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## Zinc nanoparticles in fisheries: A comprehensive review

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### Abstract

Zinc (Zn) is an essential micronutrient vital for numerous biological processes, including growth, immunity, and metabolic regulation. Its role in aquaculture, especially in nanoparticle form, has garnered significant attention due to its enhanced bioavailability, absorption, and unique physicochemical properties. Zinc plays a role in catalyzing over 300 enzymes, regulating gene expression, and supporting immune responses. The introduction of nanotechnology in zinc supplementation has revolutionized fish nutrition by offering superior efficiency and bioactivity. This review provides an in-depth exploration of zinc nanoparticles (ZnNPs) and their applications in fish nutrition and health. Key areas discussed include Zn metabolism in fish, the impact of ZnNPs on growth, haematological parameters, antioxidant responses, biochemical indices, and histopathological effects. The review highlights the potential benefits of ZnNPs, their dose-dependent effects, and toxicity concerns, presenting a holistic view of their utility and challenges. Additionally, it addresses gaps in current research and suggests future directions for sustainable aquaculture practices.

**Keywords:** Zinc nanoparticles in aquaculture, zinc metabolism in fish, zinc bioavailability and absorption

### Introduction

Zinc is the second most abundant trace element in living organisms and plays a catalytic, structural, and regulatory role in cellular processes <sup>[1, 2]</sup>. It is indispensable for numerous enzymatic functions, including DNA synthesis, protein metabolism, and cell division, making it critical for growth and immune function. Zinc deficiency can lead to severe physiological disorders, including stunted growth, weakened immunity, and impaired reproductive performance. These deficiencies are especially concerning in aquaculture, where the natural availability of zinc in aquatic ecosystems is often inadequate. Thus, fish farmers rely on dietary zinc supplementation to meet the nutritional needs of cultured species.

The advent of nanotechnology has revolutionized zinc supplementation by introducing zinc nanoparticles (ZnNPs) as an innovative alternative. Unlike conventional zinc sources, ZnNPs exhibit superior bioavailability and absorption efficiency due to their nanoscale size and large surface area. These properties enhance their interaction with biological systems, leading to improved nutrient uptake and physiological benefits. Additionally, ZnNPs possess unique antimicrobial and antioxidant properties, further augmenting their utility in aquaculture. Such advancements promise to address challenges like disease outbreaks and retarded growth, which are prevalent in fish farming, thereby improving productivity and sustainability.

Despite these advantages, the application of ZnNPs in aquaculture raises concerns regarding potential toxicity and environmental impacts. High doses or prolonged exposure to ZnNPs can induce oxidative stress, tissue damage, and disruptions in metabolic processes. Additionally, the bioaccumulation of nanoparticles in aquatic environments may pose risks to non-target organisms. Therefore, understanding the optimal levels of ZnNP supplementation and their long-term effects on fish health and the ecosystem is imperative. This review aims to consolidate existing knowledge on ZnNPs, highlighting their benefits, limitations, and

prospects in sustainable aquaculture. By addressing these aspects, it seeks to provide a framework for leveraging ZnNPs responsibly while safeguarding aquatic biodiversity.

### Zinc Metabolism in Fish

Zinc's biological importance stems from its involvement in over 300 enzymatic activities, including RNA and DNA polymerases, superoxide dismutase (SOD), and carbonic anhydrase [3]. Zinc absorption in fish primarily occurs through the gastrointestinal tract and gills, mediated by carrier and calcium-dependent mechanisms [4, 5]. Factors such as dietary composition, chemical form of Zn, and chelation with amino acids influence its bioavailability [7-8]. For instance, zinc methionine (Zn-Met) exhibits superior bioavailability compared to inorganic forms like zinc oxide (ZnO) and zinc sulfate (ZnSO<sub>4</sub>). Understanding these pathways is crucial to optimizing dietary formulations and ensuring adequate zinc levels in fish.

### Absorption and Distribution

Zinc is absorbed in freshwater fish via the gills and intestines, with mechanisms influenced by waterborne and dietary sources [5, 9, 10]. Chelation with amino acids such as histidine enhances Zn uptake and distribution in tissues. However, excessive dietary zinc competes with other bivalent minerals, potentially leading to toxicity. Studies have reported optimal Zn dietary levels for various species, such as 15-30 mg/kg for common carp and 20 mg/kg for channel catfish. Additionally, the form of zinc used in feed significantly impacts its absorption, as nanoforms often demonstrate higher efficiency. Improved zinc absorption translates to better growth and physiological resilience, making ZnNPs a valuable tool in aquafeeds [2, 11]. Furthermore, the role of dietary protein sources and other chelating agents in enhancing zinc metabolism underscores the complexity of optimizing its supplementation.

### Toxicity and Dose-Dependent Effects of Zinc Nanoparticles

The toxicity of ZnNPs varies with concentration and exposure duration [12]. While ZnNPs at low concentrations enhance growth and immunity, excessive levels disrupt physiological processes [12, 13]. For example, rainbow trout tolerate dietary Zn levels up to 1900 mg/kg without adverse effects, but higher levels reduce haemoglobin and haematocrit values, indicating haematological stress. This demonstrates the fine line between beneficial and toxic concentrations of ZnNPs, highlighting the importance of precise dosing.

### Toxicological Observations

ZnNPs induce histopathological changes in fish tissues, including liver necrosis, gill epithelial lifting, and renal vacuolation [14, 15]. The presence of ZnNPs in the cytoplasm of red blood cells and kidney glomeruli underscores their systemic distribution. These effects necessitate careful optimization of ZnNP doses in aquafeeds. Toxicological studies also reveal variations in sensitivity among species, emphasizing the need for species-specific guidelines. Moreover, long-term exposure to sub-lethal doses of ZnNPs may exacerbate oxidative stress and impair immune function, making regular monitoring of fish health a priority.

### Effects of Zinc Nanoparticles on Growth Performance

ZnNPs significantly enhance growth performance in fish due to their superior bioavailability. Studies on species like *Labeo rohita* and *Oreochromis niloticus* have demonstrated dose-dependent improvements in specific growth rate (SGR), feed conversion ratio (FCR), and weight gain [16, 18]. For instance, *L. rohita* fingerlings fed 20 mg/kg nano ZnO exhibited maximum growth [19]. Similarly, a combination of ZnNPs and selenium nanoparticles (SeNPs) further amplified growth metrics. The influence of ZnNPs on metabolic efficiency and protein synthesis further explains their growth-promoting effects.

### Comparative Analysis with Inorganic Zinc

Nano ZnO outperforms inorganic zinc forms in promoting growth and feed efficiency. In grass carp (*Ctenopharyngodon idella*), nano ZnO at 30 mg/kg achieved higher weight gain and SGR than ZnSO<sub>4</sub> [20]. However, excessive ZnNP supplementation negatively impacts growth, emphasizing the importance of dose optimization [21]. Comparative studies also highlight the role of nanoparticle properties, such as surface charge and particle size, in determining their efficacy. These findings underscore the potential of ZnNPs to transform aquafeeds when used judiciously.

### Haematological and Biochemical Implications of Zinc Nanoparticles

Haematological indices, such as red blood cell (RBC) count, haemoglobin concentration, and haematocrit levels, are vital indicators of fish health [22, 23]. ZnNPs at optimal levels enhance these parameters, but excessive concentrations induce anaemia and physiological stress. For instance, *C. idella* fed with ZnNPs showed improved RBC and haemoglobin values compared to those on inorganic zinc diets [20]. These findings reinforce the need for balanced supplementation to avoid adverse health outcomes.

### Biochemical Indicators

ZnNPs influence serum biochemical parameters, including total protein, glucose, and enzymatic activities [24, 25]. Elevated protein and glucose levels were observed in *L. rohita* fed 20 mg/kg nano ZnO, reflecting enhanced metabolic activity [26]. Moreover, ZnNPs improved digestive enzyme activities, contributing to better nutrient assimilation. These biochemical enhancements correlate with improved growth and resilience against environmental stressors. However, the potential for biochemical alterations at higher doses necessitates vigilance in monitoring fish health during ZnNP supplementation trials.

### Antioxidant Responses and Oxidative Stress

Antioxidant enzymes such as catalase (CAT), SOD, and glutathione peroxidase (GPx) are critical for mitigating oxidative stress. ZnNPs modulate these enzymes, enhancing the fish's ability to counteract reactive oxygen species (ROS). For example, ZnNP supplementation in *L. rohita* increased SOD and GPx activities while reducing malondialdehyde (MDA) levels, an indicator of lipid peroxidation. Enhanced antioxidant responses contribute to better immune function and overall health, particularly under stress conditions [19, 27].

### Synergistic Effects with Selenium Nanoparticles

The combination of ZnNPs and SeNPs has demonstrated synergistic antioxidant effects. In *O. niloticus*, such diets enhanced SOD and CAT activities, highlighting the potential for combined nanoparticle therapies in aquaculture [18]. This synergy may open avenues for designing multifunctional supplements tailored to specific species and farming conditions, maximizing benefits while minimizing risks.

### Histopathological Effects

ZnNP exposure leads to histological changes in fish tissues, serving as biomarkers of toxicity. Liver tissues exhibit vacuolization, necrosis, and blood congestion, while gills show epithelial lifting and hyperplasia. Chronic exposure also affects renal structures, with nanoparticle accumulation observed in lysosomes and glomeruli [28, 29]. These histological changes provide valuable insights into the cellular-level impacts of ZnNPs.

### Long-Term Implications

Prolonged ZnNP exposure induces ultrastructural changes, including desquamation in gill cells and vacuolation in chloride cells [13-15, 25, 28]. These findings emphasize the need for controlled usage to minimize adverse histopathological effects. Research into mitigating strategies, such as co-supplementation with protective agents, could further refine ZnNP applications in aquaculture.

### Gene Expression and Immunomodulation

ZnNPs influence the expression of growth and immune-related genes. Upregulation of growth hormone (GH) and insulin-like growth factor-1 (IGF-1) has been observed in ZnNP-fed fish, correlating with enhanced growth [28]. Additionally, ZnNPs modulate pro-inflammatory cytokines such as tumour necrosis factor- $\alpha$  (TNF- $\alpha$ ) and interleukin-1 (IL-1), improving immune responses [29, 30]. These molecular effects highlight the potential of ZnNPs to boost fish resilience against diseases.

### Antioxidant Gene Expression

ZnNP supplementation upregulates antioxidant genes, including SOD and GPx [31, 32]. For instance, *O. niloticus* exhibited increased SOD and GPx expression with ZnNP diets, enhancing oxidative stress resilience. However, excessive ZnNPs may suppress gene expression, highlighting the importance of dose regulation. Exploring gene expression profiles under varying ZnNP concentrations could provide deeper insights into their mode of action.

### Conclusion

Zinc nanoparticles offer promising benefits in aquaculture, including enhanced growth, improved immunity, and better nutrient utilization. Their superior bioavailability and physicochemical properties make them a valuable feed additive. However, their application requires careful consideration of dosage and potential toxicity to prevent adverse effects. The integration of ZnNPs into fish diets should be accompanied by regular monitoring to ensure safety and efficacy.

The long-term impacts of ZnNPs on fish health and environmental sustainability remain key areas for future research. Studies should focus on developing eco-friendly formulations, evaluating their interactions within aquatic

ecosystems, and exploring their potential synergies with other micronutrients (Mondal *et al.*, 2020; Sallam) [20]. By addressing these challenges, ZnNPs can contribute significantly to advancing sustainable practices in fisheries and aquaculture. Additionally, collaboration between researchers, policymakers, and industry stakeholders will be essential to harness the full potential of ZnNPs while minimizing risks.

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