi*, *Enterococcus faecalis*, *Pseudomonas aeruginosa*, and *Staphylococcus* *aureus*. These findings highlight the superior antimicrobial and physicochemical purification performance of GO–Ag nanomaterials compared to traditional methods, supporting their application in aquaculture water treatment systems. In marine shrimp farming, Ag NPs demonstrated potential effectiveness against pathogens such as *Vibrio spp*. and WSSV, delivered via injection, feed inclusion, or filtration systems [49]. However, concerns remain regarding their potential toxicity, bioaccumulation, and environmental safety, particularly under chronic exposure conditions. **Table 3** summarizes mechanisms and toxic effects of nanomaterials used in aquaculture water treatment.

Table 3. Nanoparticles Used in Aquaculture Water Treatment: Mechanisms and Toxic Effects.

Nanoparticle Type	Primary Mechanism of Action	Antimicrobial / Treatment Function	Reported Toxic Effects in Aquatic Species
TiO_2 NPs	Photocatalysis; ROS generation (•OH, O_2^-); membrane disruption	Effective against *Staphylococcus aureus*, *Bacillus subtilis*; degrades organic pollutants	Oxidative stress, ROS damage, reduced reproduction; toxicity modulated by salinity and UV exposure
Ag NPs	Release of Ag^+ ions; membrane damage; protein/DNA interaction	Broad-spectrum antimicrobial activity against *Vibrio spp.*, *Aeromonas spp.*; antiviral effects (White Spot Syndrome Virus)	Gill necrosis, intestinal inflammation, liver degeneration; bioaccumulation in muscle tissues
ZnO NPs	Dissolution into Zn^{2+}; ROS production; surface reactivity	Antibacterial activity; removal of organic contaminants	Reduced hatching success, oxidative stress, immune suppression; size-dependent toxicity
Graphene Oxide (GO)	Adsorption; membrane stress; improved filtration efficiency	Removal of TOC, TIC, hardness; strong antimicrobial effects when combined with Ag	Potential oxidative stress at high concentrations; limited bioaccumulation data
Magnetic Nanoparticles (Fe_2O_3, Fe_3O_4)	Adsorption; magnetic recovery; complexation with metals	Heavy metal removal (Cd^{2+}, Pb^{2+}, Cu^{2+}); antimicrobial action when functionalized	Generally low toxicity when coated; may cause oxidative stress at high doses
Nanobubbles (Ozone- and O_2-NBs)	ROS generation; enhanced gas transfer; collapse-induced microbial inactivation	Pathogen reduction (*Vibrio parahaemolyticus*); improved DO; decreased organic load	Safe in most studies; high ozone doses may irritate gill tissue

Despite these benefits, concerns remain regarding the ecotoxicity of NPs to aquatic organisms, including potential impacts on salinity and long-term ecosystem health. However, modifications such as fluorescent labelling, tyrosine coating, and the use of biocompatible carriers offer promising strategies to mitigate toxicity and enhance safety [52]. Continued research into these approaches is essential for the responsible integration of nanotechnology in aquaculture water management.

2.3.2. Adsorptive and Magnetic Nanomaterials

Magnetic and adsorptive nanomaterials have gained attention for their ability to remove dissolved pollutants such as heavy metals, phosphates, and nitrogenous compounds from aquaculture systems. These contaminants contribute to eutrophication and disease outbreaks when not adequately controlled. Recent advances in the surface modification of magnetic nanoparticles (MNPs), particularly through biopolymer coatings and silica functionalization, have significantly improved their capacity to adsorb heavy metals from aqueous environments [55]. Although most applications to date have been conducted in controlled lab settings, their strong adsorption potential and magnetic recoverability make them promising candidates for use in aquaculture wastewater treatment systems.

Aquaculture wastewater is increasingly recognized as a significant environmental concern due to nutrient loading, residual pharmaceuticals, and pathogenic contamination. While biological (e.g., bioflocs, wetlands) and physicochemical methods (e.g., advanced oxidation processes (AOPs), membranes) have been widely applied, their sustainability and long-term effectiveness remain limited [56]. Nanotechnology-based interventions, such as photocatalytic TiO_2 or adsorptive nanomaterials, offer promising alternatives that can complement or enhance these existing systems. A notable experimental study demonstrated the application of a biogenic Fe_2O_3-based magnetic cryogel, synthesized using *Bacillus subtilis* and embedded in a polyvinyl alcohol (PVA) matrix, to remediate cadmium-contaminated water in Nile tilapia culture. The magnetic cryogel not only reduced cadmium concentrations but also restored physiological, hematological, and immune parameters in the fish, highlighting its safety and efficiency in live aquaculture settings [57]. These findings support the integration of magnetic nanomaterials into sustainable aquaculture water management. Their recyclability and low residual toxicity make them attractive alternatives to conventional chemical treatments.

2.3.3. Nanobubble Technology

Nanobubble (NB) technology, comprising gas-filled cavities typically under 1 µm in diameter has gained growing interest in aquaculture for its capacity to enhance water quality and support disease mitigation. These NBs remain stable in water over extended periods, facilitating prolonged interaction with dissolved gases. Their nanoscale size enables superior gas transfer efficiency and promotes the generation of (ROS, including hydroxyl radicals and singlet oxygen, which together contribute to elevated dissolved oxygen levels and microbial suppression [58,59]. Emerging evidence indicates that NB aeration significantly improves oxygen delivery and reduces energy input compared to traditional bubble systems. In synthetic wastewater and biofilm systems, NBs have been shown to double oxygen transfer efficiency and deliver up to 80% energy savings, while also enhancing pollutant degradation and microbial control [60].

Recent studies highlight the practical benefits of NB technology in aquaculture systems. Applications of NBs particularly those infused with ozone or oxygen have proven effective in controlling pathogens such as *Vibrio parahaemolyticus* and enhancing survival rates in species like Nile tilapia and shrimp. For example, a controlled study in Vietnam demonstrated that oxygen- and ozone-enriched NBs significantly reduced *Vibrio* concentrations while improving water quality in shrimp culture ponds [61]. These findings reinforce the dual function of NBs in both oxygenation and microbial suppression. Beyond oxygen delivery, NBs can act as efficient carriers for active gases such as ozone and hydrogen, enabling targeted disinfection without leaving harmful residues associated with conventional chemical treatments. For instance, Dien et al. [62] demonstrated this using ozone NBs in a recirculating aquaculture system. The treatment significantly reduced microbial loads, including multidrug-resistant *Aeromonas hydrophila*. Bacterial concentrations were lowered by approximately 16–36%, and relative percent survival in treated Nile tilapia reached around 65%. Importantly, no adverse effects on fish health or behavior were observed during the exposure period. Ozone NB treatments have been shown to upregulate immune-related gene expression and improve disease resistance in Nile tilapia, resulting in significantly higher survival rates following bacterial challenge [63]. A comprehensive review by Yaparatne et al. [59] further emphasized that NBs generated from gases like air, oxygen, ozone, and hydrogen not only improve gas exchange but also aid in pollutant degradation and pathogen inactivation. These effects collectively lead to increased growth rates, improved harvest yields, and reduced mortality across various aquaculture species.

Long-term pilot-scale applications, including those in recirculating aquaculture systems (RAS), have shown additional benefits such as enhanced water clarity, improved nitrification, and reduced carbon dioxide accumulation [59]. Moreover, NBs have been successfully applied to manage sea lice in salmon farming and to optimize biofilter performance, supporting more sustainable and productive aquaculture operations. Despite these advantages, several challenges remain. Issues related to scalability, cost-efficiency, and potential ecological impacts of NB technology must be addressed. More comparative and long-term studies are needed to assess these aspects and to establish standardized protocols for safe and effective implementation. Nevertheless, current evidence positions NBs as a promising innovation for sustainable aquaculture development.

2.4. Environmental Monitoring and Smart Aquaculture

Precision environmental monitoring is critical in modern aquaculture for maintaining optimal water quality and ensuring healthy livestock. Traditional methods such as manual sampling and laboratory analysis are time-consuming, labour-intensive, and often lack the sensitivity required for early detection of critical parameters such as dissolved oxygen (DO), ammonia, nitrite, pH, and pathogenic microorganisms. Delays in corrective measures can lead to disease outbreaks, poor growth performance, and significant economic losses. By contrast, nanosensor-enabled monitoring systems, integrated into Internet of Things (IoT) platforms, provide continuous, real-time data and enable early detection of environmental stressors [64]. Recent systematic reviews highlight the proliferation of low-cost water quality sensors adapted for IoT applications in aquaculture. These systems monitor key parameters with sufficient accuracy and support real-time decision-making while minimizing infrastructure costs [64].

Experimental validation in Asian seabass (*Lates calcarifer*) culture systems demonstrated that IoT-based sensor arrays measuring temperature, pH, dissolved oxygen, ammonia, and conductivity can be calibrated against professional-grade instruments. This approach ensures reliable monitoring while maintaining affordability and operational scalability [65]. Incorporating nanosensor innovations such as carbon nanotube or graphene-based electrodes and metaloxide nanocomposites further enhances detection sensitivity. These nanomaterials can detect trace levels of ammonia, nitrates, heavy metals, and organic contaminants with rapid response times, a key advantage for smart aquaculture systems [66]. Foo et al. [67] emphasized the role of nanomaterials not only in contaminant sensing but also in water disinfection and pollutant degradation. Their study highlights the potential of nanotechnology-based platforms to monitor, remediate, and optimize aquaculture water systems, especially when coupled with advanced data analytics.

Recent innovations now pair nanosensors with IoT and Artificial Intelligence (AI) platforms, forming intelligent aquaculture systems capable of real-time water-quality monitoring, predictive analytics, and automated management [68,69]. These integrated platforms enable: (1) Predictive Analytics: AI-driven models on IoT sensor data offer early warnings for disease outbreaks or deteriorating water quality. (2) Automation: Systems adjust aeration, feeding, and water exchange in real time, minimizing manual intervention. (3) DataDriven Sustainability: Optimizes resources, enhances biosecurity, and reduces environmental impact.

Combining nanosensors with IoT and AI signals a shift toward fully digitized, efficient, and sustainable aquaculture production. While traditional approaches such as antibiotics and mechanical aeration remain widespread, they carry drawbacks like AMR, environmental contamination, and high costs. Cabello et al. [70] documented the link between antibiotic overuse in aquaculture and global AMR dissemination. Conversely, nanotechnology-based methods offer potential for lower chemical usage, higher efficiency, and improved sustainability. That said, uncertainties persist regarding the fate, bioaccumulation, and potential toxicity of nanoparticles in aquatic systems emphasizing the importance of robust safety assessments before widespread use.

These advances collectively position nanotechnology as a promising tool to enhance aquaculture sustainability and resilience. However, the rapid development of nano-enabled inputs demands concurrent assessment of their environmental fate, bioaccumulation potential, and human health impacts, which are addressed in the following sections.

3. Ecotoxicological Impacts of Nanomaterials

While nanotechnology holds considerable promise for advancing aquaculture, concerns regarding the environmental fate, behavior, and toxicological effects of NPs must be rigorously addressed. The unique physicochemical properties of NPs such as small size, high surface area, and reactivity allow them to interact with aquatic ecosystems in ways that differ fundamentally from bulk materials [71]. This section discusses current understanding of NP persistence, bioavailability, and ecotoxicological effects in aquaculture environments.

3.1. Environmental Fate and Transport of Nanoparticles

Nanoparticles introduced into aquaculture systems through feeds, therapeutics, or water treatment can enter surrounding water bodies and sediments via effluent discharge or direct application. Once released, their environmental behavior is shaped by key processes such as aggregation, dissolution, adsorption onto natural organic matter (NOM), sulfidation, and sedimentation, all of which influence particle mobility, transformation, and ecological impact [15,72]. **Figure 1** illustrates a conceptual overview of the fate of NPs in biological systems, illustrating the sequence from environmental exposure, uptake routes in aquatic organisms, internal distribution across organs and tissues, subsequent transformation and interaction within biological environments, and final excretion or elimination pathways. Ag NPs undergo rapid transformations in oxic and saline waters. In low-salinity systems, Ag NPs may be stabilized by NOM, whereas in high-sulfide or chloride environments, sulfidation can transform them into less bioavailable forms such as Ag_2S. These transformations reduce Ag^+ ion release and colloidal mobility, thereby lowering acute toxicity. However, sediment-associated Ag species can still pose chronic risks to benthic organisms [72]. In contrast, TiO_2 NPs exhibit different behavior, remaining suspended longer in water columns due to slower sedimentation. Their aggregation and settling behavior are sensitive to environmental factors such as pH, ionic strength, and presence of algal or organic colloids. Under UV exposure, TiO_2NPs can generate ROS, elevating risks to pelagic organisms [73].

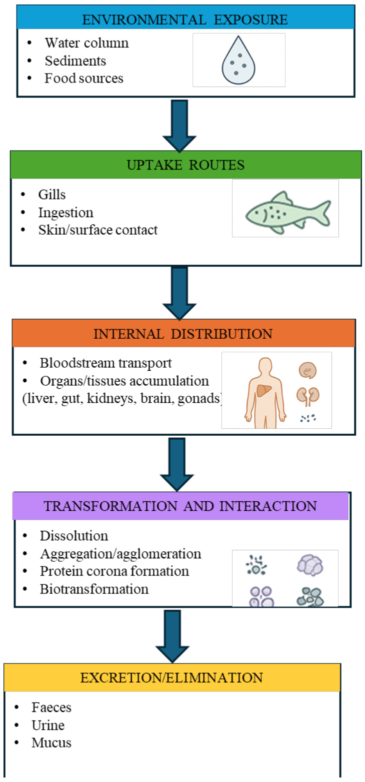

Figure 1. Conceptual overview of the fate of NPs in biological systems.

A study by Huang et al. [74] examined the toxicity of TiO_2 and Ag NPs on *Moina mongolica* under varying salinity levels in nearshore environments. Both NPs caused oxidative stress and immune responses, with Ag NPs showing stronger reproductive toxicity due to Ag^+ release. Transcriptomic analysis revealed carapace damage from NP accumulation. Salinity increased TiO_2 toxicity but reduced that of Ag NPs, highlighting salinity's key role in modulating NP effects in coastal ecosystems.

Additionally, in highsalinity environments ZnO NPs tend to aggregate and settle, reducing aqueous-phase bioavailability but increasing exposure risk for benthic organisms. Acidic or lowionic strength conditions promote dissolution, generating Zn^{2+} ions that drive toxicity [75]. For example, in early life stages of the pufferfish *Takifugu obscurus*, exposure to ZnO NPs significantly decreased hatching success and survival, and induced oxidative stress responses (MDA, SOD, CAT, GSH) and morphological deformities [76]. Similarly, studies on the marine mussel *Xenostrobus securis* showed that toxicity varied with salinity and temperature, with nanoparticle surface coatings modulating effects [77]. Algal species are particularly sensitive to Zn^{2+} release. For example, ZnO NPs inhibited growth and induced ROS-mediated stress in algae, making them effective indicators of ecosystem-level impacts [78]. Comparative toxicity assays found that small ZnO NPs had greater dissolution and stronger acute effects than nanorods or ionic Zn. Algae and bacteria exhibited lower LC_{50} thresholds

(~15 mg/L) compared to crustaceans like *Artemia* (LC_{50} ~ >40 mg/L) [79]. In marine systems, their aggregation increases with salinity, potentially reducing bioavailability in the water column but increasing sedimentation and exposure to benthic species. Furthermore, ZnO NPs can interact with NOM and phosphates, affecting dissolution rates and ecological risk profiles [80].

Understanding these transformation pathways including sulfidation, photochemical alterations, and NOM/EPS surface interactions is critical for accurate modeling of NP transport and bioavailability in aquatic ecosystems. Integrating such mechanistic insights into environmental risk assessments will improve predictive accuracy and guide the safer application of nanomaterials in aquaculture and aquatic industries.

3.2. Bioaccumulation and Biomagnification in Aquatic Organisms

Bioaccumulation of nanoparticles in aquaculture species such as fish and shrimp raises significant concerns for environmental safety and human health. Engineered NPs can be taken up through gills, ingestion, and skin, accumulating in organs like the liver, kidney, and muscle [81]. In tilapia (*O. niloticus*), ZnO NPs (10–30 nm) accumulated at significantly higher levels in gill, liver, kidney, intestine, brain, and muscle, inducing oxidative stress via elevated SOD, CAT, GSH, and lipid peroxidation biomarkers (sizedependent effects; small > large NPs) [82].

In Asian seabass (*Lates calcarifer*) under lowsalinity estuarine conditions, chronic exposure (1–50 ppm ZnO NPs for 8 weeks) resulted in substantial accumulation in the head kidney, gills, and liver, with suppressed immune gene expression, impaired growth, and increased mortality (up to 100% at 50 ppm) [83]. Sex-specific biodistribution of ZnO NPs was observed in Japanese medaka (*Oryzias latipes*). For instance, male medaka accumulated particles in brain, gills, gut, kidney, and gonads, while females showed lower brain accumulation. Reproductive behavior and fertility were impaired in both sexes, mediated by ROS induction and endocrine disruption (200 nm nZnO vs $ZnSO_4$) [84]. Collective exposure to ZnO NPs and Ag NPs in *Oreochromis mossambicus* revealed additive oxidative stress and histopathological damage; coexposure influenced bioavailability, with reduced Ag accumulation in liver but heightened ZnO NP effects [85].

Biomagnification, the transfer of NPs up the food chain remains underexplored but may pose ecological and food safety risks. For instance, trophic transfer studies in a freshwater chain (*Dunaliella salina* → *Artemia salina* → *Poecilia reticulata*) revealed that Ag NPs could biomagnify from brine shrimp to guppy fish at BMF > 1 in liver and whole body, though not from algae to shrimp (BMF < 1) [86]. A recent study emphasized how microplastics can modify biomagnification dynamics. When *Chlorella vulgaris* and *Daphnia magna* were coexposed to ZnO NPs and polystyrene microplastics (PSMPs), biomagnification of ZnO NPs occurred in Daphnia (BMF up to 1.49 in acute exposure, and 2.11 in chronic 21day exposure), whereas ZnO NPs alone showed BMF < 0.90 Accumulation occurred in the *Daphnia* intestine, with increased ROS and physiological stress [87].

Nanoparticles such as ZnO and Ag are known to bioaccumulate in aquatic organisms, particularly in organs like the liver, kidney, and gills, leading to oxidative stress and physiological disruption. Accumulation is influenced by particle properties (e.g., size, surface chemistry, shape), exposure duration, and environmental conditions (e.g., salinity and pH). While biomagnification is less studied, evidence suggests that trophic transfer can occur, especially in the presence of co-contaminants like microplastics. These findings underscore the need to consider both bioaccumulation and biomagnification in nanoparticle risk assessments and call for further research into long-term, species-specific, and combined exposure effects.

3.3. Toxicological Effects on Aquatic Biota

Engineered NP toxicity in aquatic organisms is intricately shaped by particle characteristics such as size, coating, solubility and by environmental variables like salinity, pH, and organic content, which influence bioavailability and hazard potential [15,77,88,89]. Adverse effects commonly include oxidative stress, inflammation, histopathological damage, metabolic disruption, impaired growth, reproductive dysfunction, and even genotoxicity in plankton and algae [15,88].

A recent study examined chronic dietary exposure of Nile tilapia to Ag NPs at concentrations ranging from 10 to 100 μg/L across six weeks. Fish experienced dosedependent liver damage, including congestion, fatty degeneration, fibrosis, necrosis, and marked increases in lipid peroxidation (LPO) and antioxidant enzyme activities (SOD, CAT, GPx, GR). Over time, antioxidant enzyme activity declined while oxidative damage worsened. Compared to bulk silver nitrate ($AgNO_3$), AgNPs induced more severe and progressive hepatotoxicity, highlighting their greater ecological risk through prolonged exposure [90]. In earlier work on non-vertebrate primary producers, Mahaye et al. [89] exposed the aquatic plant *Salvinia minima* to citrate- and BPEI-coated gold NPs (5–40 nm) at environmentally relevant concentrations. While root-surface binding was evident, no nanoparticle internalization occurred and plant growth remained unaffected indicating low systemic toxicity but potential for localized interaction effects. Mahaye et al. [88] also explored cytotoxicity and genotoxicity of coated gold NPs in the green alga *Pseudokirchneriella subcapitata*. Smaller, BPEI-coated NPs caused the strongest growth inhibition and chlorophylla reduction. Notably, RAPD-PCR assays revealed DNA damage in all treatments, even when cellular toxicity was limited, indicating persistent sublethal genotoxic impact. Mahaye and Musee [91] extended this work by testing cerium oxide NPs ($nCeO_2$ < 25 nm) on *P. subcapitata* across a 62.5–1000 µg/L range. While initial physiological inhibition was observed, photophysiological recovery began by 168 h. However, molecular markers still indicated DNA damage, underscoring the importance of including genotoxic assays since recovery at the physiological level may mask underlying lesions.

These combined findings illustrate the diverse effects of NPs across aquatic taxa. Fish are particularly vulnerable to dose- and time-dependent oxidative stress and histopathological damage, especially under chronic Ag NP exposure. In contrast, algae and aquatic plants, while often physiologically resilient, can exhibit molecular and genetic damage even at low concentrations. Key factors influencing toxicity include particle size, surface reactivity, and ionic release (e.g., Ag^+, Zn^{2+}), all of which are associated with heightened biological impact. Aquatic organisms, from primary producers to higher trophic levels demonstrate susceptibility to both overt and sublethal NP-induced harm. To better capture these risks, traditional acute toxicity tests should be complemented by chronic exposure studies and molecular-level endpoints. Robust environmental risk assessments must also consider nanoparticle transformation, bioaccumulation, and species-specific responses. These evaluations are critical for ensuring the safe use and regulatory approval of nano-enabled inputs in aquaculture and aquatic systems

4. Human Health Implications of Nanoparticle Exposure via Seafood Consumption

The integration of ENPs such as TiO_2, Ag, and ZnO in aquaculture practices has prompted growing concern regarding their accumulation in edible seafood tissues and the potential health risks posed to consumers. These NPs, introduced either intentionally through nano-enabled feeds and antimicrobial coatings or unintentionally via environmental contamination, have been shown to bioaccumulate in edible tissues of aquaculture species including fish, shrimp, and mollusks. Recent analytical studies confirm the presence of such particles in seafood at trace levels, raising important questions about their long-term effects on human health.

A pivotal study by Grasso et al. [92] employed single-particle inductively coupled plasma mass spectrometry (spICP-MS) to detect and quantify TiO_2 NPs in various seafood products, including tuna and clam. Their results showed detectable levels of TiO_2-NPs in all samples, with estimated dietary exposures ranging from 0.9 to 3.2 µg/kg body weight/day. These levels are considered low but still relevant for risk characterization. These findings demonstrate that ingestion of NPs via seafood consumption is plausible under real-world exposure scenarios. Supporting this, *in vivo* studies in aquatic species reveal consistent bioaccumulation of NPs in tissues consumed by humans. Kakakhel et al. [93] exposed *Cyprinus carpio* (common carp) to Ag NPs and observed significant accumulation in muscle, liver, and gastrointestinal tissues, along with histopathological changes such as gill necrosis and intestinal inflammation. These results suggest that bioaccumulated NPs can persist in edible tissues and potentially be transferred to consumers.

In addition to bioaccumulation in edible aquatic tissues, understanding the toxicodynamics of nanoparticles in the human body is crucial for accurate health risk assessment. A recent review by Pathak et al. [94] emphasizes that the toxicity of nanoparticles is not only dose-dependent but also heavily influenced by their physicochemical properties such as size, shape, and surface functional groups. Importantly, chemically synthesized NPs with synthetic capping agents often exhibit greater cytotoxicity in human cell lines compared to biosynthesized NPs due to less biocompatible surfaces. The review further notes that while inhalation remains a common route of exposure, ingestion through contaminated food such as seafood and dermal contact via consumer products also represent viable pathways. Once ingested, NPs may interact with the gastrointestinal lining or enter systemic circulation, where they can affect various organs. In vitro studies have shown that hematite NPs can induce oxidative stress in lung fibroblast MRC-5 cells by depleting glutathione and increasing the activity of antioxidant enzymes such as SOD and catalase, which may parallel potential mechanisms in the gut epithelium. These findings underscore the necessity of evaluating not only direct cytotoxic effects but also secondary systemic responses such as oxidative stress and inflammation.

Despite these indications, the actual risk to human health from consuming NP-contaminated seafood remains uncertain. This is due, in part, to the absence of standardized analytical methods for detecting NPs in complex food matrices, and limited human-specific toxicokinetic (TK) and toxicodynamic (TD) data. According to the European Food Safety Authority [16], current risk assessment frameworks are not fully equipped to account for the unique behaviors and interactions of ENPs in the human body, particularly after oral exposure. EFSA calls for the integration of realistic exposure scenarios, validated *in vitro* digestion models, and physiologically based pharmacokinetic (PBPK) modeling to improve dietary risk assessments.

In this context, the study by Lane et al. [95] provides a valuable contribution. Although focused on nano- and microplastic particles, the exposure scenarios and PBPK framework they propose are directly applicable to metallic NPs. Their model incorporates demographic variability (e.g., children, adults), multiple ingestion pathways, and probabilistic estimation of intake, offering a robust template for estimating internal exposure levels. For seafood-related exposures, this type of structured approach could enhance current NP risk assessments by integrating seafood consumption data, body burden estimates, and age-specific exposure distributions.

Yet, several challenges remain in accurately characterizing nanoparticle exposure via seafood:

1. **Analytical limitations**: Differentiating engineered NPs from naturally occurring particles in food products is complex.
2. **Lack of human biomonitoring data**: Biomarkers of NP exposure and validated absorption-distribution-metabolism-excretion (ADME) data are sparse.
3. **Synergistic toxicity**: Co-exposure with other environmental pollutants may enhance NP toxicity, but these interactions are not well understood.
4. **Cumulative exposure**: Long-term health effects from chronic, low-dose ingestion of multiple nanoparticle types remain poorly characterized.

Given these gaps, precautionary risk management is warranted. This includes continued investment in research to:

1. Improve detection and quantification of nanoparticles in aquaculture-derived food products,
2. Conduct human-relevant oral toxicological studies and long-term dietary exposure trials,
3. Develop and validate PBPK models tailored to nanomaterial ingestion,
4. Monitor exposure in vulnerable populations such as children, pregnant individuals, and immunocompromised patients.

Addressing these uncertainties will require a multidisciplinary approach. Future research priorities include the development of sensitive detection techniques for nanoparticles in complex food matrices, toxicokinetic studies specifically designed for oral ingestion, biomonitoring of chronic low-level exposures in human populations, and an emphasis on at-risk groups such as children, pregnant individuals, and those with compromised health. Establishing validated biomarkers of exposure and effect will also be critical to translate laboratory findings into meaningful human health risk assessments.

In summary, while the current evidence suggests that seafood consumption may contribute only marginally to overall human nanoparticle exposure, the scientific uncertainty surrounding long-term health effects and inter-individual variability warrants a cautious and research-driven approach. Strengthening risk assessment methodologies and filling data gaps will be essential to ensure the safe and sustainable integration of nanotechnology into aquaculture.

4.1. Gut Microbiome Interactions with Ingested Nanoparticles

Ingested ENPs such as TiO_2, Ag and ZnO can interact directly with the gut microbiota and intestinal epithelium [96–98]. Recent reviews identify the microbiome as an important early target of dietary NP exposure [99,100]. Across *in vitro* gut models and rodent studies, these materials have been associated with dysbiosis, reduced microbial diversity, and shifts in microbial metabolic activity. Reported mechanisms include particle size and surface properties, metal-ion release (notably from Ag and ZnO), and oxidative stress–mediated effects on epithelial and microbial function [99,100]. Controlled *in vivo* work demonstrates that repeated oral TiO_2 exposure can alter microbial α-/β-diversity, modify amino-acid and lipid metabolic pathways, and increase indicators of oxidative stress and low-grade inflammation [101]. Broader evaluations of inorganic NPs used as food additives consistently report reductions in beneficial commensals such as Lactobacillus and shifts in the Firmicutes/Bacteroidetes ratio, patterns commonly associated with dysbiosis and perturbed mucosal homeostasis [102].

Evidence also suggests that NP-induced microbiome changes may be more pronounced under pre-existing gut inflammation. In colitis-prone models, exposure to TiO_2 or AgNPs has been shown to decrease overall diversity, increase mucus production, and enrich mucus-degrading taxa such as *Akkermansia muciniphila*, collectively contributing to worsened epithelial inflammation and impaired barrier integrity [96].

Although most evidence derives from animal or in vitro systems, the convergence of findings supports the microbiome as a relevant pathway through which chronic NP ingestion may influence host metabolic and immune processes. Current reviews highlight the need for standardized gut-relevant exposure models and incorporation of microbiome endpoints into food-safety assessment [99,100].

4.2. Current Knowledge Gaps and Methodological Challenges

While Section 4 focused on human health risks from dietary nanoparticle exposure, the broader scientific literature on nano-enabled aquaculture exhibits additional limitations that hinder comprehensive risk assessment and regulatory development.

4.2.1. Methodological Inconsistencies

Studies often differ in how nanoparticles are synthesized, characterized, and applied. Variations in particle size, surface chemistry, and dispersion protocols lead to poor reproducibility and incompatible toxicity results across species and systems.

4.2.2. Short-Term and Laboratory-Focused Studies

Most investigations are based on short-term trials in controlled laboratory settings. These fail to account for long-term, low-dose, or cumulative exposures that occur under realistic aquaculture conditions. Field or mesocosm studies simulating natural environmental dynamics are largely absent.

4.2.3. Narrow Taxonomic and Endpoint Focus

Research has disproportionately focused on common fish models such as *Oreochromis niloticus* and *Cyprinus carpio*, while overlooking economically important invertebrates like shrimp and mollusks. Additionally, endpoints such as immune modulation, microbiome changes, and reproductive impacts are understudied.

4.2.4. Human Health Extrapolation Gaps

Oral bioavailability, nanoparticle transformation in the digestive tract, and long-term effects on human systems are not well defined. *In vitro* and animal models dominate current research, with limited translation to real-world human dietary exposures.

4.2.5. Regulatory and Analytical Barriers

Despite rising commercialization of nanotechnology, international regulatory frameworks remain inconsistent, and no global standards exist for permissible nanoparticle residue levels in seafood. Analytical challenges, including distinguishing ENPs from natural colloids in food matrices, further complicate enforcement [16,103].

5. Risk Governance and Mitigation Strategies for Nano-Enabled Aquaculture

As established in Section 4, ENPs may accumulate in aquaculture products consumed by humans. The growing application of nanotechnology thus demands comprehensive regulatory oversight and evidence-based mitigation strategies. **Table 4** gives a summary of regulatory and mitigation approaches to nano-enabled aquaculture inputs.

5.1. International Regulatory Perspectives

5.1.1. United States (FDA)

The U.S. Food and Drug Administration evaluates nano-enabled feed additives and veterinary drugs under the Federal Food, Drug, and Cosmetic Act. FDA's Guidance for Industry #220 emphasizes case-by-case assessments of particle characterization, toxicity, and residue levels, although it does not mandate nano-specific aquaculture guidelines [104].

Table 4. Summary of Regulatory and Mitigation Approaches to Nano-Enabled Aquaculture Inputs.

Domain	Key Measures	Challenges
Regulatory Oversight	Tiered risk assessment (EFSA), FDA case-by-case evaluations	No seafood MRLs, definition inconsistency
Analytical Monitoring	spICP-MS, AF4, electron microscopy; HACCP integration	High cost, validation gaps in complex matrices
Safe-by-Design	Biodegradable coatings, reduced surface charge, biopolymer-based carriers	Early development costs, lack of standards
Risk Communication	Labeling, certification schemes, consumer outreach	Distrust of nanotechnology, regulatory inertia
Surveillance	Long-term dietary and environmental monitoring, field studies	Biomarker gaps, ethical/economic hurdles

5.1.2. European Union (EFSA)

The European Food Safety Authority applies a tiered risk assessment strategy for nanomaterials. The 2021 EFSA guidance requires data on *in vitro* digestion, absorption, bioaccumulation, and long-term toxicology. However, Maximum Residue Limits (MRLs) for NPs in seafood remain undefined [16].

5.1.3. Codex Alimentarius and OECD

While the Codex Alimentarius Commission provides food safety benchmarks, it lacks nano-specific guidelines for aquaculture. OECD, through its Working Party on Manufactured Nanomaterials, has made progress in harmonizing nanoparticle testing protocols, including for particle size, toxicity, and environmental fate [103].

5.2. Persistent Challenges in Oversight and Enforcement

1. **Lack of Harmonized Definitions**: Inconsistent definitions of what constitutes a nanomaterial complicate regulatory alignment across countries [94].
2. **Analytical Gaps**: Reliable detection in seafood products is hindered by matrix complexity. Advanced tools like single-particle ICP-MS and asymmetric flow field-flow fractionation (AF4) are promising but not yet universally adopted [92].
3. **Dynamic Transformations**: Nanoparticles may un-

dergo agglomeration, oxidation, or digestion-dependent transformations that influence bioavailability and toxicity, complicating exposure modeling [105].

4. **Trade Barriers**: Divergent regulations, particularly the EU's precautionary stance, may restrict imports of nano-enabled aquaculture products, affecting global market access [16].

5.3. Mitigation Strategies for Consumer Safety

The growing presence of ENPs in aquaculture systems and seafood products necessitates a multi-layered risk mitigation strategy. Addressing potential consumer safety concerns requires interventions at the material design stage, within analytical monitoring protocols, through coordinated regulation, and across consumer communication and surveillance mechanisms.

5.3.1. Safe-By-Design Nanomaterials

Safe-by-Design is a proactive approach that integrates toxicological considerations into the initial stages of NP development. By engineering NPs with biodegradable coatings such as chitosan, alginate, or polyethylene glycol (PEG), researchers can reduce persistence in aquatic organisms and improve clearance from human tissues after ingestion. Adjusting surface charge toward neutrality further limits bioavailability by reducing NP interactions with epithelial and mucosal surfaces. Another important strategy is the substitution of traditional metal-based NPs like Ag or ZnO with safer, biopolymer-based carriers such as liposomes or poly lactic-co-glycolic acid (PLGA). These alternative carriers have shown promise in delivering functional benefits such as nutrient delivery or immunostimulation while minimizing systemic toxicity and environmental accumulation [94,105].

5.3.2. Enhanced Analytical Monitoring

Reliable detection and quantification of NPs in aquaculture inputs and seafood products are essential for risk assessment and regulatory compliance. Techniques such as spICP-MS, AF4, and transmission electron microscopy (TEM) provide the resolution necessary to characterize particle size, shape, and composition in complex biological matrices. However, challenges remain in standardizing these methods for routine use. Regulatory agencies and research institutions must develop validated protocols and inter-laboratory comparisons to ensure consistency and accuracy. Integrating these methods into existing food safety frameworks, including Hazard Analysis and Critical Control Point (HACCP) systems, will facilitate early detection of nanoparticle residues before products reach consumers.

5.3.3. Regulatory Harmonization and Policy Alignment

A major hurdle in governing nano-enabled aquaculture is the lack of international regulatory alignment. Definitions of nanomaterials vary among jurisdictions, leading to inconsistent oversight and potential trade barriers. Establishing harmonized criteria for nanoparticle classification, safety evaluation, and labeling is essential. Agencies such as EFSA and the FDA have issued guidance documents, but specific thresholds for nanoparticle residues in seafood such as MRLs have yet to be universally established. Collaborative platforms like the Codex Alimentarius and OECD provide opportunities for harmonizing regulatory practices by promoting standardized test methods, tiered risk assessment frameworks, and mutual recognition agreements. These efforts would reduce regulatory fragmentation and ensure a more predictable environment for producers and exporters.

5.3.4. Transparent Risk Communication and Consumer Engagement

Consumer perception is a critical factor influencing the adoption and marketability of nano-enabled aquaculture products. Transparent communication regarding the use of nanotechnology, especially when residues may remain in edible tissues, can help build public trust. Mandatory labeling that discloses the presence and purpose of nanoparticle applications allows consumers to make informed choices. Educational campaigns, outreach materials, and certification schemes can further demystify nanotechnology and emphasize its potential to enhance food safety, nutritional value, and sustainability. These initiatives should be driven by evidence-based messaging and supported by regulatory bodies and industry stakeholders alike.

5.3.5. Post-Market Surveillance and Long-Term Monitoring

Risk mitigation does not end at the point of product approval. Long-term surveillance is necessary to assess chronic exposure risks and detect emerging issues. This includes biomonitoring of human populations with high seafood consumption, as well as those with increased physiological vulnerability such as children, pregnant individuals, and immunocompromised patients. The development of validated biomarkers for nanoparticle exposure and effect would greatly improve the reliability of epidemiological studies. In parallel, environmental field trials and mesocosm studies are needed to validate laboratory findings under realistic aquaculture conditions. Together, these monitoring systems provide a safety net that ensures consumer protection even as nanotechnology applications continue to evolve.

The application of nanotechnology in aquaculture offers transformative potential for enhancing sustainability, productivity, and disease management. However, its successful integration into the seafood supply chain depends on a comprehensive governance framework that accounts for the unique physicochemical properties of nanoparticles and their interactions within biological systems. While regulatory efforts by EFSA, the FDA, and the OECD have laid the groundwork for oversight, gaps in residue limits, analytical validation, and public communication persist. A robust risk mitigation strategy, anchored in Safe-by-Design nanomaterials, advanced detection tools, regulatory harmonization, and transparent communication will be essential for building consumer trust and maintaining market integrity. As scientific knowledge progresses, a responsive, interdisciplinary approach that includes long-term health and environmental surveillance will be necessary to ensure that the benefits of nanotechnology in aquaculture are realized without compromising human health or ecological stability.

5.4. Regulation and Trade Impacts

Regulatory actions targeting specific nanomaterials have already influenced international seafood trade. A notable example is the European Union's 2022 removal of titanium dioxide (E171) as a food additive following EFSA's conclusion that it could no longer be considered safe. This decision prompted reformulation of certain processed seafood products such as surimi and coated items that previously used whitening or texturizing agents containing TiO_2, creating additional compliance requirements for exporters to the EU. Differences in regulatory approaches, such as the EU's nanospecific risk-assessment framework versus the FDA's case-by-case guidance, can also generate trade uncertainty when data expectations diverge. Ongoing initiatives by the OECD Working Party on Manufactured Nanomaterials and Codex expert groups aim to harmonize testing methods and definitions, helping reduce regulatory fragmentation and facilitate smoother trade of nano-enabled aquaculture products.

6. Conclusions

Nanotechnology presents transformative opportunities for aquaculture by offering innovative tools to enhance productivity, disease control, and environmental sustainability. Applications such as nanoparticle-based drug delivery, nano-formulated feed supplements, and antimicrobial coatings have shown promise in improving aquaculture efficiency. However, the increasing use of ENPs also raises concerns regarding their persistence, bioaccumulation, and potential toxicity in aquatic organisms and humans via seafood consumption.

Although current research demonstrates beneficial effects of nanomaterials in controlled settings, several knowledge gaps persist. These include the lack of long-term and field-based studies, limited data on oral bioavailability and chronic toxicity in humans, and challenges in nanoparticle detection in complex food matrices. Regulatory frameworks vary significantly between countries and are often not well adapted to the unique properties of nanomaterials. In addition, there are no globally harmonized maximum residue limits or standardized risk assessment protocols specific to nano-enabled aquaculture products.

Looking forward, the development of green nanotechnology using biologically derived synthesis methods could help reduce environmental impact while improving safety and cost-efficiency. Smart and biodegradable nanomaterials responsive to environmental triggers may enable targeted release of nutrients and therapeutics, reducing nanoparticle persistence in aquatic systems. Integration of nanosensors with digital monitoring platforms offers potential for precision aquaculture, enabling real-time tracking of water quality, disease outbreaks, and nutrient delivery. Furthermore, conducting comprehensive life cycle assessments will be essential to evaluate the environmental, economic, and social impacts of nano-enabled technologies across the aquaculture value chain.

To ensure safe and sustainable deployment, future efforts must focus on: (1) Long-term dietary exposure studies, (2) PBPK modeling for ingested nanoparticles, (3) Development of biomarkers for human exposure, (4) Harmonization of international regulatory standards, (5) establishing clear nanoparticle residue thresholds in seafood, and (5) Investing in consumer engagement strategies such as transparent labeling and public education. Collectively, these efforts will enable nanotechnology to support global food security while upholding environmental and public health standards.

Priority Recommendations

1. Develop harmonized international definitions and test protocols for engineered nanoparticles in aquaculture to reduce variability in safety assessments and facilitate regulatory alignment.
2. Strengthen analytical detection and exposure-monitoring capacity, including validated methods for quantifying ENPs in water, sediments, and edible tissues.
3. Adopt Safe-by-Design nanomaterial development, integrating biocompatibility, degradability, and minimized bioaccumulation early in material synthesis.
4. Expand long-term and environmentally realistic toxicity studies, including chronic low-dose exposure, trophic transfer analyses, and gut microbiome interactions.
5. Improve data sharing and regulatory transparency, especially through OECD, Codex, FAO/WHO platforms, to support science-based decision-making and reduce trade uncertainty.
6. Encourage multi-stakeholder collaboration among regulators, researchers, and industry to accelerate risk-benefit evaluation and responsible adoption of nano-enabled aquaculture technologies.

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Conflicts of Interest

The author declares no conflict of interest.

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