



Review

Limitations and Novelties of Nanotechnology in Aquaculture: A Focus on Nanocarriers and Encapsulation Strategies

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Abstract

Modern aquaculture is essential for meeting the increasing global demand for fish and seafood, but its rapid expansion has exposed limitations that threaten long-term sustainability. Major challenges include high disease outbreaks, low nutritional efficiency, and the instability and poor solubility of nutraceuticals and plant-derived compounds. These challenges often create a self-reinforcing feedback loop, amplifying the detrimental effects of one another. Conventional approaches, including antibiotics, chemical treatments, aquafeeds, and chemotherapeutic agents, have shown limited effectiveness, partly due to inefficient delivery systems that can contribute to environmental contamination and antimicrobial resistance. This review discusses nanotechnology-enabled strategies to improve these traditional methods, focusing on nanocarriers and nanoencapsulation techniques, and also mentioning other synthesized nanoparticles and microencapsulation strategies. These systems have succeeded in reducing oxidative degradation and improving bioavailability by enhancing the stability and activity of encapsulated bioactives. The review also evaluates their functional performance, limitations, environmental effects, interactions with different organisms, and regulatory constraints in the industry. Overall, while safe and scalable use of biodegradable nanoscale delivery systems in modern aquaculture has shown great potential, it still depends on careful design, harmonized regulations, and economically feasible manufacturing.

Keywords: nanocarriers; aquaculture; encapsulation; nanotechnology



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1. Introduction: Current Challenges in Modern Aquaculture Using Conventional Strategies and Solutions Found in Nanoscience

Aquaculture has become one of the most important industries thanks to its key role in helping meet the increasing global demand for food, since fish and seafood supplied ~3.2 billion people with almost 20% of their average per capita intake of animal protein, not to mention that just 150 g of fish protein can provide ~50–60% of the daily protein requirement of an adult [1]. Besides protein supply, fish and seafood provide essential amino acids, fatty acids, and key micronutrients such as iodine and selenium, which are not easily replaced by many terrestrial foods [1–4]. These contributions have supported coastal economies, strengthened food security, and reduced pressure on capture fisheries through more sustainable production pathways at a global scale [1,4]. As a result, modern

aquaculture technologies are now a critical pillar of global food security and nutrition [1,4]. However, the rapid expansion of aquatic farms worldwide has also increased the structural limitations that threaten their productivity and long-term sustainability [3,5]. Among these limitations, this review highlights three interrelated challenges: disease outbreaks, inadequate delivery of functional compounds, and the instability or low solubility of bioactive compounds. These limitations were highlighted and studied in this review due to their constant presence in modern aquaculture, and despite the immense and lasting research and development in the aquatic industry, continue to limit the productivity and sustainability of fish and seafood production [1,4–6]. Additionally, they do not operate independently; these limitations form a dangerous self-reinforcing feedback loop in which they could intensify or become the cause of one another [3,5].

This review defines the first limitation as disease outbreaks in intensive aquatic farming systems. Bacterial, viral, parasitic, and fungal pathogens continue to drive major mortality events, particularly in shrimp and finfish production, where high concentration densities accelerate the transmission and the scale of the possible disease outbreak, as well as poor conditions related to the presence of heavy metals, ammonia, food and antibiotic residues, among others, in the localized environment of aquatic farms [7,8]. These issues build up over time, and the high fish density, chronic stress, and poor water quality (i.e., unstable physicochemical parameters such as temperature, pH, or dissolved oxygen) typically found in aquatic farms can increase the fish's susceptibility to infection and worsen outcomes during disease outbreaks [5–7,9,10].

Modern technologies in aquaculture have attempted to control disease outbreaks through water-quality management, vaccination, antibiotics, chemotherapeutic agents, probiotics, immunostimulants, and improved feed formulations, among other methods. These measures have proven to be valuable and, in some cases, highly effective [11].

Vaccination is one of the most important preventive strategies against infectious diseases, while antibiotics and chemotherapeutics can reduce pathogen loads during outbreaks. Probiotics, β -glucans, plant-derived compounds, and other immunostimulants are also used to improve gut health, stress tolerance, immune response, and disease resistance [9,12]. However, these methods may still suffer from oxidative degradation of sensitive compounds, water-soluble nutrients can diffuse rapidly into the surrounding environment before ingestion (in open or semi-open systems), and poor bioavailability of functional additives such as antioxidants, immunostimulants, and phytochemicals [5,13,14]. Similarly, bioactive compounds incorporated into feed matrices may degrade under light, temperature, or moisture exposure, leading to incomplete efficacy, environmental residues, toxicity risks, development of pathogen resistance, and poor delivery efficiency [9,15–18].

These losses reduce growth performance and feed efficiency while increasing organic and nutrient, nitrogen and phosphorus loading in aquatic farms [4,5,15,17]. Nutrient leaching and uneaten feed are particularly relevant because they connect feed inefficiency with water-quality deterioration. In aquatic farms, a fraction of the supplied feed may remain uneaten or lose soluble nutrients before ingestion, increasing the release of organic residues and nitrogenous wastes into the environment. These inputs can reduce dissolved oxygen, increase ammonia concentration, promote microbial proliferation, and accelerate water-quality deterioration [6,9,10,15,19]. Therefore, inadequate retention of nutrients and bioactive compounds in aquafeeds does not only reduce feed efficiency but also contributes directly to environmental stress within aquatic farms, reinforcing the same conditions that favor disease outbreaks and poor physiological performance in and around aquaculture systems [1–4,9], continuing to negatively affect both the aquatic farm productivity and its environment, reinforcing sustainability concerns and raising doubts regarding the long-term viability of the aquatic farm [5,6,10,15].

These facts highlight a fundamental issue among these conventional strategies: they commonly fail to reach their expected efficiency due to their inability to deliver, protect, and maintain their active compounds (i.e., vaccines, probiotics, immunostimulants) effectively within these intensive aquatic farms. The stronger the disease outbreak, the higher the concentration of biochemical compounds that may be required. A higher concentration of biochemical compounds leads to environmental residues that could cause more disease outbreaks. Hence, inadequate delivery represents the second limitation to discuss in this review and a major bottleneck in aquatic farms [1,2,5,14,15].

Finally, the instability and low solubility of many promising aquafeeds (e.g., vaccines, nutraceuticals, among others) cause current mitigation strategies against disease outbreaks and nutritional inefficiencies to become less effective, and in some cases, detrimental. The reason is that many molecules have nonpolar regions, such as carbon chains or lipid-based groups, which interact poorly with water [6,15,16]. Moreover, pH, light and temperature have critical effects on chemically reactive groups or unstable bonds within molecules. Therefore, the very same molecular structure that increases the positive effects of bioactive compounds often makes them unstable or poorly sensitive to environmental changes [20]. Once again, conventional chemical treatments and antimicrobial agents are effective but also introduce residues, causing toxicity risks. On the other hand, while natural approaches (i.e., probiotics, essential oils, among others) exhibit positive biological activity depending on the extraction method and formulation, their practical application is often limited by poor aqueous solubility and rapid degradation, requiring more environmental management in aquatic farms, which further complicates aquaculture operations [6,7,21]. These issues make evident the gap between the efficiency of controlled experimental conditions and field performance, and this limitation is not caused by formulation challenges but instead by biological limitations. Thus, the aquaculture industry requires approaches that improve precision and minimize environmental burden while sustaining productivity [11].

Across fisheries and aquaculture, research on nanotechnology, and more precisely, nanocarrier systems and encapsulation strategies, has emerged as a promising technological framework to develop new delivery systems capable of protecting bioactive molecules, enhancing bioavailability, reducing nutrient leaching losses, and enabling targeted or sustained release to address and mitigate these key limitations [8,14,21–23]. By operating at the nanoscale, such systems (i.e., nanocarriers) support “stimuli-responsive properties” (such as time-controlled release and monitoring of bioactive delivery) while the small size and high surface-to-volume ratio of nanocarriers can improve cellular interaction, absorption, and stability of delivered compounds [14,23–25].

Novel immunostimulant platforms (e.g., chitosan and β -glucan nanoparticle systems) are described as capable of improving vaccine efficacy and duration of protection [11,23]. Additionally, nanoencapsulation has been described as a way to address the poor stability and low bioavailability of many nutraceuticals by stabilizing poorly soluble compounds and enabling either rapid-dissolving or sustained-release formats that better match physiological uptake [8,20,23,25].

As such, this review attempts to discuss this novel technology and its function to improve upon the conventional strategies as a way to further mitigate disease outbreaks, inadequate delivery and the instability of bioactive compounds. It is important to understand that, while nano-enabled approaches are not isolated solutions to single problems, they represent integrated strategies capable of simultaneously improving the efficacy of the aquaculture industry as a whole.

2. Nanotechnology: Nanocarriers and Nanoencapsulation Strategies to Mitigate the Limitations in the Aquaculture Industry

Nanotechnology has been increasingly incorporated into aquaculture research due to many of the industry's persistent limitations [5–8,11,15,16]. Disease outbreaks, inefficient nutrient delivery, and the instability or poor solubility of the biological compounds form a self-reinforcing feedback loop: poor water quality and high stocking densities increase the risks of disease outbreaks; disease management often relies on therapeutic compounds with limited delivery efficiency, and unstable or poorly absorbed aquafeeds may fail to produce consistent and positive biological responses while contributing to environmental loading (more residues). While nano-enabled approaches encompass a wide range of tools, such as nanosensors, antifouling materials, and water remediation or filtration systems, the most biologically and technologically relevant advances in modern aquaculture focus on nanocarrier systems and encapsulation strategies, offering cutting-edge solutions for overcoming physicochemical and biological limitations inherent to aquatic production systems (i.e., farming) [6,8,11,16].

Conventional feed-based administration may expose active compounds to dilution, nutrient leaching, enzymatic degradation, or incomplete absorption before they reach the target tissue [3,9,26]. Therefore, nanocarriers and nanoencapsulation systems can improve the performance of vaccines, antimicrobial agents, immunostimulants, antioxidants, and nutraceutical compounds by protecting them from premature degradation and improving their interaction with biological barriers [21,22,27,28]. This protection further mitigates the limitations of instability and low solubility of bioactive compounds. Additionally, polymeric nanoparticles, chitosan-based systems, PLGA nanoparticles, virus-like particles, and lipid-based carriers have been explored as platforms capable of improving antigen stability, oral delivery, immune stimulation, and resistance against bacterial or viral pathogens [12,18,22–24,27,29–39]. In turn, providing the bioactive compounds an adequate and controlled delivery system. As such, nanotechnology does not simply introduce new disease-control agents; rather, it improves the delivery and functional persistence of existing agents, protecting them from their low solubility or instability, and potentially reducing repeated dosing, which in turn vastly improves their efficiency against disease outbreaks, without leaving residues or needing additional environmental management in aquatic farms [6,8,11,15,16,20,23,24,40].

The way nanocarriers address inadequate delivery in aquatic farms is by entrapping bioactives within protective matrices, improving their retention during water exposure, and enabling more gradual or site-relevant release during gastrointestinal transit. This is particularly important for oral delivery systems, where the goal is not only to preserve the compound before ingestion but also to release it at a biologically useful point during digestion, thereby improving bioaccessibility, bioavailability, and biological response [12,15,16,26,32].

It is important to understand that nanocarriers are nanostructural delivery vehicles engineered to transport, protect, and release active compounds in a controlled manner [5,9,12,26,32]. They commonly fall within the 10–500 nm range, and their performance depends on a combination of factors including particle size (compared to the targeted area), surface characteristics, composition, morphology, and responsiveness to the surrounding environment as they reach the targeted area [11]. In aquaculture, reported nanocarrier systems include lipid nanoparticles, polymeric nanoparticles, chitosan-based nanoparticles, nanoemulsions, nanospheres, and nanocapsules [11,12,18,22,23,26,32,34–39,41].

In contrast, nanoencapsulation is the fabrication and loading technique by which the bioactive compounds are entrapped within nanoscale matrices or shells (i.e., core-shell architectures, matrix dispersion, electrostatic assembly, or polymer crosslinking) [7,20,28]. Therefore, nanoencapsulation is a methodological technique, whereas nanocarriers are

the resulting engineered structures/matrices [6,11,15,24]. Furthermore, the instability or low solubility of bioactive compounds is mostly mitigated through nanoencapsulation, which reduces oxidative degradation, hydrolysis, and photodegradation by isolating these compounds within biopolymeric, lipid-based, or polysaccharide-based matrices. At the same time, nanocarriers may improve the dispersion of hydrophobic compounds and increase interfacial contact with biological membranes, regulating release kinetics, enhancing cellular interaction and absorption efficiency [7,13–17,22].

The distinction between nanocarriers and nanoencapsulation is important because instability, aggregation, or inconsistent release may happen due to the carrier composition, newly created surface, or encapsulation efficiency. Without knowing the distinction between the fabrication method and the structural design, it becomes difficult to determine whether technological shortcomings originate from the material's properties or the need for further modification/optimization [11,29].

The following table (Table 1) presents the most widely known and most studied types of nanocarriers used in the recent advances in modern aquaculture.

Based on the information from Table 1, it is possible to observe how nanoencapsulations of immunostimulants, antioxidants, antimicrobial agents, vaccine antigens, and nutraceutical compounds have improved growth performance, stronger immune responses, enhanced oral vaccine efficiency, and greater resistance to pathogens [12,23,26,27,30,32–35,42,43].

Therapeutic nanocarriers, particularly poly (lactic-co-glycolic acid) (PLGA) nanoparticles and chitosan-based nanoparticles, have also been explored as delivery vehicles because they can improve antigen stability, bioavailability, intestinal residence time, and protective efficiency against bacterial and viral pathogens [12,34,35,44]. For example, PLGA nanoparticles carrying plasmid DNA vaccines improved nanoparticle absorption and survival in rainbow trout, while rifampicin-loaded PLGA nanoparticles increased survival in zebrafish embryos [12,34,35]. However, PLGA systems also have formulation limitations, since double-emulsion solvent evaporation may generate heterogeneous particle sizes, reduce antigen entrapment efficiency, or cause payload denaturation at the oil–water interface. Therefore, although PLGA nanoparticles are promising for oral vaccination and antimicrobial delivery, their scalability, reproducibility, and payload stability require further optimization [12,34,35,44].

Virus-like particles and chitosan-based systems provide additional examples of nanoscale delivery applied to disease control [32]. In white leg shrimp, virus-like particles produced through recombinant bacterial expression delivered VP28 double-stranded RNA, forming particles of approximately 30 nm and improving dsRNA efficacy against WSSV; encapsulated RNA increased survival by 16.7% compared with non-encapsulated RNA. These results suggest that VLPs can protect fragile nucleic acids and improve antiviral activity, although their practical application depends on structural stability and batch-to-batch consistency [32]. Similarly, chitosan/ β -glucan nanoparticles containing inactivated *Streptococcus agalactiae* antigen improved vaccine stability, antibody stimulation, and survival in Nile tilapia. In this experiment, nanoparticles were synthesized at a 2:1 chitosan: β -glucan ratio, using β -glucan at 2 mg/mL, 5 min sonication, 0.22 μ m filtration, stirring at 800 rpm for 60 min, centrifugation at $15,000 \times g$ for 30 min, washing, lyophilization, and incorporation into commercial feed [23]. The vaccine formulation used formalin-inactivated *S. agalactiae*, with 0.01 mL of vaccine at 3×10^9 CFU/mL mixed with 5 g of feed, equivalent to approximately 3×10^7 CFU/g feed. In the experimental design, 300 *Nile tilapia* fingerlings were distributed into 12 tanks, with 25 fish per tank and triplicate groups; fish received vaccine feed for 7 days, normal feed for 7 days, a 7-day booster, and were challenged on day 30 post-vaccination. Survival ranged from 33.33% to 75.56%, with the chitosan/ β -glucan vaccine group showing the strongest protective

response. Nevertheless, this system also shows that oral vaccine performance remains dependent on formulation, needed for batch-to-batch consistency [23].

Table 1. Detailed information regarding the most recent nanocarriers, the loaded bioactive, the reported features from the nanocarriers, the species tested and the main reported results or outcomes of the successful nanocarrier applied to aquaculture studies.

Nanocarriers	Bioactive/Payload	Species Tested	Reported Features	Main Reported Outcome	Reference
PLGA nanoparticles	Plasmid DNA vaccine	Rainbow trout (<i>Oncorhynchus mykiss</i>)	Double-emulsion system; particle size ~200–1000 nm.	Improved nanoparticle absorption and survival after viral challenge	[12]
PLGA nanoparticles	Rifampicin	Zebrafish (<i>Danio rerio</i>) embryos	Rifampicin-loaded PLGA nanoparticles.	Increased survival	[34]
PLGA nanoparticles	Fadrazole/letrozole	Guppy (<i>Poecilia reticulata</i>)	PLGA-loaded aromatase-inhibitor system, drug loading of approximately 43.6%. Averaging 222 nm particles.	Used for monosex population production. Improved efficiency in hormonal sex control	[35]
Virus-like particles, VLPs	Double-stranded RNA VP28	Whiteleg shrimp (<i>Litopenaeus vannamei</i>)	Recombinant bacterial expression system; particle size 30 nm; encapsulated RNA improved survival by 16.7% compared with non-encapsulated RNA.	Increased efficacy of dsRNA delivery against WSSV	[32]
Chitosan nanoparticles	Pumpkin seed oil	Whiteleg shrimp (<i>Litopenaeus vannamei</i>)	Ionotropic gelation; particle size 20–80 nm.	Improved growth, digestive enzymes, immune response, histological condition, and survival against <i>Vibrio parahaemolyticus</i>	[30]
Chitosan nanoparticles	Hollow nanocapsules/Fluorescein isothiocyanate (FITC), dsRNA delivery	Black tiger shrimp (<i>Penaeus monodon</i>) post-larvae	Oral delivery system.	Survival rate of 86.63% and effective silencing of Monodon baculovirus (MBV) structural gene	[27]
Chitosan nanoparticles	GRHa hormone	Goldfish (<i>Carassius auratus</i>)	Oral delivery; 100 µg GRHa kg ^{−1} body weight; feeding every 3 days for 40 days.	Prolonged elevated hormone levels and increased ova diameter	[42]
Chitosan/β-glucan nanoparticles	Inactivated <i>Streptococcus agalactiae</i> antigen	Nile tilapia (<i>Oreochromis niloticus</i>)	Sonication; reported particle size at ~500 nm.	Higher vaccine stability, antibody stimulation, and improved survival	[23]
Chitosan-conjugated nanotherapeutic system	Vitamin C	Rainbow trout (<i>Oncorhynchus mykiss</i>)	Chitosan-conjugated vitamin C; controlled release over 48 h, 185 nm diameter.	Stimulated immune response	[33]
Chitosan tripolyphosphate (CS/TPP) nanoparticles	Plasmid DNA vaccine	General fish, species not specified	Synthesized by ionic gelation process. Reported 79.9% protection.	Improved vaccine protection	[26]

Table 1 also illustrates the controlled delivery function through chitosan nanoparticles that prolonged GRHa hormone activity in goldfish [42] and PLGA nanoparticles loaded with aromatase inhibitors for monosex population production in guppy [35]. Other chitosan-based systems, including pumpkin seed oil-loaded chitosan nanoparticles, VP28 DNA-loaded chitosan nanoparticles, and chitosan–dextran sulfate/silica nanoparticles carrying dsRNA against the MBV p74 gene, further demonstrate the role of nanocarriers in improving immune response, antiviral intervention, gene silencing, and survival in shrimp and fish models [23,26,27,30,33,42].

Overall, although not all systems directly demonstrate solubility enhancement, the evidence indicates that nanocarriers and optimized nanoencapsulation strategies can improve the functional use of nutraceuticals, plant-derived compounds, vaccines, hormones, antimicrobials, nucleic acids, and other sensitive payloads by increasing stability during feed processing and water exposure while promoting controlled release during digestion [12,23,26,27,30,32–35,42].

Keeping that in mind, advances in nanocarrier engineering focus not only on reducing particle size but also on optimizing surface properties, improving encapsulation efficiency, and tailoring release mechanisms. For example, lipid-based nanocarriers (e.g., lipid nanoparticles) can encapsulate both hydrophilic and lipophilic compounds. Furthermore, they can improve colloidal stability, reduce aggregation, and promote targeted interactions with biological membranes or tissues thanks to the modifications added to their surface [22]. These developments indicate a transition from simple nanoparticle inclusion toward the planned design of carrier–bioactive interactions, interfacial characteristics, and release dynamics focused on overcoming the instability and solubility barriers that limit many nutraceuticals and plant-derived compounds in aquaculture.

In summary, nanocarriers are optimized delivery systems, designed to address instability, inefficient absorption, and uncontrolled dispersion of bioactive compounds in aquatic farms. Their relevance lies in enhancing the performance and reliability of existing therapeutic and nutritional strategies without further modification of the biological compound [8,16]. A clear understanding of these technologies is essential to critically assess the novelty and limitations of nanotechnology in the modern aquaculture industry.

Alongside nanocarriers, the following table (Table 2) presents some of the most successful nanoscale feed additives used in modern aquaculture:

Table 2. Detailed information regarding the most recent nano-enabled feed additives used in aquaculture research, the functional component, the reported features, the species tested and the main reported results or outcome of the successful feed additive.

Nano-Enabled Feed Additive	Functional Component	Species/Pathogen Tested	Reported Features	Main Reported Outcome	Reference
Silver nanoparticles	Silver	Marine shrimp (juvenile), pathogen <i>Vibrio harveyi</i> , zebrafish.	Size reported as <100 nm in various studies, some as small as 10 nm; feed additive dose reported as 500 mg kg ^{−1} ; long-term treatment in <i>Vibrio harveyi</i> -infected juvenile marine shrimp reduced mortality by 71% at higher AgNP doses.	Antibacterial activity against pathogenic bacteria; potential improvement of gut microbiota and disease resistance; developmental toxicity of coated silver NP in zebrafish embryos.	[45–49]

Table 2. Cont.

Nano-Enabled Feed Additive	Functional Component	Species/Pathogen Tested	Reported Features	Main Reported Outcome	Reference
Gold nanoparticles	Gold	Used against <i>Heretosporis saurida</i> and <i>Candida isolates</i> . Tested on <i>Manila clam</i> (<i>Ruditapes philippinarum</i>).	Size reported as ~5 nm; antifungal activity reported at 1 $\mu\text{g mL}^{-1}$ in cell-line context.	Bactericidal, antifungal, and antiviral activity. Can cause cellular internalization, producing toxic effects.	[50–53]
Zinc oxide nanoparticles	Zinc oxide	Juvenile Grass Carp (<i>Ctenopharyngodon idella</i>); various fishes and invertebrates (general).	Size reported as <100 nm; dietary supplementation at 30 mg kg^{-1} feed in grass carp.	Improved percentage weight gain, specific growth rate, feed conversion ratio, survival, and growth rate. Produces adverse effects with excessive zinc exposure.	[54,55]
Iron nanoparticles	Iron	Giant Freshwater Prawn (<i>Macrobrachium rosenbergii</i>) Post-Larvae, Bagridae Catfish (<i>Clarias batrachus</i>).	Size reported as <50 nm; dietary inclusion 20 mg kg^{-1} of feed produced the most favorable growth and survival in Giant Freshwater Prawn; 40 mg kg^{-1} for 60 days in <i>Clarias batrachus</i> produced best growth/feed utilization response.	Improved growth, survival, and feed utilization; strong dose-dependent response (needs constant monitoring).	[17,56]
Selenium nanoparticles	Selenium	<i>Nile tilapia</i> (<i>Oreochromis niloticus</i>), Mahseer Fish (<i>Tor putitora</i>).	Size reported as ~20 nm; application as growth promoter at 0.5, 1 and 2 mg kg^{-1} ; <i>Nile tilapia</i> fed 2.5 mg kg^{-1} SeNPs showed 51.9% higher growth rate than control; common carp at 1 mg kg^{-1} showed improved growth and Se deposition; mahseer response reported near 0.68 mg n-Se kg^{-1} dry feed.	Improved growth (1 gm in average weight and 2.75 cm in average length in <i>Nile tilapia</i>), antioxidant status, muscle selenium deposition, feed conversion, and immune-related performance.	[57–59]
Copper nanoparticles	Copper	Zebrafish (<i>Danio rerio</i>)	Size reported as <50 nm; dietary exposure at 500 mg kg^{-1} meal.	Altered gut microbial population; increased bacterial diversity, but some common intestinal taxa were absent.	[48]
Chitosan nanoparticles as feed additive	Chitosan	<i>Nile tilapia</i> (<i>Oreochromis niloticus</i>)	Size reported as ~200 nm; dietary inclusion 1 g kg^{-1} .	Improved fish health and immunostimulatory performance.	[37]
Nano-nutrient complex	Fe, Zn, Cu, and Se nanoparticles	<i>Nile tilapia</i> (<i>Oreochromis niloticus</i>)	Chemically synthesized nano-nutrient complex; dietary inclusion at 30 mg kg^{-1} and 60 mg kg^{-1} for 60 days; NNC60 produced the strongest response.	Improved final weight and length; increased muscle protein, fat, vitamin C, and essential amino acids.	[60]

The nano-enabled feed additives summarized in Table 2 differ from nanocarriers because they do not primarily function as protective delivery vehicles for an external payload. Instead, their effects derive from the intrinsic biological activity of the nanoscale material itself. And while Chitosan NPs follow a similar performance to the nanocarriers discussed in Table 1, it is particularly evident that metallic nanoparticles (e.g., silver, gold, etc.) are mainly associated with antimicrobial activity [17,37,45–60].

Silver nanoparticles (AgNPs) have been tested in different sizes, including 10, 30–40, and 100 nm, and their antibacterial activity was shown to be size-dependent. Smaller AgNPs, especially 10 nm particles, showed stronger bactericidal activity and lower cytotoxicity within the tested dose range, while 100 nm particles were less effective and more cytotoxic [45–48]. In aquaculture-related applications, Table 2 reports AgNPs below 100 nm used as feed additives at 500 mg kg^{-1} , with long-term treatment reducing mortality by 71% in *Vibrio harveyi*-infected juvenile marine shrimp. These findings suggest that AgNPs may help address disease outbreaks through antibacterial activity and potential improvement of gut microbiota and disease resistance. However, their limitation is also clear: antimicrobial efficacy is closely linked to particle size, concentration, and exposure context, leading to excessive or poorly controlled use that may raise cytotoxicity, residue, and environmental safety concerns [45–49]. Additionally, these NPs show antimicrobial potential, although the available evidence is less directly aquaculture-specific. In the articles referenced in this review, gold nanoparticles (AuNPs) were supported on zeolite materials, with gold contents between 2.3 and 2.8 wt%. The most effective material, Au-faujasite, contained highly dispersed particles of approximately 5 nm and eliminated 90–95% of *Escherichia coli* and *Salmonella typhi* colonies. Table 2 similarly reports gold nanoparticles of approximately 5 nm with bactericidal, antifungal, and antiviral activity. These results support their relevance as antimicrobial nanoadditives, particularly for pathogen-control strategies. Nevertheless, their application in aquaculture remains limited by the absence of species-specific feeding trials, concentration-response data, and direct evidence in fish or shrimp farming systems. Therefore, gold nanoparticles should be presented as promising antimicrobial nanoadditives, but not yet as established aquaculture feed additives, this leaves an opportunity for future work [50–53].

At single glance, silver nanoparticles (AgNPs) have received considerable attention due to their widespread industrial and biomedical applications and their relatively high ecotoxicity, primarily associated with the release of Ag^+ ions, oxidative stress induction, trophic transfer, and bioaccumulation in aquatic organisms [49]. In contrast, gold nanoparticles (AuNPs) generally exhibit lower intrinsic toxicity owing to their high chemical stability and multiple applications; however, prolonged exposure, together with particle size and surface functionalization, may enhance tissue accumulation and induce sublethal biological effects [53].

Zinc oxide nanoparticles (ZnO-NPs) and iron oxide nanoparticles (FeO-NPs) provide clearer examples of nano-enabled mineral supplementation. ZnO-NPs were synthesized by co-precipitation and tested as dietary zinc sources in juvenile grass carp at 30 and 60 mg kg^{-1} diet over 90 days [54]. The ZnO-NPs had a crystallite size of 50–60 nm, and the 30 mg kg^{-1} treatment produced the best growth response, including improved percentage weight gain, specific growth rate, feed conversion ratio, and hematological performance, with no mortality during the trial. Similarly, dietary iron oxide nanoparticles below 50 nm were supplemented to *Macrobrachium rosenbergii* post-larvae at 0, 10, 20, 30, 40, and 50 mg kg^{-1} for 90 days [17]. The best response occurred at 20 mg kg^{-1} , where survival reached 90.83% compared with 80.03% in the control, final weight increased to 1.72 g compared with 0.85 g, and feed conversion ratio (FCR) improved to 0.86 compared with 1.34. Polynomial regression estimated an optimal dietary requirement of $24.56 \text{ mg kg}^{-1} \text{ Fe}_2\text{O}_3$.

nanoparticles [17,56]. These examples show that nano-mineral additives can address inadequate nutritional performance by improving growth, feed utilization, mineral uptake, and physiological condition. However, both systems also show a narrow functional window: higher zinc or iron supplementation may reduce performance or increase stress responses, indicating that nanoforms are not automatically safer or more beneficial than conventional mineral sources [17,54,56]. And while selenium nanoparticles (SeNPs) have emerged as a promising alternative because they retain high biological activity while exhibiting lower toxicity than inorganic selenium compounds, the evidence shows similar limitations based on the concentration of NPs. SeNPs were synthesized using high-energy ball milling, characterized by XRD and TEM, and incorporated into *Nile tilapia* diets at 0.5, 1.0, and 2.0 mg kg⁻¹. The NPs showed an average size distribution of 30–50 nm, approximately 40 ± 12 nm in aqueous solution, and a zeta potential of −50 ± 7 mV. The optimal inclusion level was 1 mg kg⁻¹, producing the highest relative growth rate, specific growth rate, condition factor, and improved nutritional quality, with a survivability of 95.37% [57]. In contrast, the 2 mg kg⁻¹ treatment reduced survival to 54.73%, demonstrating that even essential micronutrients can become detrimental when supplied in excessive concentrations of NPs [57–59]. Uncertainties remain regarding their long-term environmental persistence, potential for bioaccumulation, and possible ecotoxicological effects [59].

As expected, copper nanoparticles (CuNP) show a similar limitation. Table 2 reports dietary CuNP exposure at 500 mg kg⁻¹ meal in zebrafish, associated with altered gut microbial population, increased bacterial diversity, and disappearance of some common intestinal taxa [48]. Indicating that CuNPs can bioaccumulate and induce oxidative stress, tissue damage, metabolic disorders, and increase mortality rates in fish. Therefore, while CuNPs may influence microbial communities and have antimicrobial relevance, their toxicological profile makes them one of the most concerning and dangerous nanoadditives to use in aquatic farms [48]. From this information, copper nanoparticles (CuNPs) and zinc oxide nanoparticles (ZnO NPs) are considered of greater environmental concern than the previously discussed NPs because of their high dissolution potential, leading to the release of Cu²⁺ and Zn²⁺ ions that induce oxidative stress, membrane damage, developmental abnormalities, and reduced growth and reproductive performance in algae, invertebrates, and fish [48]. Iron oxide nanoparticles (Fe₃O₄ and γ-Fe₂O₃), on the other hand, have been shown to exhibit relatively low persistence in aquatic and terrestrial environments because they can be transformed into naturally occurring iron species. Nevertheless, elevated concentrations may alter bacterial communities and sediment geochemistry [17,56].

It is easy to understand that the physicochemical properties of metallic nanoparticles, including particle size, surface charge, surface coating, and dissolution rate, directly influence their environmental persistence, bioavailability, bioaccumulation, and ecotoxicological effects in aquatic and terrestrial ecosystems [61–64]. Overall, although the environmental risks associated with metallic nanoparticles vary considerably with material type, their increasing production and release into the environment underscore the need for comprehensive assessments of their persistence, bioaccumulation, and toxicity to ensure their safe and sustainable application [48,61,65–67].

In summary, Table 2 shows that nano-enabled feed additives may help mitigate disease outbreaks, offer antimicrobial protection and slightly increase growth in fishes through a controlled delivery system, but their benefits are strongly limited by their particle size, concentration, species, and environmental behavior.

3. Functional Performance and Critical Limitations of Nanoencapsulation Techniques in Aquaculture

The worth of nanocarriers and nanoencapsulation techniques is determined by their performance under realistic conditions in aquatic farms. These innovative delivery systems must retain bioactive compounds during water exposure and gastrointestinal transit, while enabling release in biologically relevant areas [6,15,68]. Therefore, the critical question is not whether a carrier is smaller or more complex, but whether it can reproducibly improve stability, release control, bioavailability, and biological response under conditions that resemble commercial aquaculture. In this context, it is their “bioavailability” that is the central determinant of the bioactive compound’s effectiveness.

Bioavailability is closely associated with the effectiveness of bioactive compounds and encompasses the processes of digestion, absorption, metabolism, distribution, and delivery to the site of action, ultimately determining their physiological impact. Two closely related concepts are bioaccessibility and bioactivity [4–6,64,68]. Bioaccessibility is the proportion of a compound released from food during digestion that becomes available for absorption. Compounds that are not bioaccessible cannot be absorbed effectively and are unlikely to have physiological effects. Conversely, bioactivity refers to the biological response triggered when the compound reaches its target site. Therefore, bioaccessibility impacts bioavailability, which in turn affects the compound’s ability to elicit a physiological response [61–63,67].

As mentioned before, encapsulation technologies primarily intervene at the level of bioaccessibility by facilitating controlled release while protecting compounds from premature degradation, allowing compounds with low solubility or instability to survive in different environments. The physicochemical properties of bioactive compounds (i.e., molecular weight, degree of polymerization, glycosylation, conjugation, among others) strongly influence bioaccessibility. High molecular weight in bioactive compounds often faces membrane permeation barriers and can be highly susceptible to environmental degradation during processing and digestion. It is important to note that these interconnected factors can have their effects reduced due to many situations, such as exposure to oxygen, temperature variations, light, pH changes, and enzymatic activity [69–71].

The techniques used for nano-encapsulation employ natural and (less frequently) synthetic biopolymers, such as chitosan, sodium alginate, maltodextrin, gum arabic, albumin, whey protein, and β -cyclodextrin, thanks to their biocompatibility, biodegradability, and capacity to form stable molecular matrices and networks [70]. These materials contain functional groups that promote interaction with bioactive compounds and enhance retention within the corresponding matrix. Among the most relevant properties of these materials is their ability to form nanoscale carrier systems that increase the available surface area and enhance interfacial contact with the biological environment. This characteristic may promote processes such as the absorption, stability, and bioavailability of the encapsulated compounds [38,71,72]. However, the biological performance of nanocarrier systems is determined by the interplay of multiple physicochemical, structural, and physiological factors rather than by any single attribute alone. Key determinants include surface charge, matrix composition, morphology, degradation behavior, release kinetics, and responsiveness to environmental cues such as pH, temperature, and enzymatic activity. Furthermore, species-specific physiological features, including digestive processes, metabolic regulation, and biological barriers, critically influence nanocarrier–host interactions. Together, these parameters govern the fate, bioavailability, and functional efficacy of encapsulated bioactive compounds [16,41].

The stability and performance of encapsulated systems depend on the interactions established between wall materials and bioactive compounds. These interactions are

mostly divided into hydrogen bonding, hydrophobic interactions, and electrostatic forces, as described in Figure 1 [38,71,72].

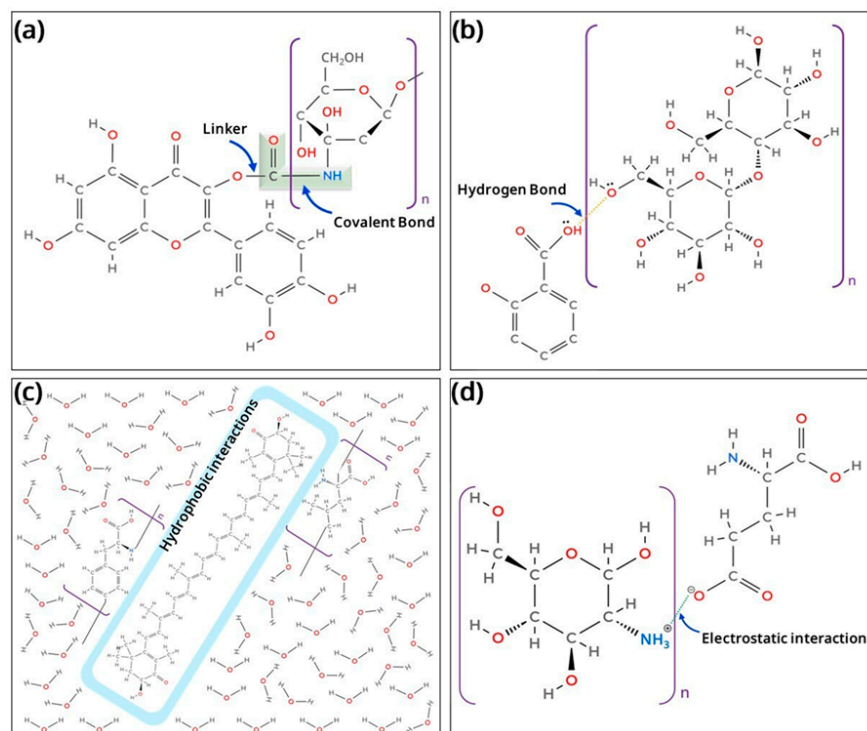


Figure 1. Classification of the main types of interactions occurring between wall materials and bioactive compounds: (a) covalent bonding; (b) hydrogen bonding; (c) hydrophobic interactions; (d) electrostatic interactions.

The hydrogen bonds stabilize molecular networks through directional dipole–dipole interactions [72]. Then, hydrophobic interactions promote aggregation of nonpolar domains in aqueous environments and enhance the encapsulation resistance of lipophilic compounds [70,72]. Finally, electrostatic interactions are caused by attraction between functional groups with opposite charges; these interactions are known for their strong influence on pH and ionic strength. The combined contribution of these interactions determines encapsulation efficiency, structural integrity, and their capability to release the loaded compound in the relevant area [72].

The affinity and stability of such bindings depend on intrinsic molecular properties and extrinsic environmental factors (e.g., pH, ionic strength, solvent composition, and temperature). Molecular size and the flexibility of their matrices further influence the strength of the molecular/atomic interaction. And while larger molecules may offer multiple binding sites and stronger interactions, their excessive steric hindrance may reduce the accessibility or affinities of reactive groups. Therefore, particle size is heavily influenced by the objective or function expected from the nanocarriers; some larger molecules may offer significant advantages compared to smaller particles depending on the circumstances. [70,72]. Keeping this in mind, encapsulation strategies to protect unstable compounds and grant a controlled-delivery system can be divided into microencapsulation and nanoencapsulation.

4. Critical Differences and Performance Between Microencapsulation and Nanoencapsulation Strategies

It is important to understand that micro- and nanoencapsulation differ in scale and functional objectives. Microencapsulation (i.e., particles between 1 and 5000 μm

in size) [70,73] and is primarily used to enhance technological stability during feed processing, storage, and gastrointestinal transit. Therefore, its main objective is not rapid systemic absorption like other smaller nanoscale delivery systems, but long-term protection of sensitive compounds, reducing nutrient loss, and gradually releasing the compound after ingestion. In this sense, microencapsulation is particularly useful for feed-based applications where the encapsulated compound must remain stable over longer periods of time within a relatively larger targeted area.

Microencapsulation has been reported to be quite successful across different species. Further results regarding microencapsulation techniques are illustrated in the following table (Table 3):

Table 3. Detailed information regarding the most recent microencapsulation used in aquaculture research, the loaded bioactive, the reported features, the species tested and the main reported results or outcome of the successful micro-encapsulated particle.

Microencapsulation/ Micro-Carrier System	Bioactive/Payload	Species Tested	Reported Features	Reported Outcome	Reference
Co-encapsulated probiotic with algae-derived polysaccharides	<i>Bacillus aryabhatai</i> CKNJH11	Asian seabass (<i>Lates calcarifer</i>)	Co-encapsulation of probiotic bacteria with algae-derived polysaccharides.	Improved growth performance and immunity.	[74]
Microencapsulated inulin	Inulin prebiotic	Striped catfish (<i>Pangasianodon hypophthalmus</i>)	Microencapsulated prebiotic formulation.	Enhanced growth, digestive enzyme activity, and immune response.	[73]
Microencapsulated astaxanthin from <i>Haematococcus pluvialis</i>	Astaxanthin	Common carp (<i>Cyprinus carpio</i>)	Microencapsulated microalgal pigment/antioxidant.	Improved growth, muscle quality, antioxidant system, and related gene expression	[75]
Alginate-based particles	Shrimp enzymes from fishery waste	Fishes in general, not specified	Electrohydrodynamic atomization used to immobilize shrimp enzymes in alginate-based particles.	Proposed strategy to convert fishery waste into functional aquafeed additives.	[76]
Alginate-coated chitosan particles	Antigen	Indian carp (exact species not specified), various fish species (not specified)	Extrusion; microsphere size 1000 nm.	Improved antigen integrity and productive performance.	[31]
Encapsulated probiotic	<i>Lactobacillus plantarum</i>	Rainbow trout (<i>Oncorhynchus mykiss</i>)	Encapsulation used to improve probiotic functional stability.	Improved probiotic potential and helped reduce lead toxicity effects.	[77]
Microencapsulated antigens	<i>Piscirickettsia salmonis</i> antigens	Fish oral immunization context; salmonid relevance	Microencapsulation optimized for antigen stability and oral immunization.	Improved antigen stability for fish oral immunization.	[78]
Microencapsulated organic acids and salts	Organic acids/acidifiers	Pacific white shrimp/whiteleg shrimp (<i>Litopenaeus vannamei</i>)	Dietary microencapsulated organic acid system.	Improved growth performance, immunity, and disease resistance.	[79]

Table 3. Cont.

Microencapsulation/ Micro-Carrier System	Bioactive/Payload	Species Tested	Reported Features	Reported Outcome	Reference
Wax-coated lipid microcapsules	Algal feed nutrients	European flat oyster (<i>Ostrea edulis</i>)/bivalve broodstock	Microencapsulated algal feed designed to reduce nutrient loss before ingestion.	Supported replacement of live algal feed for commercial bivalve broodstock.	[80]
Alginate and alginate–bentonite microcapsules	Shrimp proteases/exogenous enzymes	<i>Nile tilapia</i> (<i>Oreochromis niloticus</i>)	Alginate and alginate–bentonite microcapsules for intestinal enzyme delivery.	Enabled intestinal delivery of exogenous shrimp proteases.	[81]
PLGA microparticles	Formalin-killed <i>Aeromonas hydrophila</i> cells	Fishes in general, not specified	PLGA microparticle-encapsulated killed bacterial cells; single-shot vaccine strategy.	Improved vaccine efficacy against <i>Aeromonas hydrophila</i> infection.	[82]

From Table 3, alginate–bentonite microcapsules enabled intestinal delivery of exogenous shrimp proteases in *Nile tilapia* (*Oreochromis niloticus*) [81], alginate-coated chitosan particles that improved antigen integrity and productive performance in Indian carp, chitosan-conjugated vitamin C systems that provided controlled release over 48 h and stimulated immune response in rainbow trout [31], while wax-coated lipid microcapsules reduced nutrient loss before ingestion and supported the replacement of live algal feed in European flat oyster (*Ostrea edulis*) broodstock [80]. Similarly, co-encapsulation of *Bacillus aryabhattai* with algae-derived polysaccharides improved growth performance and immunity in Asian seabass (*Lates calcarifer*) [74], and microencapsulated inulin enhanced growth, digestive enzyme activity, and immune response in striped catfish (*Pangasianodon hypophthalmus*) [73]. Other systems, including microencapsulated astaxanthin, organic acids, probiotics, antigens, and PLGA microparticles, have been associated with improved antioxidant status, probiotic stability, oral immunization, disease resistance, and vaccine efficacy in common carp, rainbow trout, whiteleg shrimp, salmonid-relevant models, and fish vaccination contexts [73,75,77–79,82,83]. These examples show that microencapsulation is a robust strategy for improving feed additive stability, oral delivery, and biological performance across multiple aquaculture species.

In contrast, nanoencapsulation and nanocarrier systems operate at a much smaller scale, usually below 500 nm [70,72,84,85], and are more strongly associated with enhanced surface interaction, improved absorption, immune recognition, and controlled, rapid delivery of sensitive payloads. The nanocarriers summarized in Table 1 include PLGA nanoparticles carrying plasmid DNA vaccines, virus-like particles delivering dsRNA, chitosan/ β -glucan nanoparticles encapsulating inactivated bacterial antigens, chitosan nanoparticles carrying pumpkin seed oil or VP28 DNA constructs, chitosan–dextran sulfate/silica systems delivering dsRNA, and chitosan-conjugated systems delivering vitamin C. These systems are mainly directed toward disease outbreak control and biologically precise delivery, with reported outcomes including improved nanoparticle absorption, increased survival rate, increased dsRNA delivery efficiency, antibody stimulation, controlled release, and immune stimulation [28,44,70,86,87].

Therefore, based on the evidence illustrated in Tables 1 and 3, microencapsulation is better suited for protecting feed additives, probiotics, prebiotics, enzymes, pigments, organic acids, antigens, and algal nutrients during feed production, storage, water exposure,

and digestion [73,75–79,82,83,86]. Nanoencapsulation, in contrast, is more suitable for high-value or biologically fragile payloads that require improved absorption and molecular interaction or protection, targeting much more precise areas within the organism. This distinction is particularly important for nucleic acid-based strategies, vaccine delivery, and gene-silencing systems, where nanocarriers such as PLGA nanoparticles, chitosan-based nanoparticles, and virus-like particles may offer advantages that larger microcapsules are unable to reproduce [28,44,70,86].

Despite these advantages, both approaches have important limitations to consider. Microencapsulation is less effective when the target application requires cellular/molecular uptake, tissue penetration, or rapid interaction with biological membranes. Larger particle size can reduce interfacial contact with intestinal surfaces and may limit the delivery of compounds that require close interaction with the targeted cells. Microencapsulated systems also depend strongly on wall material stability, water-leaching resistance, and release behavior under gastrointestinal conditions. Thermal treatments during feed extrusion may compromise probiotic viability or alter the structural integrity of encapsulated systems [88], while digestive enzymes, pH shifts, and intestinal transit time may affect the release profile of enzymes, antigens, and other bioactives [89]. Essentially, microencapsulations are more susceptible to environmental changes than nanoencapsulations. Thus, microencapsulation can improve stability and sustained release, but it does not guarantee precise or targeted delivery on the same level as nanoencapsulation.

That being said, nanoencapsulation presents a different set of challenges. Because nanocarriers are designed to interact more closely with tissues, their performance depends heavily on particle size, morphology, surface charge, encapsulation efficiency and payload retention [70,72]. Environmental variables such as pH, salinity, ionic strength, digestive enzymes, and organic matter may further alter nanoparticle stability and release behavior [29,85]. In addition, highly hydrophobic or light-, heat-, and oxygen-sensitive compounds can be difficult to stabilize even after encapsulation, especially when their chemical structure favors degradation or poor aqueous dispersion, causing the batch-to-batch reproducibility of nanoencapsulation to vary in morphology more often than microencapsulations [69,76,85]. Therefore, nanoencapsulation may improve bioavailability and biological interaction, but these benefits depend on whether the formulation is properly optimized.

Nanocarriers also raise broader safety and implementation concerns. Their smaller size and higher surface reactivity may improve delivery, but these same properties may increase the risk of tissue accumulation, unexpected biological interactions, environmental dispersion, and nanotoxicity, particularly important when dealing with metallic NPs [15,76,90,91]. In contrast, microencapsulation is generally more compatible with conventional feed-manufacturing approaches, although with lower delivery precision. Both technologies also face practical limitations related to production cost, encapsulation efficiency, batch-to-batch reproducibility, scalability, and quality control. Positive outcomes obtained under controlled experimental conditions do not necessarily translate directly into commercial aquaculture, where feed extrusion, storage, water exposure, species-specific digestion, and farm-level variability may alter performance [84,86,91].

It is important to notice that, in modern aquaculture, not just encapsulation techniques are on the rise but also biodegradable nano- and microcarriers are emerging as promising oral delivery systems due to their biocompatibility, biodegradability, and low toxicity, while also protecting bioactive compounds from environmental breakdown and harsh gastrointestinal conditions after feed ingestion [11,16,25,28,29,40,69,70,78].

While all these carrier systems aim to improve stability, controlled release, and bioavailability, they offer unique functional benefits. Chitosan boosts mucoadhesion, intestinal

absorption, and innate immune responses. In contrast, PLGA allows for precisely controlled degradation and sustained release, making it ideal for vaccines and long-term therapeutic delivery [11,30,33,35,36,44]. Lipid-based systems offer exceptional versatility for encapsulating both hydrophilic and lipophilic compounds while promoting targeted delivery and improved cellular uptake [22,25,89,91,92]. Conversely, alginate-based particles enable pH-sensitive release, safeguarding sensitive bioactives throughout gastric transit and aiding intestinal delivery, while their compatibility with composite formulations also boosts encapsulation efficiency and improves mechanical stability [74,76,81,88]. Consequently, the selection of an appropriate carrier should not rely on a single material but rather on the physicochemical characteristics of the encapsulated compound, the desired release profile, and the physiological requirements of the target aquatic species, thereby maximizing production performance, health, and disease resistance.

In summary, microscale carriers have been demonstrated to be an effective strategy for enhancing technological stability and sustained release across multiple aquaculture species without the need for a nanoscale design and despite a few drawbacks. On the other hand, nanoscale carriers offer enhanced bioavailability, immune modulation, and are more consistent in terms of antioxidant performance when rapid absorption or controlled delivery is required, compared to microencapsulation [25,86].

Overall, microencapsulation and nanoencapsulation should be considered complementary technologies. The decision to use micro- or nanoencapsulation should be made on a case-by-case basis, considering the payload, target species, route of administration, expected biological effect, environmental risk, production cost, and industrial scalability. In both techniques (micro- and nanotechnologies), achieving precise, controlled release, ensuring structural stability under processing conditions, minimizing environmental risks, and ensuring scalable production remain critical challenges, regardless of particle size [16].

Functional performance must therefore be evaluated by studying biological responses and by assessing reproducibility, environmental compatibility, and industrial feasibility. Given the increase in production costs and scalability, it is strongly recommended to conduct a case-by-case assessment of whether the projects require carriers in the micro- or nanoscale.

5. Environmental, Toxicological and Regulatory Constraints of Nanotechnology in the Aquaculture Industry (Progress)

Thus far, it has been well-established that aquaculture is currently one of the fastest-growing food production sectors worldwide, driven by increasing demand for high-quality protein and the overexploitation of capture fisheries [80]. Within this expanding sector, micro- and nanoencapsulation technologies have emerged as promising tools to enhance nutritional efficiency, stability, and precise controlled release of bioactive compounds in many aquatic organisms [25,93]. However, the transition from experimental application to large-scale implementation requires careful consideration of environmental behavior, toxicological implications, and regulatory feasibility. The functional advantages described in previous sections must therefore be evaluated alongside potential ecological and public health risks.

One of the principal environmental concerns associated with nanocarriers in aquaculture is their possible release into aquatic systems through uneaten feed, fecal excretion, or incomplete digestion. Once introduced into water bodies, nanoparticles may undergo aggregation, dissolution, sedimentation, or interaction with natural organic matter, thereby altering their physicochemical properties and environmental behavior [49,94]. These processes are strongly influenced by pH, salinity, ionic strength, temperature, and the presence

of dissolved organic compounds, which collectively determine colloidal stability, transport dynamics, and persistence [95,96].

Aggregation may reduce dispersion in the water column but increase sediment deposition, potentially exposing benthic organisms. Conversely, stable nanosuspensions may enhance mobility and increase contact with planktonic organisms, including microalgae that form the base of aquatic food webs [97–100]. Numerous studies have documented that engineered nanomaterials can induce oxidative stress, inflammatory responses, membrane damage, and behavioral alterations in aquatic organisms [53,101–106]. However, most of the available evidence has been generated using metallic nanoparticles, which generally exhibit greater environmental persistence and bioaccumulation potential than biodegradable nanoencapsulation systems. Therefore, direct extrapolation of these findings to protein-, polysaccharide-, or lipid-based nanocarriers should be approached with caution. Although similar nanoscale-dependent mechanisms may occur in nanoencapsulated systems, particularly when structural degradation modifies particle behavior or surface reactivity, biodegradable carriers are expected to present a lower environmental burden due to their capacity to degrade into naturally occurring compounds. Nevertheless, comparative studies evaluating the environmental fate and toxicological profiles of different nanocarrier systems under realistic aquaculture conditions remain limited and warrant further investigation.

Environmental concentration modeling suggests that nanomaterial levels in aquatic systems may occur in the ng L^{-1} range or lower under typical scenarios [19,107–109]. Nevertheless, localized accumulation near aquaculture facilities, particularly in sediment compartments, may result in higher exposure levels. Chronic low-dose exposure and long-term ecological consequences remain insufficiently characterized, especially under realistic farming conditions. The formation of biomolecular coronas in aquatic environments may further modify bioavailability, transport, and toxicity profiles [101], complicating predictive assessment.

Bioaccumulation represents another critical dimension of risk evaluation. Residual nanoparticles have been found to accumulate in tissues such as the liver, gills, or muscle, depending on particle size, surface charge, and coating characteristics [104,110]. Although inclusion levels in aquafeeds are typically low (often mg kg^{-1} in feed translating to ng g^{-1} or lower in tissues) [109–112], concerns persist regarding chronic dietary exposure through fish and shellfish consumption. Toxicity associated with nanomaterials often depends less on bulk chemical composition and more on structural parameters such as size, morphology, and exposure duration [113–115]. The enhanced cellular interaction characteristics of nanoscale materials may increase biological uptake, potentially amplifying systemic exposure even at low concentrations. The interconnected pathways of environmental release, organismal uptake, tissue accumulation, and potential transfer to consumers are summarized in Figure 2.

Reported toxicological effects in aquatic species include oxidative stress, histopathological alterations, hepatotoxicity, immune modulation, and genotoxic responses [39,53,85,98,100,101,108,115–121]. While biodegradable polymeric or lipid-based nanocarriers are generally considered safer than metallic nanoparticles, nanoscale dimensions may still influence membrane permeability, inflammatory signaling, and molecular interactions. Moreover, interactions with other environmental contaminants may produce synergistic effects [8]. It is important to note that many toxicological studies have been conducted under controlled laboratory conditions using exposure concentrations that may exceed those expected in commercial aquaculture systems. Consequently, the ecological relevance of some reported adverse effects remains uncertain and warrants further evaluation under realistic farming

conditions. These uncertainties underscore the importance of comprehensive toxicological frameworks that integrate acute, chronic, and multigenerational assessments.

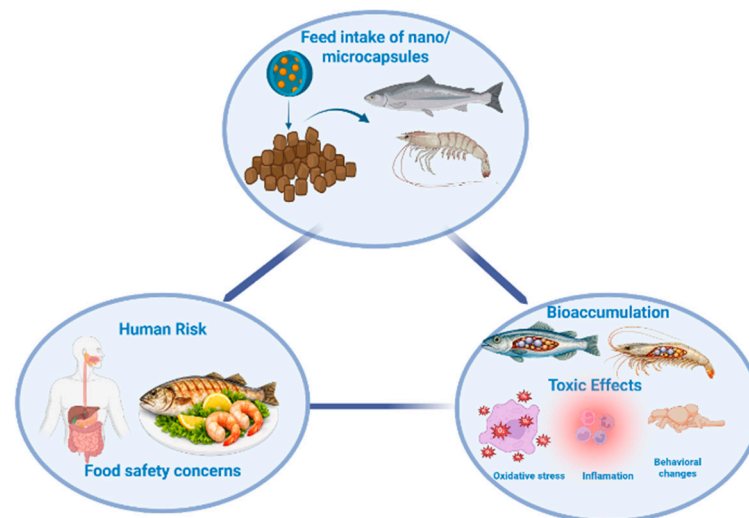


Figure 2. Schematic representation of environmental and biological pathways associated with nano- and microencapsulated feed in aquaculture systems. Uneaten feed and excreted nanoparticles may disperse in aquatic environments, undergo aggregation or sedimentation, interact with non-target organisms, accumulate in tissues of cultured species, and potentially transfer to consumers. Reported biological effects include oxidative stress, inflammatory responses, and behavioral alterations.

Biodegradable design strategies offer a promising pathway to mitigate environmental impact. Encapsulation systems composed of proteins, lipids, and polysaccharides may degrade into naturally occurring byproducts, potentially reducing persistence and bioaccumulation risks [121]. Compared with non-biodegradable nanomaterials, these systems may offer improved environmental compatibility while maintaining the functional benefits of controlled release and enhanced bioavailability. Improved nutrient absorption and reduced feed waste from encapsulated formulations may also decrease organic loading and nutrient discharge in aquaculture systems [122–126], contributing to better water quality and reduced eutrophication pressure [118,127]. However, biodegradability should not be assumed to guarantee environmental safety, as degradation products, degradation rates, and environmental conditions may influence ecological outcomes. Therefore, evaluating the complete life cycle of encapsulation systems remains essential for assessing their long-term sustainability.

Beyond environmental and toxicological considerations, regulatory frameworks remain heterogeneous and, in many cases, insufficiently developed for nanoscale applications in aquaculture. In the United States, the FDA provides guidance for nanomaterials in food and feed, while within the European Union, regulatory instruments such as the Novel Foods Regulation and REACH govern nanoscale substances [123,124,128,129]. EFSA has developed specific guidance for nanoscale risk assessment in food and feed, and the EU remains among the most proactive regions in establishing regulatory standards for nanomaterials. In contrast, many aquaculture-producing countries still lack specific regulatory frameworks for nano-enabled feed additives, creating uncertainty for product registration, commercialization, and international trade.

International initiatives, including the OECD Program on Manufactured Nanomaterials and the NANOMET project, aim to harmonize testing methodologies and regulatory approaches [68,130]. At the global level, the United Nations Strategic Approach to International Chemicals Management (SAICM) addresses nanomaterial safety within broader chemical governance frameworks [129,131]. Nevertheless, aquaculture-

specific nanoregulations remain limited, and variability in definitions, testing requirements, and labeling policies complicates regulatory approval and cross-border trade [1,15]. This lack of harmonization may also slow technology transfer from academic research to industrial implementation.

Economic and implementation constraints further influence adoption. Nanoencapsulation technologies often require specialized production methods and strict quality control to maintain reproducibility, increasing operational costs [80]. While laboratory-scale studies have demonstrated promising improvements in nutrient delivery, bioavailability, and controlled release, scaling these technologies to commercial production remains challenging. Factors such as manufacturing costs, process standardization, long-term stability, quality assurance, and regulatory compliance must be addressed before large-scale implementation can be achieved. In regions where aquaculture is central to food security, financial and infrastructural limitations may further restrict technological integration [129].

In summary, while nanocarriers and nanoencapsulation systems offer substantial potential to improve feed efficiency, immune performance, and therapeutic delivery, their large-scale application must be accompanied by rigorous evaluation of environmental fate, toxicological impact, bioaccumulation risk, and regulatory compliance (Figure 3). The sustainability of nano-enabled aquaculture depends not only on functional performance but also on environmental compatibility, consumer safety, economic feasibility, and harmonized governance. Future progress will depend on the successful translation of laboratory-scale innovations into commercially viable products through coordinated efforts among researchers, industry stakeholders, regulatory authorities, and policymakers. Advancing these technologies responsibly requires balancing innovation with precaution, ensuring that environmental protection and public health considerations evolve in parallel with technological progress. Successful implementation, therefore, requires multidisciplinary collaboration to ensure safe, economically viable, and socially acceptable deployment, as illustrated in Figure 3 [131].

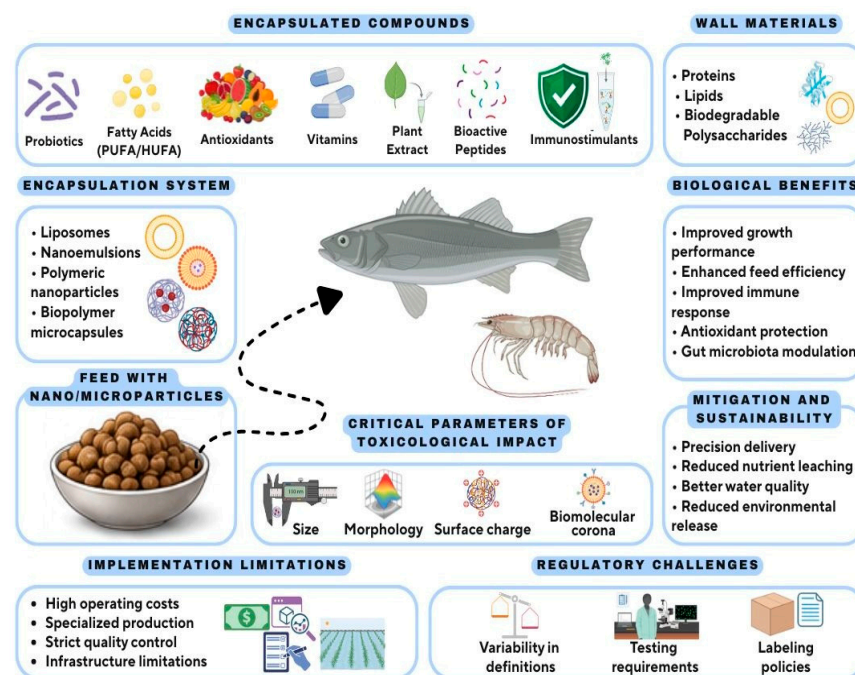


Figure 3. Schematic overview of nano- and microencapsulation systems in aquaculture nutrition, highlighting encapsulated bioactive compounds, wall materials, biological benefits, mitigation and sustainability, critical parameters of toxicological impact, implementation limitations, and regulatory challenges.

6. Conclusions and Future Directions: Perspective for Sustainable Nano-Aquaculture

The rapid development of nanocarrier systems and encapsulation strategies in aquaculture reflects a broader shift from empirical feed supplementation toward engineered delivery platforms. Through these new delivery systems, nanotechnology has managed to further mitigate the detrimental effects that come from inefficient nutrient delivery and the instability of poor solubility of bioactive compounds that prevented conventional strategies from effectively combating disease outbreaks in aquatic farms [1–7,13–16].

This conceptual distinction between nanocarrier and encapsulation is essential for guiding future innovation, as advances in performance will depend not only on material selection but also on precise control over encapsulation efficiency, surface chemistry, and environmental responsiveness [15,29].

Additionally, encapsulation strategies were further discussed in Sections 2–4; in both the micro- and nanoscale, encapsulation strategies complement one another depending on the species. Microscale carriers have shown strong potential for improving technological stability, feed additive protection, and sustained release across multiple aquaculture species without requiring nanoscale design. Nanoscale carriers, in contrast, are more appropriate when the objective is to enhance bioavailability, immune modulation, antioxidant performance, rapid absorption, or controlled delivery of sensitive payloads [87,93]. Therefore, the decision to use micro- or nanoencapsulation should be made on a case-by-case basis, considering the payload, target species, route of administration, expected biological effect, environmental risk, production cost, and industrial scalability. Regardless of particle size, achieving precise controlled release, maintaining structural stability during processing and digestion, minimizing environmental risks, and enabling scalable production remain major challenges [16].

Integration of biodegradable and biocompatible materials remains a key direction for sustainable development. Biopolymer-based matrices derived from chitosan, alginate, proteins, and lipids offer promising pathways for reducing environmental persistence and bioaccumulation risks [33,98]. However, biodegradability must be evaluated across complete degradation pathways, including intermediate products and long-term ecological interactions. Coupling delivery efficiency with environmental compatibility will be central to responsible implementation.

This consideration is especially important for metallic nanoparticles and other inorganic nano-enabled additives. Their physicochemical properties, including particle size, surface charge, surface coating, dissolution rate, aggregation behavior, and ion release, directly influence environmental persistence, bioavailability, bioaccumulation, and ecotoxicological effects in aquatic and terrestrial ecosystems [59,69]. Although risks vary considerably depending on material type, concentration, exposure route, and environmental conditions, the increasing production and release of metallic nanoparticles emphasize the need for comprehensive assessments of persistence, bioaccumulation, and toxicity before their broad application in aquaculture [59,69].

Another important advance involves species-specific optimization. Differences in gastrointestinal physiology, immune architecture, and metabolic responses across fish and crustacean species necessitate tailored nanocarrier formulations rather than universal platforms [11,87]. Advances in transcriptomic and proteomic tools may enable more precise evaluation of immunomodulatory and metabolic effects, supporting the development of targeted nanoformulations for disease prevention and nutritional enhancement. Scalability and industrial feasibility represent equally critical determinants of future success. Early stage fabrication techniques must evolve into reproducible, cost-effective production systems compatible with commercial feed extrusion processes [3,76]. Harmonized

characterization protocols and batch-to-batch consistency will be necessary to bridge the translational gap between experimental validation and field-level performance. Beyond technical scalability, successful commercialization will require addressing manufacturing challenges, including production costs, raw material availability, process standardization, and quality control. Furthermore, effective technology transfer from research institutions to industry will depend on pilot-scale validation and field trials conducted under commercial aquaculture conditions. Market adoption will ultimately be driven not only by biological performance but also by economic feasibility, regulatory approval, compatibility with existing feed manufacturing infrastructure, and the ability to demonstrate clear advantages over conventional feed additives [1,8,86,93,110].

Additionally, the delivery system, especially in vaccines and nutraceuticals, required even higher precision under realistic feed and digestive conditions (e.g., within aquatic farms). These shortcomings are generally tested by trying to further improve the interactions between the nanoparticles/nanocarriers in fish at molecular and cellular levels.

Moreover, the shift to explore these interactions, as well as improving the reproducibility of the experiments in realistic conditions, tends to align with safety regulations and environmental risks. After all, there are many regulatory challenges, namely unresolved safety assessments related to bioaccumulation, development of higher toxicity, oxidative stress and long-term ecological risks. Said regulations (e.g., FDA, EFSA, REACH, Novel Foods Regulations, among others) can differ from country to country, further limiting the implementation of nanoscience in aquaculture worldwide. From a regulatory perspective, future progress will depend on clearer nanospecific guidelines within aquaculture frameworks. International coordination through regulatory bodies and scientific networks will be required to establish standardized risk assessment methodologies, particularly for long-term exposure and bioaccumulation studies [1,25,94,95]. Transparent safety evaluations and environmental monitoring schemes will strengthen public confidence and facilitate market adoption.

Future directions and work must prioritize rational design approaches grounded in physicochemical characterization. Particle size distribution, surface charge (often characterized as zeta potential), encapsulation efficiency, degradation kinetics, and release profiles should be standardized and systematically reported to enable reproducibility across studies [5,8,93]. The next generation of nanocarriers should move beyond passive protection and toward stimuli-responsive systems capable of modulating release under defined gastrointestinal or environmental conditions. Such systems may enhance therapeutic precision while minimizing premature dispersion into aquatic environments.

In conclusion, nanocarrier systems and encapsulation strategies represent significant technological advances with the potential to improve feed efficiency, immune resilience, and therapeutic delivery in aquaculture. However, their long-term success for future work will depend on improvements in early-stage fabrication methods, standardized evaluation, scalable production, and environmentally responsible implementation. It is important to recognize that a significant portion of current research remains focused on translating promising laboratory-scale nanoencapsulation systems into robust and reproducible technologies suitable for practical application. Although substantial advances have been made in fabrication methods, challenges related to batch-to-batch consistency, process standardization, and scale-up remain for certain nanoencapsulation techniques. Variations in particle size distribution, encapsulation efficiency, and release behavior may arise depending on the production method and operating conditions, highlighting the need for standardized characterization protocols and manufacturing practices to ensure reproducibility and industrial applicability.

Ultimately, this review concludes that the future direction of nanocarriers and encapsulation strategies in aquaculture lies not in technological novelty alone, but in their capacity to integrate functional performance, environmental stewardship, economic feasibility, and regulatory compliance. The transition from promising experimental systems to widely adopted industry tools will require multidisciplinary collaboration among material scientists, aquaculture specialists, toxicologists, regulators, and industry stakeholders.

By aligning material innovation with environmental safety and regulatory harmonization, nanotechnology can meaningfully contribute to the development of a more efficient and sustainable aquaculture industry.

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Abbreviations

The following abbreviations are used in this manuscript:

AgNPs	Silver nanoparticles
ZnO-NPs	Zinc oxide nanoparticles
SeNPs	Selenium nanoparticles
CuNP	Copper nanoparticles
AuNPs	Gold nanoparticles
FCR	Feed conversion ratio
EFSA	European Food Safety Authority
EPA	Environmental Protection Agency
EU	European Union
FAO	Food and Agriculture Organization of the United Nations
FDA	Food and Drug Administration
NLCs	Nanostructured lipid carriers
NPs	Nanoparticles
REACH	Registration, Evaluation, Authorization and Restriction of Chemicals
SAICM	Strategic approach to International Chemicals Management
WSSV	White spot syndrome virus

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