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REVIEW ARTICLE

Antibiotic resistance in aquaculture and aquatic organisms: a review of current nanotechnology applications for sustainable management

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Abstract

Aquaculture has emerged as one of the world's fastest-growing food industries in recent years, helping food security and boosting global economic status. The indiscriminate disposal of untreated or improperly managed waste and effluents from different sources including production plants, food processing sectors, and healthcare sectors release various contaminants such as bioactive compounds and unmetabolized antibiotics, and antibiotic-resistant organisms into the environment. These emerging contaminants (ECs), especially antibiotics, have the potential to pollute the environment, particularly the aquatic ecosystem due to their widespread use in aquaculture, leading to various toxicological effects on aquatic organisms as well as long-term persistence in the environment. However, various forms of nanotechnology-based technologies are now being explored to assist other remediation technologies to boost productivity, efficiency, and sustainability. In this review, we critically highlighted several ecofriendly nanotechnological methods including nanodrug and vaccine delivery, nanoformulations, and nanosensor for their antimicrobial effects in aquaculture and aquatic organisms, potential public health risks associated with nanoparticles, and their mitigation measures for sustainable management.

Keywords Antibiotics · Antibiotic resistance · Aquaculture · Aquatic organisms · Nanotechnology · Sustainable management

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Introduction

Antibiotics have been identified as one of the most important types of emerging contaminants (ECs) due to their widespread use in human and veterinary medicine, as well as their long-term persistence in the environment (Sodhi et al. 2021; Okoye et al. 2022a). Antibiotic use increased from 21.1 to 34.8 billion defined daily doses in 76 countries between 2000 and 2015, and it is anticipated to reach 126 billion defined daily doses in 2030 if no policy changes are made. Antibiotics, however, are discharged into the environment in their natural forms or as metabolites in 30 to 90% of cases, posing a hazard to ecosystems (Wang et al. 2021a). Antibiotics have helped to reduce mortality rates in developing nations by reducing deaths from infectious infections, but the costs of antibiotic contamination continue to be a major issue.

Antibiotic-resistant bacteria enter aquatic habitats through human and animal sources. These bacteria can pass their genes on to water-based microorganisms, which contain their resistance genes (Kraemer et al. 2019). Antibiotic-resistant genes and other new pollutants have spread across the globe, posing a multidimensional threat (Felis et al. 2020). Antibiotics and other developing pollutants have comparable origins and travel routes; thus, they will eventually coexist in aquatic habitats. There is a knowledge gap about their treatment alternatives and management for their efficient removal because these pollutants were only recently introduced or recognized. Furthermore, despite technological developments, existing treatment technologies are not designed to eliminate these ECs, and there are no published health regulations that provide direction on how to handle these contaminants (Gogoi et al. 2018).

Aquatic resources have played a crucial part in meeting the massive demand for animal protein and, as a result, in food security in recent decades. Contamination of the environment and the frequency of diseases, on the other hand, are seen as critical issues in aquaculture and aquatic ecosystem. In this regard, new technological ways have been paved to successfully cope with such issues. Nanotechnology, as a novel and revolutionary technique, offers a wide range of applications and enormous potential in aquaculture and seafood preservation. It has the potential to develop new technologies for drug management and vaccine development, ensuring the protection of fisheries resources against disease-causing microorganisms (Nasr-Eldahan et al. 2021).

Various forms of nanotechnology-based systems are now being used to boost productivity, efficiency, and sustainability. Recent efforts have been made in the fields of health management, enhancement of fish and shellfish development by dietary supplementation with nutraceuticals, seafood processing, and preservation, as well as water purification (Shah and Mraz 2020). As a result, nanotechnology has a key role to play in the development of aquatic resources efficiency and environmental effect. To achieve a better understanding of the persistence and toxicity of these pollutants in aquatic environments, researchers must first figure out how antibiotics interact with other developing contaminants (Hairom et al. 2021; Fajardo et al. 2022). This study discusses antibiotics resistance in the aquatic environment reported in recent studies, including antibiotics use and residues in aquaculture and aquatic ecosystems, antibiotic resistance in aquatic organisms, toxicological effects of antibiotics, remediation strategies for antibiotics resistance in aquaculture and aquatic ecosystems, and the roles of nanotechnology in aquaculture and aquatic organisms. This review highlights the current progress in the applications of nanoparticles for remediation of antibiotics resistance, the potential human health risks associated with nanotechnology, and its mitigation measures for sustainable management.

Antibiotics use and residues in aquaculture and aquatic ecosystems

Antibiotics are natural or synthetic substances used as antibacterial drugs to kill or inhibit the growth and spread of bacterial pathogens. Antibiotics are employed prophylactically, therapeutically, or metaphylactically in animal husbandry (Patel et al. 2019; Okoye et al. 2022b) and aquaculture (Lozano et al. 2017; Lulijwa et al. 2020; Schar et al. 2020). Antibiotics are also utilized to boost growth in aquaculture. The different classes of antibiotics used in aquaculture include aminoglycosides, quinolones, sulfonamides, tetracyclines, macrolides, chloramphenicols, β-lactams, nitrofurans, lincosamides, and polymyxins (Sun et al. 2020). Antibiotics usage in aquaculture is largely unregulated in many developing nations, leading to indiscriminate antibiotic use (Budiati et al. 2013), and even where laws do exist, stringent compliance is largely nonexistent. Many developed countries have animal husbandry and aquaculture regulatory authorities entrusted with, among other things, approving and regulating antibiotic usage in aquaculture and ensuring rigorous compliance. The permitted antibiotics, regulatory systems, amount of antibiotics utilized, and manner of farming vary greatly between countries, making it impossible to determine current levels of antimicrobial usage in aquaculture around the world (Chen et al. 2018). For example, Vietnam has the most authorized antibiotics (30), followed by Chile (19) and South Korea (17), while Brazil, the UK, and the USA have the fewest (Table 1). The most often used antibiotics in aquaculture are oxytetracycline, florfenicol, and sulfadiazine(Lulijwa et al. 2020; Sun et al. 2020).

Table 1 List of authorized antibiotics for aquacultural use in major aquaculture-producing countries

Country	Number of authorized antibiotics	Type of antibiotics	References
Bangladesh	12	Sulfamethazine, sulfamethizole, sulfamethoxazole, amoxicillin, chlortetracycline, doxycycline, erythromycin, oxytetracycline, penicillin G, sulfadiazine, trimethoprim, tylosin	(Ali et al. 2016; Hossain et al. 2017)
Vietman	30	Danofloxacin, dicloxacillin, difloxacin, emamecyin, erythromycin, flumequine, neomycin, amoxicillin, benzylpencillin, ciprofloxacin, cloxacillin, colistin, chlortetracycline, cypermethrim, sulfamonomethoxine, sulfamethoxazole, sulfamethazine, spectinomycin, oxolinic acid, ormetoprinm, oxytetracycline, oxacillin, paromomycin, sarafloxacin, sulfadimethoxine, sulfadiazine, tetracycline, tilmicosin, trimethoprim, tylosin	(Lulijwa and Kajobe 2018)
Thailand	14	Amoxicillin, ormetoprim, penicillin, sulfadiazine, sulfadimethoxine, sulphamonomethoxine, sulfadimethoxine +, sulphaguanidine, enrofloxacin, norfloxacin, oxytetracycline, trimethoprim, tribrissen, tetracycline	(Lulijwa and Kajobe 2018)
China	13	Neomycin, norfloxacin, oxolinic acid, sulphadiazine, doxycycline, enrofloxacin, florfenicol, flumequine, sulphamethazine, sulphamethoxazole, sulphamonomethoxine, thiamphenicol, and trimethoprim	(Liu et al. 2017; Lulijwa et al. 2020)
UK	5	Oxytetracycline, sarafloxacin, cotrimazine, oxolinic acid, amoxicillin	(Preena et al. 2020)
Italy	6	Tetracycline, amoxicillin, flumequine, sulfadiazine, oxytetracycline	(Preena et al. 2020)
USA	4	Florfenicol, oxytetracycline, sulfa/trimethoprim, sulfadimethoxine/ormetoprim	(Preena et al. 2020)
South Korea	17	Amoxicillin, ciprofloxacin, chlortetracycline, enrofloxacin, sulphamethoxazole, sulfadimethoxine, erythromycin, florfenicol, nalidixic acid, ormetoprim, oxolinic acid, oxytetracycline, sulfadiazine, sulphachloropyridazine, sulphamethazine, trimethoprim, tetracycline	(Lulijwa et al. 2020)
Brazil	2	Florfenicol, oxytetracycline	
Chile	19	Furazolidin, gentamyin, neomycin, norfloxacin, oxolinic acid, oxytetracycline, sulphadiazine, amoxicillin, chloramphenicol, doxycycline, enrofloxacin, erythromycin, florfenicol, flumequine, sulphamethazine, sulphamethoxazole, sulphamonomethoxine, thiamphenicol, trimethoprim	(Preena et al. 2020)

In several countries, antibiotics are used inadvertently by fish farmers without identifying the exact causes of fish infection(Rahman et al. 2021). The most common route for the administration of antibiotics in aquaculture is by mixing the antibiotic substance with aquaculture feed. Other routes of administration of antibiotics include pond sprinkling and injection(Liu et al. 2017). All antibiotic administration methods, aside from injection, have a direct impact on aquatic animals as well as the aquatic environment. Studies have confirmed that antibiotics are not effectively metabolized by fish (Sun et al. 2020), and it has been estimated that 75% of the antibiotics fed to fish are excreted back into the pond water (Burridge et al. 2010). Indeed, several studies have revealed that antibiotics accumulate in the aquaculture environment, leading to antibiotic residue buildup in pond water, sediments, animal tissues, and cultured aquatic products with negative effects for human and environmental health (Lulijwa and Kajobe 2018; Chen et al. 2018). The presence of antibiotic residues in cultured aquatic products could be systemically toxic to consumers and has a direct negative impact on the complex microflora that inhabits the human gastrointestinal system with potentially adverse implications (Monteiro and Andrade 2018). Chloramphenicol residues raise the risk of cancer and, at lower concentrations, aplastic anemia. Other side effects of residual antibiotics include penicillin hypersensitivity, gentamicin mutagenicity and nephropathy, and sulfamethazine, oxytetracycline, and furazolidone immunopathology and carcinogenic consequences (Beyene 2016).

Aquaculture farm effluents containing residual antibiotics are commonly discharged into aquatic bodies such as rivers or into farmlands where they serve as manure. From these places, the residual antibiotics can enter the food chain leading to unpleasant consequences. Residual antibiotics can also affect phytoplankton and zooplankton diversity (Ferreira et al. 2007; Song et al. 2016). These antibiotics, including sulfonamides, quinolones, and tetracyclines, have also been implicated in the disruption of zooplankton early developmental processes (Park and Kwak 2018) and phytoplankton chlorophyll production (Song et al. 2016). This disruption, in turn, may lead to alterations in the food chain, with consequences at every level of the ecosystem. Several factors such as exposure concentration and physiochemical properties influence the residual level of different antibiotics in an aquaculture environment, aquatic animals, and their products. It is generally accepted that antibiotics such as quinolones (especially enrofloxacin, norfloxacin, and ofloxacin) with poor water solubility tend to accumulate more in aquatic environments and aquatic products, and are classified as "pseudopersistent" emerging contaminants (Tang et al. 2017). Residual antibiotics in aquatic environments and ecosystems are widely recognized as an emerging threat to both humans and the environment, and this has prompted many studies aimed at finding effective biological, chemical, and physical methods to remove residual antibiotics in wastewater effluents and natural waters. However, the majority of these studies have focused on removing antibiotics from hospital effluent, pharmaceutical firms, and livestock farms; there has been little study explicitly focused on aquaculture wastewater treatment to remove residual antibiotics (Senarathna et al. 2021). Although the same methodology can be applied to aquaculture wastewater, field-specified studies or research are very necessary. The emerging hazard posed by indiscriminate use of antibiotics in aquaculture and the resulting antibiotic residues in aquatic environments is a complex phenomenon that requires global approaches and efforts from governments, relevant organizations, and stakeholders. It is also very imperative to implement effective and sustainable methods for monitoring antibiotic levels in the environment in order to mitigate this problem.

Toxicological effects of antibiotics in aquaculture and aquatic organisms

Antibiotics belonging to various classes are utilized by humans in the treatment of various diseases such as trichomoniasis, dermatophytosis, infection of the urinary tract, human immunodeficiency virus (HIV), as well as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (Becker et al. 2020; Girijan et al. 2020; Trivedi et al. 2020; Das 2021). However, due to continuous exposure to these drugs, certain effects (short and long term) are being induced upon humans, especially in the gut which inhabits various species of bacteria, viruses, fungi, and archea (Table 2).

Antibiotic-resistance bacteria

Different classes of antibiotics have been produced as a result of high demand in treating various diseases. Contrariwise, the irresponsible and reckless use of antibiotics has led to the introduction of bacterial, fungal, and viral strains that are resistant (Zaman et al. 2017). In the past, the manufacture of novel antibiotics varied directly to the development of resistant strains, but currently, the conventional method in disease-fighting is directed towards modifying existing antibiotics to fight evolving and re-evolving pathogenic resistance worldwide (Zaman et al. 2017).

Antibiotic resistance entails the ability of a drug to inhibit microbial (bacteria, fungi, viruses) growth efficiently. Antibiotics are always active against these microbes, but when the microorganisms display resistance or low sensitivity, it necessitates an antibiotic concentration that is higher above the normal to have effects on them (Zaman et al. 2017). The gut of humans serves as a source of diverse microbial genes that are resistant to antibiotics. Different classes of antibiotics such as vancomycin, bacitracin, cephalosporin, and tetracycline have been reported to have genes that are resistant to them within the human gut (Field and Hershberg 2015).

The microbiome in the guts of humans controls the immune system, metabolism of the body, as well as the entire functioning of human health (Chauhan 2017). Antibiotic formulations are utilized for managing and fighting off infections caused by microbes. Their consistent usage has resulted in targeted microbes (bacteria, fungi, and viruses) developing immunity over time (Yadav 2022). The development of this resistance or immunity for antibiotics by these microbes is brought about by gene mutation (Laxminarayan and Brown 2001), and selective pressure and their mechanisms for resisting antibiotics are shown in Table 3.

However, the resistance exhibited by these microbes is not without effects on the intestinal flora of humans. The resistance to antibiotics by microbes has resulted in high mortality and infections that threaten human lives (Zaman et al. 2017). For instance, Freire-Moran et al. (2011) reported that about 25,000 people in Europe die as a result of drug resistance to bacterial infections.

Cystic fibrosis which is a respiratory disease is caused by *Burkholderia cenocepacia*, *Staphylococcus aureus*, *Hemophilus influenza*, and *Pseudomonas aeruginosa* which are resistant to multi-drugs (Carmody et al. 2010). *Streptococcus pneumoniae*, *Klebsiella* sp., *P. aeruginosa*, *S. aureus*, *H. influenza*, and *Acinetobacter baumannii*, which show resistance to carbapenem class of antibiotics, result in severity of pneumonia (Singla et al. 2015; Martin et al. 2016). Bacteria that are resistant to isoniazid and rifampicin used in treating patients with tuberculosis have been reported to hinder tuberculosis treatment in them (Yadav 2022). According to Chattaway et al. (2016), *E. coli* which has resistance to quinolone antibiotics increases the risk of having enteric infections. Diseases such as gastrointestinal inflammation, cholera, shigellosis, salmonellosis, and listeriosis are all triggered by bacteria that are resistant to antibiotics (Abdulamir et al. 2014; de Vasconcelos et al. 2016).

Table 2 Toxicological effects of antibiotics on different biomarkers

Class of antibiotics	Types	Effects	References
Cephalosporins	Ceftriaxone	Depletion of *Enterobacteriaceae* Excessive growth of Candida and Enterococci species *Clostridium difcile* infection	(Sullivan et al. 2001)
Nucleoside reverse transcriptase inhibitors (NRTIs)	Zidovudine, lamivudine	Inhibition of reverse transcriptase	(Adriaenssens et al. 2011)
Synthetic nucleoside analogues	Acyclovir	Inhibition of DNA polymerase by virus	(Adriaenssens et al. 2011) (Bule et al. 2019)
Antimicrobials	Nitrofurantoin	Inhibition of protein synthesis in DNA and RNA of bacterial cell wall	(Stewardson et al. 2015)
	Β-Lactams	Increase in microbial load of fecal sample Impairment of carbohydrate metabolism	(Hernández et al. 2013) (Panda et al. 2014)
Lincosamides	Clindamycin	Disruption of microbiota in gut *Clostridium difcile* infection (CDI)	(Rashid et al. 2015)
Glycopeptides	Vancomycin	Reduction in species like *Enterococcus*, *Clostridia*, Bacteroides and Bafidobacteia Enhances the growth of *Lactobacillaceae*, *Enterobacteriaceae* and Enterococci Reduction of Firmicutes in human gut	(Yin et al. 2015) (Reijnders et al. 2016)
Macrolides	Erythromycin, azithromycin, and clarithromycin	Shift in the intestinal flora composition Affects the metabolism of human gut	(Korpela et al. 2016)
Glycopeptides-carbapenem	Vancomycin-imipenem	High sugars and arabinitol in feces	(Choo et al. 2017)
Aminoglycosides, glycopeptides, and carbapenem	Gentamicin, vancomycin, and meropenem	Increase in Enterobacteriaceae Reduction in Bifidobacterium as well in species that produce butyrate	(Palleja et al. 2018)
Penicillins	Penicillin G	Inhibition of the synthesis of cell wall	(Grenni et al. 2018)
Aminoglycosides and tetracycline	Gentamicin and oxytetracycline	Inhibition of the synthesis of protein	(Grenni et al. 2018)
Nitroimidazole	Metronidazole	Inhibition of DNA synthesis	(Grenni et al. 2018)
Antihelminthes	Albendazole, praziquantel	Inhibition of microtubules polymerization Enhances the permeability of parasite to calcium	(Grenni et al. 2018)
Quinolones	Ciprofloxacin	Loss of microbial diversity in human gut Inhibition of nucleic acid synthesis which acts on DNA girase	(Grenni et al. 2018) (Lulijwa et al. 2020)
Sulfonamides	Sulfamethoxazole	Interference with the synthesis of folic acid	(Grenni et al. 2018) (Lulijwa et al. 2020)
Azole antifungal	Ketoconazole	Inhibition of the synthesis of ergosterol	(Sallach et al. 2021)
Antifungals	Amphotericin B, griseofulvin	Alters cytoplasmic membrane Microtubule alteration	(Sallach et al. 2021)
Antimicfrobials, macrolides, and protein-pump inhibitors	Clarithromycin, metronidazole, and omeprazole	Perturbations of microbiota in gut when used in treating infections caused by *Helicobacter pylori*	(Yang et al. 2021)
Penicillin, beta-lactamase inhibitors	Amoxicillin + clavulanic acid	Aerobic gram-positive cocci were wiped totally High resistance of enterobacteria	(Yang et al. 2021)
Polymyxin, penicillins	Colistin + amoxicillin	Alteration in gut microbiota Induction of antibiotic resistome	(Li et al. 2021) (Yang et al. 2021)

Antibiotic resistance in aquatic organisms

Aquatic organisms fall into four major categories including microorganisms, plants, vertebrates, or invertebrates. Each of these groups are composed of complex species and sub-species, all of which interact with each other in the aquatic environment at different trophic levels (Liao et al. 1AD). Antibiotics are regarded as emerging contaminants in aquatic environments posing a serious problem as most of the waste water treatment facilities have not been well equipped to eliminate these emerging contaminants (Pal et al. 2015; Gogoi et al. 2018; Michael-Kordatou et al. 2018; Rodríguez-Molina et al. 2019; Liu et al. 2021). Recent studies have shown that many antibiotics are now finding their way into aquatic environments and knowledge of their interactions with aquatic organisms is scarce (Gogoi et al. 2018; Guha Roy 2019; Gomes et al. 2020; Liu et al. 2021). Therefore, it is important to research and continuously update our current knowledge on the roles antibiotics play in aquatic environments and how they interact with aquatic organisms.

Table 3 Mechanism of antibiotic resistance

Antibiotic	Resistance mechanism	References
Tigecycline, minocycline	Alteration of target Production of efflux pump Monooxygenation	(Dean et al. 2003) (Zaman et al. 2017)
Synercid	Acetylation Carbon–Oxygen lyase Production of efflux pump Alteration of target	(Werner et al. 2002) (Zaman et al. 2017)
Penicillins, monobactams, penems, and cephalosporins	Hydrolysis Efflux pump production Alteration target	(Zaman et al. 2017)
Cephalosporins	AmpC beta-lactamase ESBLs	(Zaman et al. 2017)
Clindamycin	Nucleotidylation Production of efflux pump Alteration of target	(Zaman et al. 2017)
Linezolid	Production of efflux pump Alteration of target	(Zaman et al. 2017)
Ciprofloxacin	Production of efflux pump Acetylation Alteration target production	(Zaman et al. 2017)
Chloramphenicol	Acetylation Production of efflux pump Alteration of target	(Zaman et al. 2017)
Streptomycin, spectinomycin, and gentamicin	Acetylation Phosphorylation Nucleotidylation Efflux pump production Alteration of target	(Zaman et al. 2017)
Sulfamethoxazole	Alteration of target Production of efflux pump Overproduction of dihydropteroate synthase (DHFR) Mutation of dihydrofolate reductase (DHPS)	(Zaman et al. 2017)
Teicoplanin, vancomycin	Reprogramming peptidoglycan biosynthesis	(Zaman et al. 2017)
Daptomycin	Alteration of target	(Zaman et al. 2017)
Erythromycin, azithromycin	Hydrolysis Phosphorylation Glycosylation Production of efflux pump Alteration of target Ribosomal methylation of binding sites	(Sedaghat et al. 2017) (Zaman et al. 2017)
Rifampin	Production of efflux pump ADP-ribosylation Mutations in RNA polymerase gen Alteration of target Enzymatic degradation	(Kakoullis et al. 2021)
Aztreonam	Extended-spectrum-β-lactamases (ESBLs)	(Kakoullis et al. 2021)

Antibiotic resistance in any environments is considered as serious public health concern (Larsson and Flach 2021). The continued accumulation of antibiotics in aquatic environments has led to the rise of antimicrobial resistant genes (ARGs) in this environment (Richardson and Kimura 2019; Saima et al. 2020; Liu et al. 2021). The type of ARGs circulating within a certain region has been noted to vary significantly based on temporal and spatial distribution (Liu et al. 2021; Valdés et al. 2021). For example, in a study conducted on various water bodies in China, it was observed that the type of antibiotics found in a specific water body was related to the locally available industry infrastructures, mode of antibiotic disposal by pharmaceutical companies, and the type of antibiotic used in the livestock industry in that specified area (Liu et al. 2021). In this section, the possible mechanisms by which ARGs may interact with aquatic organisms as summarized in Fig. 1. In addition, areas where nanotechnology may be applied to disrupt these interactions are discussed. Despite these remedies, it is also important to note that the possible fate of nanomaterials in aquatic environments is yet to be fully established and need to be studied before use as continuous use may prove toxic in aquatic environments if not checked (Fajardo et al. 2022).

Antibiotic presence in aquatic environment is well documented, and overtime, aquatic microorganisms get exposed to these antibiotics acquiring ARGs which they pass to other organisms (Michael-Kordatou et al. 2018; Saima et al. 2020; Sun et al. 2020; Liu et al. 2021; Valdés et al. 2021). For example, antibiotic selective pressure exerted in aquatic environments promotes easy contact between microorganisms and ARGs, further facilitating easy exchange and recombination of genetic material (Fig. 1A). This results in formation of antibiotic resistant bacteria (ARBs) or microorganisms that are capable of infecting other aquatic microorganisms (Michael-Kordatou et al. 2018; Saima et al. 2020). The process of selective pressure leading to ARBs can be tackled by nanotechnology. Recently, nanotechnological approaches have been used to eliminate ARBs in aquatic environments (Fajardo et al. 2022). Asides from eliminating ARBs, nanomaterials can be used to eliminate other contaminates that take part in selective pressure, e.g., those from pharmaceutical and cosmetic industries (Hairom et al. 2021). If the causes of ARBs or contaminates involved in selective pressure can be identified early, formation of tailored nanomaterials against the ARBs or other contaminants can be done.

Asides from, or in conjunction with, selective pressure, aquatic microorganisms can accumulate to form complex

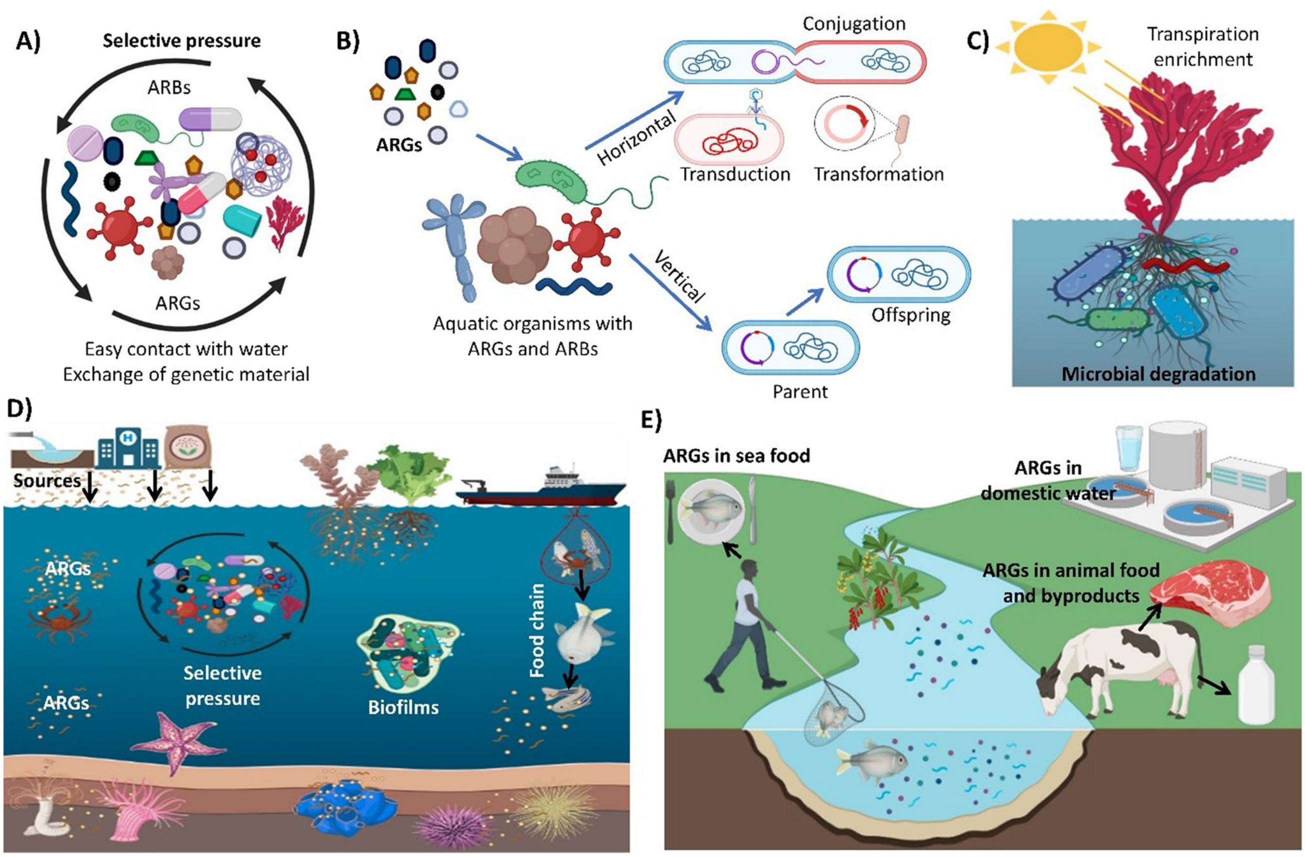

Fig. 1 Antimicrobial resistance in aquatic organisms and possible fate. **A** Selective pressure may enhance the genetic transfer of ARGs. **B** Transfer of ARGs in various microbial communities including biofilms. **C** Uptake of ARGs by floating aquatic plants. **D** Presence of ARGs in aquatic environments from varying sources. The ARGs can be picked up by various organisms and transferred from one organism to another by various mechanisms including food chains, selective pressure, and genetic material transfer by microbial communities. **E** Possible fate of ARGs. Humans and animals may get exposed to RGs from infected fish or water

microbial communities (e.g., biofilms), where genetic material is exchanged (Parrish and Fahrenfeld 2019; Fabra et al. 2021). These complex microbial communities are harder to eliminate due to their complex nature. In such places, genetic materials is transferred from one microorganism to the other through various channels such as horizontal transmission (e.g., conjugation, transduction, and transformation) or to the next generations through vertical transmission as seen in Fig. 1B (Michael-Kordatou et al. 2018). During the transfer of genetic materials, there is a possible risk of mutations leading to the development of novel ARGs that can induce ARBs and cause wide spread bacterial resistance (Wei et al. 2019). Nanotechnological approaches like coupling of nanomaterials with surfactants or antibiotics can be used to disrupt antimicrobial resistant biofilm communities (Li et al. 2021). Recent research has shown that environmental biofilms including aquatic biofilms are efficient binding matrices for nanomaterials probably due to the extracellular polymeric substances (EPS) holding the biofilms together. This shows potential in developing nanomaterials that can clear these microbial biofilms, especially those containing ARBs and ARGs in aquatic environments.

Continued bioaccumulation of ARGs in aquatic environments leads to their presence within various trophic levels. In aquatic food chains, antibiotics have been detected in fish (He et al. 2014; Chen et al. 2017; Tang et al. 2020). The concentrations of antibiotics in aquatic organisms may vary based on feeding habits, position in food chain, and location in the aquatic environment. For example, a study on fish caught in wild waters showed that the concentrations of antibiotics in fish increased progressively from herbivorous to omnivorous to carnivorous (He et al. 2014; Tang et al. 2020), probably because carnivorous fish are the top consumers in the aquatic food chain (He et al. 2014; Tang et al. 2020). Aquatic plants can accumulate antibiotics in their roots, and the antibiotics will be further degraded by other microorganisms which enrich the roots facilitating uptake of the antibiotics by these plants (Fig. 1C) (Liu et al. 2021). Chronic exposure of fish, plants, and other aquatic organisms to ARGs make them toxic and a potential health risk to people and animals that consume them (Fig. 1D, E) (Miranda et al. 2018; Sun et al. 2020). Apart from direct human consumption of seafood, people are also at a risk of exposure of ARGs when consuming meat or byproducts of animals exposed to ARGs and ARBs from aquatic environments. One way of reducing the risks is elimination through nanotechnological approaches. For example, studies have showed that nanoparticles can be used to eliminate ARB in fish in vitro (Shaalan et al. 2016; Nasr-Eldahan et al. 2021). However, the long-term effect of nanotechnology when treating fisheries and other aquatic organisms need to be determined as they may be toxic (Fajardo et al. 2022). The rise of new ARGs may prove difficult to eliminate by the normal waste disinfection procedures posing further risks in the water used domestically (Pal et al. 2015; Gogoi et al. 2018; Michael-Kordatou et al. 2018; Rodríguez-Molina et al. 2019; Liu et al. 2021). Therefore, continuous monitoring of the accumulation of antibiotics, ARGs, ARBs, and modes of transmission will be useful in tackling rising antimicrobial resistance changes in aquatic environments. There already exists nanotechnological approaches for cleaning aquatic systems (Fajardo et al. 2022), and knowledge of the types of ARGs and ARBs in aquatic environments can help in formulation of better nanotechnological water treatment procedures to reduce or completely eliminate their presence in both domestic and wild water.

Nanotechnology, aquaculture, and aquatic ecosystems

Nanoparticles synthesis

Since the beginning of nanoscience, high yield and low-cost nanomaterial synthesis have been a major issue. The ability to produce nanoparticles with varied shapes, monodispersity, chemical composition, and sizes is critical for their use in aquaculture and fish medicine (Shah and Yoon 2017). The synthesis of metallic nanoparticles with desired properties is carried out through different approaches, including bottom-up and top-down. The bottom-up strategy entails synthesizing nanoparticles and assembling them into the final composite product. This type of synthesis can be performed either biologically or chemically. The bottom-up approach has a significant benefit in that it can synthesize metallic nanoparticles with no flaws and chemical composition homogeneity. The "top-down" technique, mediated by chemical or physical approaches, reduces the starting material to its size. The downside of this process is the nonuniformity of morphology, which affects the physical and chemical properties of the generated nanoparticles. While physical and chemical methods are widely used, biological nanoparticle synthesis is still in its infancy (Sakhare et al. 2022).

Physical synthesis

The most important physical approaches are evaporation–condensation and laser ablation. Physical synthesis has several advantages over chemical approaches, including the absence of solvent contamination in the produced thin films and the uniformity of NP distribution. Physical synthesis using microwaves has been used for silver nanoparticles, which involves the physical reduction of silver using various microwave radiation frequencies. When compared to a thermal approach with the same temperature and exposure, this process performed faster and yielded a larger concentration of silver nanoparticles. The larger the particle obtained, the greater the concentration of silver nitrate utilized, the longer the reaction time, and the higher the temperature (Jiang et al. 2006).

Chemical synthesis

Chemical synthesis with organic and inorganic reducing chemicals is the most frequent method for producing nanoparticles. For example, several reducing agents such as ascorbate, sodium citrate, elemental hydrogen, N,N-dimethylformamide (DMF), sodium borohydride ($NaBH_4$), and Tollens reagent are utilized for the reduction of silver ions ($Ag+$) in aqueous or nonaqueous solutions. At room temperature, nanoparticles can be made by combining the appropriate metal ions with reduced polyoxometalates, which act as reducing and stabilizing agents. Polyoxometalates are water-soluble and can perform multielectron redox reactions in a stepwise manner without disrupting their structure. Illuminating a deaerated solution of polyoxometalate/S/Ag + resulted in the formation of silver nanoparticles. Furthermore, one-step green chemistry production and stabilization of silver nanostructures in water at room temperature using mixed-valence polyoxometalates have been described (Iravani et al. 2014).

Biological synthesis

Finding environmentally acceptable and cost-effective methods to synthesize nanoparticles is a hot topic. The use of biological approaches is seen to be crucial in this strategy. Bacteria, fungi, and plants are the three main categories of organisms that produce biologically produced nanoparticles. To make the required nanoparticles, microbial enzymes or plant phytochemicals with antioxidant or reducing characteristics work on precursor molecules. A solvent medium for synthesis, an environmentally acceptable reducing agent, and a nontoxic stabilizing agent are the three basic components of a biosynthetic nanoparticle system (Shaalan et al. 2016).

Silver nanoparticles made from *Origanum vulgare* leaf extract were found to have antibacterial and cytotoxic properties when tested against a human lung cancer cell line. The green production of silver and gold nanoparticles using cashew nut shell liquid showed bactericidal efficacy against many fish infections. Silver nanoparticles made from tea leaf extract (*Camellia sinensis*) were found to have a bactericidal effect against *Vibrio harveyi* in juvenile *Feneropenaeus indicus*. For green manufacture of zinc oxide nanoparticles (ZnO-NPs), an *Aloe* leaf extract broth was employed, which demonstrated stronger bactericidal activity than nanoparticles made by traditional chemistry. *Aeromonas hydrophila* bacteria is used as a reducing agent in a unique process for biologically synthesizing zinc oxide nanoparticles. This procedure is both ecologically friendly and cost-effective (Shaalan et al. 2017).

Nanoparticles application in aquaculture and aquatic organisms

Antimicrobial activities of nanoparticles

In aquaculture, one of the biggest challenges was infection disease control caused by microbial pathogens. Due to the indiscriminate use of antibiotics in fish farming, many disease-causing microbes in fish have acquired resistance to commonly used antibiotics. This has prompted the need for new therapeutic approaches to overcome this challenge. The use of nanoparticles as alternative antimicrobials to combat the emergence of microbial resistance to antibiotics in aquaculture has been proposed as a solution to antimicrobial resistance (Swain et al. 2014; Dar et al. 2020). Various metal nanoparticles have shown promising antimicrobial effects against bacterial, fungal, and viral pathogens (Table 4) through different mechanism such as damaging of the microbial cell membrane/cell wall, disruption of protein transports, inactivation of vital enzymes and others (Fig. 2) (Nasr-Eldahan et al. 2021).

a) Silver nanoparticles (Ag-NPs)

   Silver nanoparticles are the most studied nanoantibacterial agent. In contrast to antibiotics that generally act through one mechanism only (Antony et al. 2013), Ag-NPs act against disease-causing bacteria through multiple mechanisms, enabling them to overcome bacterial resistance (Knetsch and Koole 2011). The antimicrobial mechanism of AgNPs is not fully understood. Researchers have hypothesized various possible mechanisms that may be related to changes in the morphology and structure of the bacterial cells induced by the size of nanoparticles in relation to the large surface-to-volume ratio and their shape (Rai et al. 2009). These physiochemical variables play an important role in the antibacterial action of AgNPs (Beyth et al. 2015). The nanoparticles' small size allows for greater interaction with the bacterial cell as well as easier penetration (Rai et al. 2009). AgNPs are thought to attach to the cell membrane via electrostatic charges, in which the nanoparticle's positive surface charge electrostatically attaches to the cell membrane's negative charge, promoting nanoparticle membrane adhesion. Nanoparticles enable the release of Ag + ions, which bind to bacteria cell membrane protein, triggering changes to the structure of the cell membrane, including permeability and leading to cell death (Sondi and Salopek-Sondi 2004). They can also attach to cytochrome and nucleonic acids, causing cell damage and preventing cell division (Huang et al. 2012). Silver nanoparticles have been demonstrated to exhibit strong antibacterial activity against multidrug-resistant bacterial strains (Prakash et al. 2015). Silver nanoparticles made with citrus lemon juice as a reducing agent showed antibacterial and anti-cyanobacterial action against *Staphylococcus aureus* and *Edwardesiella tarda* bacteria, as well as anti-cyanobacterial activity against *Oscillatoria* species (Swain et al. 2014). Silver nanoparticles had high inhibitory effects against Candida species as an antifungal drug, similar to the commercial antifungal Amphotericin B (sanjemban). There has been limited research especially on the therapeutic use of silver nanoparticles with antifungal and antiviral properties in aquaculture.

b) Zinc oxide nanoparticles (ZnO-NPs)

The antibacterial and antifungal properties of zinc oxide nanoparticles have attracted a lot of attention (Gunalan et al. 2012; Sirelkhatim et al. 2015). However, the specific antibacterial toxicity mechanism of ZnO-NPs is unknown and still contested. However, it has been hypothesized that their antibacterial effect is owing to the particles' disruption to the bacterial cell membrane, causing cytoplasmic contents to leak out of the cell (Sirelkhatim et al. 2015). ZnO-NPs have been shown to prevent the growth of *Aermonas hydrophila*, *Edwardseilla tarda*, *Citrobacter* spp., *Staphylococcus aureus*, *Vibrio species*, *Bacillus cereus*, *Pseudomonas aeruginosa*, and *Flavobacterium branchiophilum* in the field of aquaculture (Swain et al. 2014). Antibacterial activity of ZnO-NPs against a fish bacteria pathogen (*Vibrio harveyi*) was demonstrated in a study, and the antibacterial activity increases as the particle size of the ZnO-NP decreases (Vaseeharan et al. 2010). Another intriguing study found that ZnO-NPs generated biologically using *Aermonas hydrophila* have antibacterial action against *E. coli*, *Enterococcus faecalis*, *Pseudomonas aeruginosa*, *Aspergillus flavus*, and *Candida albicans* (Jayaseelan et al. 2012). Several investigations have found that ZnO-NPs are nontoxic to human cells, which has necessitated their use as antibacterial agents, lethal to microbes, and have good biocompatibility with human cells (Padmavathy and Vijayaraghavan 2008; Siddiqi et al. 2018).

c) Titanium dioxide nanoparticles (TiO_2-NPs)

Few research has been performed on the use of TiO_2-NPs as therapeutic agents in aquaculture. After being activated by light, TiO_2-NPs were found to have a bactericidal impact against fish bacterial infections such *Streptococcus iniae*, *Edwardsiella tarda*, and *Photobacterium damselae* (Cheng et al. 2011). TiO_2-NPs can form extremely active hydroxyl -OH, superoxide ion -O, peroxyl radical -OOH, and other free radicals with high oxidation capability when exposed to ultraviolet light. These free radicals can interact with biomacromolecules such as lipids, proteins, enzymes, and nucleic acid molecules in microorganisms, and destroy their cell structures through a series of chain reactions (Sonawane et al. 2003). However, a study suggested that TiO_2-NPs can affect the immune system of fish by decreasing the antibacterial activity of fish neutrophils, making the fish less resistant to bacterial infections (Jovanović et al. 2015).

d) Gold nanoparticles (Au-NPs)

Due to their low toxicity to eukaryotic cells, there is currently a lot of interest in studying the antibacterial effects of gold nanoparticles (Li et al. 2014). In aquaculture, gold nanoparticles have the potential to be efficient antibacterial agents and reduce mortality caused by microbial infection (Saleh et al. 2016). The use of gold nanoparticles as an antibacterial agent to inhibit the growth of common waterborne pathogens including *Salmonella typhi* and *E. coli*, which are becoming resistant to traditional bactericides, has been investigated (Lima et al. 2013). There have been several studies on gold nanoparticles as antibacterial treatments in aquaculture (Vaseeharan et al. 2010). Au-NPs were found to limit the growth of multi-drug resistant bacterial isolates (Li et al. 2014), including fish bacterial isolates (Velmurugan et al. 2013). In a similar study, gold nanoparticles have been shown to have antifungal action against Candida species, and their efficacy was size-dependent, with smaller gold nanoparticles having stronger antifungal effects (Wani and Ahmad 2013). It has been claimed that Au-NPs work against bacteria by interfering with the oxidative phosphorylation process and modifying the potential of the bacterial cell membrane, resulting in a drop in the activity of F-type ATP synthase and a net reduction in ATP generation and metabolism.

Nanoparticles for drug delivery

Recently, there have been significant advances in the utilization of nanoparticles to deliver therapeutic drugs to their target locations (Obeid et al. 2017). A perfect drug delivery system includes numerous critical characteristics, including the delivery system's safety, biocompatibility, and biodegradability, as well as the stability of the drug,

Table 4 Studies of nanoparticles for remediating antibiotic resistance in aquaculture

Metal NPs	Purpose	Remark	Ref
CuO, ZnO, Ag and Ag–TiO_2	Antibacterial agents against aquaculture diseases	Broad spectrum of antibacterial antifungal activities against fungi like *Penicillium* and *Mucor* species	(Swain et al. 2014)
Ag_3PO_4 loaded hydroxyapatite nanowires	Water treatment	Excellent antibacterial activities towards *E. coli* and *S. aureus* in water	(Li et al. 2015)
γ-Fe_2O_3 NPs	Oxytetracycline (OTC) administration in zebra fish	The dynamics related to OTC release is still unclear	(Chemello et al. 2016)
MoS_2 nanofilms	Water disinfection and purification	Inactivation of bacteria under light irradiation via the generation of ROS	(Liu et al. 2016)
Nanozyme	Antibiotics for drug-resistant bacteria	Enhanced antibacterial functions against *E. coli* and *S. aureus* *in vitro* and *in vivo*	(Cao et al. 2019)
Se-NPs	Studies of the immune response and histopathological alterations induced by sublethal cadmium (Cd) toxicity in Nile tilapia (*Oreochromis niloticus*)	Improvement of the growth, immunity and antioxidant power of *O. niloticus* and alleviate the pathological disorders induced by Cd toxicity	(Abu-Elala et al. 2021)
Algae-coated Se NPs	Antibacterial agent against *Vibrio harveyi* in human and shrimp cell	High performance and nontoxic	(Mansouri-Tehrani et al. 2021)
Cu_3P NPs	Impeding antibacterial resistance in fishery water	The multiple enzyme-like activities of the NPs and the action of ROS produced by their oxidase- and peroxidase- like activities facilitates their inherent activities for glutathione depletion and the lipid peroxidation	(Chao et al. 2022)
AgNPs	Antibiotic-resistant *Aeromonas veronii* infections in Nile tilapia, Oreochromis niloticus (L.)	The treatment increased fish survival; improved hematological, immunological, and antioxidant activities; and optimized liver and kidney function	(Elgendy et al. 2022)

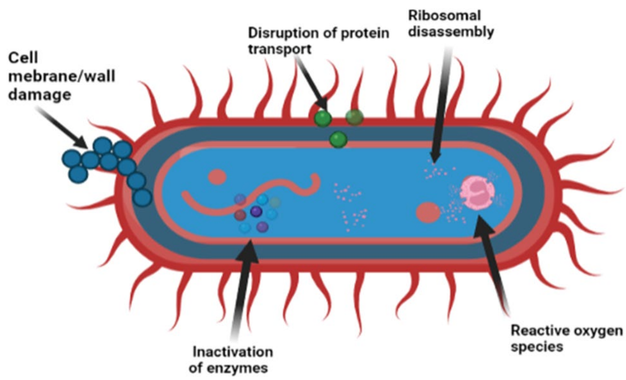

Fig. 2 Action of metal nanoparticles against pathogenic bacteria

specificity of delivery, and minimal or no side effects (De Jong and Borm 2008). Nanoparticles have piqued interest as medication delivery methods due to their small size and ability to pass biological barriers such as the blood–brain barrier. Nanoparticles also have a large surface area to volume ratio, which allows them to interact with more conjugates and compounds (Wang et al. 2011). The most studied nanoparticles for drug delivery in aquaculture are chitosan nanoparticles and PLGA nanoparticles.

a) PLGA nanoparticles

Because of its versatility, PLGA is an ideal choice for drug administration due to its versatility. It is a biocompatible and biodegradable copolymer made up of poly lactic acid and poly glycolic acid, and one of the nanoparticles that the Food and Drug Administration (FDA) has approved for human use. As a result, numerous studies on the viability of employing PLGA as a drug carrier have been done (Makadia and Siegel 2011). PLGA nanoparticles were combined with the anti-mycobacterial drug rifampicin and fed to zebra fish embryos infected with *Mycobacterium marinum* in a study. When compared to rifampicin alone, the rifampicin-PLGA nanoparticles had a greater therapeutic impact against *Mycobacterium marinum* and a higher embryo survival rate (Fenaroli et al. 2014).

b) Chitosan nanoparticles

Chitosan nanoparticles are ideal drug carriers because of their compatibility and biodegradability. They are made of a biocompatible, nontoxic, and biodegradable polymer that is easily excreted through the kidneys (De Jong and Borm 2008). As a result of the extremely small size, they are capable of penetrating through biological barriers in vivo and delivering medications to the infection site, thereby enhancing drug efficacy (Wang et al. 2011). Chitosan nanoparticles also have the added advantage of offering a gradual and controlled drug release, which improves drug stability and efficacy. In an aquacultural study, vitamin C was coupled with chitosan nanoparticles and administered to *Oncorhynchus mykiss*. Because of the significant synergism between chitosan and vitamin C, the vitamin was released up to 48 h after oral delivery, and the fish innate immune system was stimulated (Alishahi et al. 2011). In another research, chitosan nanoparticles were employed as a hormone delivery system to boost fertility in *Cyprinus carpio*. Luteinizing hormone-releasing hormone was conjugated with chitosan nanoparticles in one group and compared to luteinizing hormone-releasing hormone conjugated with chitosan-gold nanoparticles in another group. The result shows that when compared to the group injected with hormone alone, the nanoparticle-treated groups exhibited an increase in blood hormone levels with sustained release of hormones (Rather et al. 2013).

Trace metals and polymeric nanoparticles as nanofeed formulations for aquatic organisms

The advancement in the field of nanotechnology has spread across many areas of scientific inventions, especially in the biomedical fields and agriculture/aquaculture. Nanoparticles, owing to their small sizes have been observed to possess large surface area and pore size which enables them to penetrate complex systems. Therefore, the feed of aquatic organisms formulated with nanotrace elements is 100% more beneficial to the organism than the conventional bulk inorganic trace elements, as the former could be delivered quickly in the body of the organism and reduce the level of pollution of the aquatic environment derived from the bulk feedstuff (Nasr-Eldahan et al. 2021). The incorporation of nanofeed formulation and nanodrug design for the aquatic organisms will undoubtedly improve the bioavailability and bioaccessibility of nutrients, improve their metabolism and allow the nutrient to be delivered to active sites as well as regulate the antibiotic resistance in the aquatic ecosystem (Shah and Mraz 2020). These micro- or nanonutrients provided by these formulations in the feed of aquatic-being can penetrate the cells more efficiently and intensify the number of nutrients and rate of absorption in their digestive tracts (Fajardo et al. 2022). Their small sizes and biodegradability can also accelerate the ease of the feed distribution in the various tissues/organs and facilitate easy excretion from the body to avert potential toxicity (Zhao et al. 2011). Trace elements such as Mn, Cu, Se, Zn, Fe, etc. have been explored for the practical formulation of diets for aquaculture animals to improve growth rate, reproduction efficiency, and disease prevention (Liang et al. 2015; Ma et al. 2015). Meanwhile, the supplementation of these trace compounds or with other feed enrichments tends to further stimulate increased antioxidant enzyme activity, and osmotic stress tolerance, salinity stress tolerance amongst others (Table 5) (Shao et al. 2012; Silva-Aciares et al. 2013; Sun et al. 2013). Typically, ginger (*Zingiber officinale*) as a dietary supplement with probiotic bacterium *Bacillus coagulans* have shown good growth performance, hematological parameters, and nonspecific immune parameters in *Catla* (Bhatnagar and Saluja 2021). The application of nanocomposite materials obtained from natural biopolymers, such as cellulose, chitosan, protein, and lipids, into aquatic feeds has expanded the alternatives of aquatic nanofeeds and improved the nutritional benefit and nourishment parameters for adequate growth and development (Martins et al. 2018). These derived materials incorporate a wide variety of additives, such as antioxidants, antifungal agents, antimicrobials, colors, and other nutrients (Dursun et al. 2010). Also, these polymer nanoparticles (PNPs) constitute a substantial amount of the crude fiber, crude protein, crude lipids, carbohydrates, etc. that is necessary for the aquatic feed formulation (Kumaran et al. 2020). For example, chitosan nanoparticles were shown to improve the survival rate, growth performance, and meat quality of tilapia (*Oreochromis nilotica*) after being fed at 5.0 g/kg of diet for a period of 60 days (Wang and Li 2011). In another investigation, the nanoparticles containing rhodamine B in zein or chitosan biopolymers were coated in the feed of freshwater amphipod *Hyalella azteca*. Although the feeding trials showed that both zein and chitosan nanoparticles significantly release rhodamine B into the water at a lower rate than food dyed with rhodamine B alone, the Zein nanoparticles also showed better retention ability than chitosan nanoparticles (Gott et al. 2014). Recent investigations have shown that various nanostructures such as nanohydrogels and nanofibers derived from natural biopolymers have been successfully used to encapsulate and improve the distribution efficiency of numerous bioactive compounds such as phenolics, essential oils, carotenoids, and vitamins in aquatic feeds (Jiménez-Fernández et al. 2014; Fernández-Díaz et al. 2017; Akbari-Alavijeh et al. 2020; Lima et al. 2021).

Nanotechnology in preventing and remediating antibiotic pollution and antimicrobial resistance in aquaculture and aquatic ecosystems

Nanotechnology is a vital tool for remediating antibiotic pollution and antibiotic resistance in the aquatic ecosystem and aquaculture. Several existing and novel nanosystems can potentially be adopted for managing antibiotics and antibiotic resistance (Nasr-Eldahan et al. 2021). Going forward, we shall expand on these nanosystems under two broad approaches. In this first approach, we shall discuss nanosystems available as prophylaxis for preventing the widespread of antibiotic resistance and antibiotic pollution in the aquatic environment and aquaculture. In the second approach, possible remediation nanosystems for management or treatment of already polluted environment with antibiotic and antibiotic resistance was extensively reviewed (Fig. 3).

Some prophylactic/preventive nanotechnological systems for managing the spread of antibiotic resistance

Some prophylaxis nanosystem exist that help prevents antibiotic pollution and the emergence of antibiotic resistance microbe in aquaculture and aquatic environment. Generally, this preventive approach adopts alternative nanosystems for managing the microbial load in the aquaculture and preventing the unscrupulous discharge of antibiotic-rich effluents from pharmaceutical manufacturing industries. Some of these systems include the use of nano-derived natural products as an alternative antimicrobial agent for aquaculture, the adoption of nanoprobiotics/prebiotics to boost the vitality and immune resistance of aquaculture, the application of nanoparticles as control release of antibiotics in aquaculture, and the use of nanosensors/detector for estimating the level of antibiotics pollution in pharmaceutical industries.

The use of the nano-derived natural products in aquaculture

Natural products are sustainable alternatives to synthetic antibiotic chemicals in preventing or treating pathogenic attacks in aquaculture. Antimicrobial natural products consist of metabolites, phytochemicals, essential oils, and bioactive peptides from vast plants, animals, and microorganisms. Nanoparticles can be synthesized from natural products and have been proven to have improved antimicrobial potency in combating pathogens and microbial colonization for many reasons. First, nanoparticles synergistically contribute to killing the microbes by other antimicrobial mechanisms. Secondly, nanoparticles improve the specificity and precise delivery of these natural products targeted against microbial infection. Finally, the nanoparticles and natural products duos ensure their long-lasting antimicrobial effects in aquaculture and aquatic environments, just as other synthetic antibiotics, without fostering antimicrobial or multidrug resistance. Specifically, nanoparticle ensures a programmable and controlled release of natural product to boost the vitality and productivity of aquaculture (Fajardo et al. 2022). Several physical and chemical methods such as microemulsion, thermal decomposition, polyol, electrochemical synthesis, microwave synthesis, chemical vapor deposition, gamma radiation, and others have been applied to synthesize nano-derived natural products. The

Table 5 Nanoparticles as aquatic nanofeed formulation or supplemented with other nutrient enrichment for different aquatic species

Nanoparticle	Function	Amount	Test duration	Aquatic species	References
TiO_2 NPs	Decrease in locomotive behavior	1 mg/L	14 days	Rainbow trout	(Boyle et al. 2013)
Cu NPs	Induced higher malonaldehyde concentration in tissues by overwhelming total superoxide dismutase activity, total glutathione concentration and Na^+/K^+-ATPase activity	20 or 100 µg Cu/L	25 days	*Epinephelus coioides*	(Wang et al. 2014)
Nanoselenium	Enhanced the antioxidant defense system and growth	2 mg	8 weeks	Card feed	(Ashouri et al. 2015)
Fe NPs + *Lactobacillus casei*	Improved growth parameters	50 µg/kg + 108 CFU/g	60 days	Rainbow trout	(Mohammadi and Tukmechi 2015)
Au NPs in in acetaminophen	Protect the liver against oxidative damage, tissue damaging enzyme activities, and acetaminophen-induced hepatic damage	2.5 mg/kg + 500 mg/kg	24 h	Carp fish (*Cyprinus carpio* L.)	(Kunjiappan et al. 2015)
Copper oxide (CuO) NPs	Increased activities of all of the antioxidant enzymes, and decreased the activity of carbonic anhydrase	100 µg/L	21 days	Sea anemone, *Exaiptasia pallida*	(Siddiqui et al. 2015)
Manganese-oxide NPs	Improvement in growth performance, digestive enzyme activities and muscle biochemical compositions	3.0–18 mg/kg	90 days	Prawn feed	(Asaikkutti et al. 2016)
Cu NPs	Regulating better survival, growth and immune response of the organism	20 mg/kg	90 days	*Macrobrachium rosenbergii* postlarvae	(Muralisankar et al. 2016)
Cu NPs and vitamin C	Improved growth and health performance	0/0–2/1200 mg/kg	60 days	Red sea bream	(El Basuini et al. 2017)
Zn, Se, and Mn nanometals	Improved stress resistance and bone mineralization	86 mg/kg, 1.9 m/kg, and 3.3 mg/kg, respectively	20 days	Dah seabream larvae	(Izquierdo et al. 2017)
Aloe vera NPs	Improved growth factors	1%	60 days	Siberian sturgeon (*Acipenser baerii*)	(Sharif Rohani et al. 2017)
Ginger NPs	Enhanced growth, fish cognition, immunity and prevention of motile *Aeromonas septicaemia* disease	0.5–1 g/kg	30 days	*Cyprinus carpio*	(Korni and Khalil 2017)
Chitosan and polycaprolactone NPs loaded with ascorbic acid	Lower toxicity in the development of the zebra fish, decreased activity of the enzyme acetylcholinesterase (AChE) but did not affect the swimming behavior	57.4 and 179.6 mg/L	90 days	Zebra fish larvae	(Luis et al. 2021)
Thymbra spicata (TS) plant extract loaded chitosan PNPs	Improves the performance of the plant extract in growth, blood parameters, immunity, and stress response	200–400 g/kg	8 weeks	Rainbow trout (*Oncorhynchus mykiss*)	(Ghanbary et al. 2022)

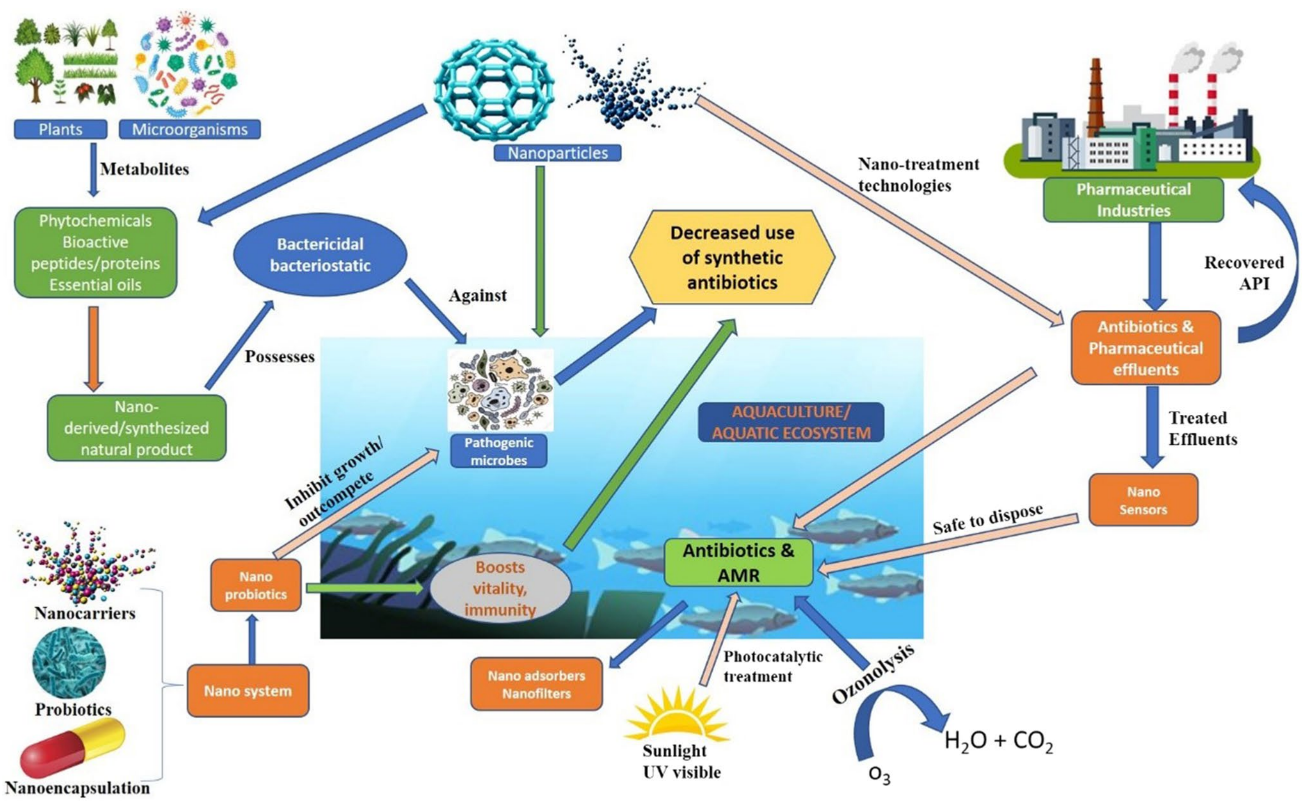

Fig. 3 Application of nanotechnology in combating antimicrobial and antibiotic resistance in aquaculture and aquatic ecosystems

final product of these syntheses is usually nano-sized of diverse shapes such as spherical, prismatic, hexagonal, globular, cuboid, as well as irregular shapes (Table 6).

In a recent study by Ghetas et al. (2022), a spherical green synthesized nanoparticle from the solvent extraction of *Origanum vulgare* leaves was reported with impressive antibacterial and antifungal effects against bacterial and fungi pathogens of Nile tilapia and sea bass. The antibacterial activities against *Streptococcus agalactiae*, *Aeromonas hydrophila*, and *Vibrio alginolyticus* were reported as a zone of inhibition between 23.7 and 31.3 mm observed on treatment with 10 μL nanoparticles/disk. Similarly, the fungi pathogens such as *Aspergillus flavus*, *Fusarium moniliforme*, and *Candida albicans* showed a zone of inhibition of 11–18 mm, on treatment with the same concentration (10 μL/disk) (Ghetas et al. 2022). Another study showed that gold nanoparticles synthesized from fucoidan polysaccharide of *Fucus vesiculosus* had significantly more excellent antibacterial and antibiofilm activities against *Aeromonas hydrophila* (ZI 23.2 mm) than chloramphenicol (ZI 17.3 mm) (Vijayakumar et al. 2017). Other studies summarized in Table 6 are convincing evidence of the potential of nano-derived natural products as an alternative for antibiotic usage in aquaculture, hence minimizing the advent of antibiotic resistance.

The use of nanoprobiotics to boost the vitality and immune resistance of aquaculture

Nanoprebiotics are an emerging nanosystem application for formulating and efficiently delivering probiotics to living organisms. For several decades, when administered in sufficient amounts, probiotics have been applied to boost several host organisms' health and vitality. Generally, these probiotics are administered orally, through diet formulations, to populate the gut and outcompete pathogenic species (Hill et al. 2014; Varankovich et al. 2015). Probiotics can be used to confer protection against pathogenic microbes through various mechanisms; hence, they are a better alternative than the use of antibiotics and a more sustainable approach to preventing the emergence of antibiotic resistance (Watts et al. 2017).

Probiotics have recently gained attention in aquaculture and aquatic ecosystems because they improve overall productivity and resistance to pathogens via several multidimensional mechanisms (Fig. 4). Hasan and Banerjee (2020) reported, among others, that probiotics improve body weight, digestion rate, fecundity, antioxidant enzymes, and stress tolerance of aquacultures. At the same time, it downregulates pathogenic bacteria, viral infection, cortisol levels, and enteric colonization. The beneficial functions

Table 6 Studies on the use of nano-derived natural product (green synthesis) in aquaculture

Aquaculture	Nanoparticles	Natural products	Shape and size	Aquaculture pathogen	Bioactivities	References
Salmonid fish and cod	Chitosan Ag nanocomposites	Chitosan	Spherical (281 nm)	Cold water vibriosis caused by bacteria *Aliivibrio salmonicida*	Bacteriostatic and bactericidal with MIC and MBC of 50 μg/mL and 100 μg/mL, respectively	(Dananjaya et al. 2016)
Tilapia (*Oreochromis mossambicus)*	Au-NPs	Polysaccharide fucoidan from *Fucus vesiculosus*	Spherical and triangular (10–100 nm)	*A. hydrophila*	Antibacteria and anti-biofilm with a ZI of 23.2 mm at 100 μg/mL, greater than chloramphenicol (ZI 17.3 mm)	(Vijayakumar et al. 2017)
Cirrhinus mrigala fingerlings	Ag-NPs	*Azadirachta indica* (Neem)	Spherical (35.4 nm)	*Aeromonas hydrophila*	Antibacterial (with a 74% survival rate of treated fingerlings) and immune-modulatory	(Rather et al. 2017)
Goldfish, *Carassius auratus*	Ag-NPs	Aqueous extract of garlic, *Allium sativum*	Spherical	*Bacillus licheniformis* and *Pseudomonas aeruginosa*	Antibacteria	(Saha and Bandyopadhyay 2019)
Nile tilapia, *Oreochromis niloticus*	Chitosan nanoparticles (CNP)	Chitosan	Pentagon and hexagon (35 nm)	Bacteria [*Aeromonas hydrophila*, *Aeromonas sobria*, and *Aeromonas sobria* (at 0.156 to 2.5 μg/mL dosage)] Fungi [*Aspergillus flavus*, *Mucor* sp., and *Candida* sp. (ZI 35 mm at 20 μg/mL dosage)]	- Bacterial cell wall destruction - Antifungal	(Abdel-Razek 2019)
Labeo rohita fingerlings	Zinc oxide NPs	*Spinacia oleracea* (Spinach)	Spherical (22.61 nm)	*Saprolegnia* sp.	Feed additives for growth and improved biochemical and hematological parameters	(Thangapandiyan and Monika 2020)
Fish (not specific)	Zein nanoparticles	*Zein proteins, Eugenol*, and *garlic essential oils*	Spherical (150 nm)	*Aeromonas hydrophila*, *Edwardsiella tarda*, and *Streptococcus iniaein*	Antibacteria	(Luis et al. 2020)
Fish (not specific)	Ag-NPs	Red algae *Portieria hornemannii* extract	Spherical (70–75 nm)	*Vibrio harveyi*, *Vibrio parahaemolyticus*, *Vibrio vulnificus*, and *Vibrio anguillarum*	Antibacterial with ZI of 16–28 mm	(Fatima et al. 2020)
Longfin yellowtail	AuNPs	Aqueous extracts of *Turnera diffusa* (oplopanone, γ-eudesmol, hydroquinone-β-d-glucoside (arbutin), and inositol)	Spherical (24 nm)	*Vibrio parahaemolyticus and Aeromonas hydrophila*	Antimicrobial Antioxidant Immunomodulation	(Reyes-Becerril et al. 2021)

Table 6 (continued)

Aquaculture	Nanoparticles	Natural products	Shape and size	Aquaculture pathogen	Bioactivities	References
Fish (not specific)	Cu(II) nanoflowers	Juice and peel of blood orange	Spherical	*Yersinia ruckeri* (causative for enteric red mouth disease in fish)	Antibacterial with a ZI of 30.66–33.66 mm at 0.5 µg/mL	(Demirbas 2021)
Fish (not specific)	Ag-NPs	Gum arabic	Spherical (10 nm)	*Aeromonas hydrophila and Pseudomonas aeruginosa* with a ZI of 22 and 20 mm and an MIC of 1.625 µg/mL and 3.25 µg/mL, respectively	Antibacteria and antibiofilm	(El-Adawy et al. 2021)
Tilapia (*Oreochromis mossambicus*)	Ag-NPs	Polysaccharides of *Caulerpa racemosa*	Spherical (88 nm)	*Pseudomonas aeruginosa*	Antibacteria Antioxidant	(Thanigaivel et al. 2022)
Nile tilapia and Sea bass	Ag-NPs	*Origanum vulgare* leaves extract	Irregular (100 nm)	Bacteria (*Streptococcus agalactiae*, *Aeromonas hydrophila*, and *Vibrio alginolyticus*) Fungi [*Aspergillus flavus*, *Fusarium moniliforme*, and *Candida albicans*]	- Antibacterial with a ZI 23.7–31.3 mm at 10 µL/disk of the green AgNPs - Antifungal (ZI 11–18 mm at 10 µL/disk)	(Ghetas et al. 2022)

of probiotics are associated with their ability to produce enzymes, antibiotics, hydrogen peroxide, bacteriocins (proteinaceous toxins), and siderophores (Watts et al. 2017; Uma & Rebecca 2018). Some basic mechanisms of probiotics are potent antimicrobial agents for aquaculture. These basic mechanisms are the competitive exclusion of harmful bacteria, the creation of adverse habitats of pathogenic bacteria, the stimulation of host immunity against pathogens, and antiviral activities. In addition to their antimicrobial activities, probiotics enhance water quality by fostering the degradation of aquaculture and aquatic ecosystems' organic and inorganic contaminants.

In recent years, nanosystems such as nanoencapsulation, nanoparticles, nanobeads, nanofibers, nanoemulsion, and nanolayers have been adopted to deliver probiotics in humans and various animals. However, this approach is still novel for aquaculture as there are only sparsely available studies (Fajardo et al. 2022). The adoption of nano-derived probiotics is a prophylaxis measure against the excessive use of antibiotics and the rise of antibiotic resistance in aquaculture. The nano-derived probiotics have improved the functionality, bioavailability, viability, and stability of the beneficial microbes in the host systems. Moreover, nanoparticles associated with probiotics possibly improve their anti-oxidative properties for better management of cellular damages due to the diseased state. Despite this number of benefits from nanoformulation of probiotics, there may be a noticeable increase in toxicity if the concentration of the formulations is not optimized.

There have been several recent studies on applying probiotics in aquaculture and aquatic ecosystems; however, studies on their nanoformulations are limited. Sam-on and colleagues isolated three bacteria, *Bacillus subtilis*, *Bacillus velezensis*, and *Bacillus pumilus*, from the gut of giant freshwater prawn. Following the in vitro testing of these bacteria as probiotics, it was observed that *Bacillus velezensis* expressed higher antimicrobial activity against *Aeromonas hydrophila* (23.7 mm) and *Aeromonas veronii* (25 mm). The high resistance of *Bacillus* spp. to 0.3% bile salt and the activities of protease, amylase, and lipase as exhibited by them further certifies their functionality as probiotics of great importance in aquatic environments (Sam-on et al. 2022). Another study examined different *Bacillus* strains from mangrove environments as probiotics used in dietary of (Rohu) *Labeo rohita*. Different concentrations of *Bacillus* spp.; *B. amyloliquefaciens* of 10^6 cfu/g and 10^9 cfu/ g; *B. subtilis* of 10^6 cfu/g and 10^9 cfu/g; *B. megaterium* of 10^6 cfu/g and 10^9 cfu/g; all three bacteria in the same proportion of 10^6 cfu/g and 10^9 cfu/g; and control without probiotics were experimented with Rohu fingerlings with an average weight of 5.02 ± 0.85 g for 45 days, after which they subjected to *Aeromonas hydrophila*, and survival rate was observed for 10 days. The combination of the three bacteria (10^6 cfu/g)

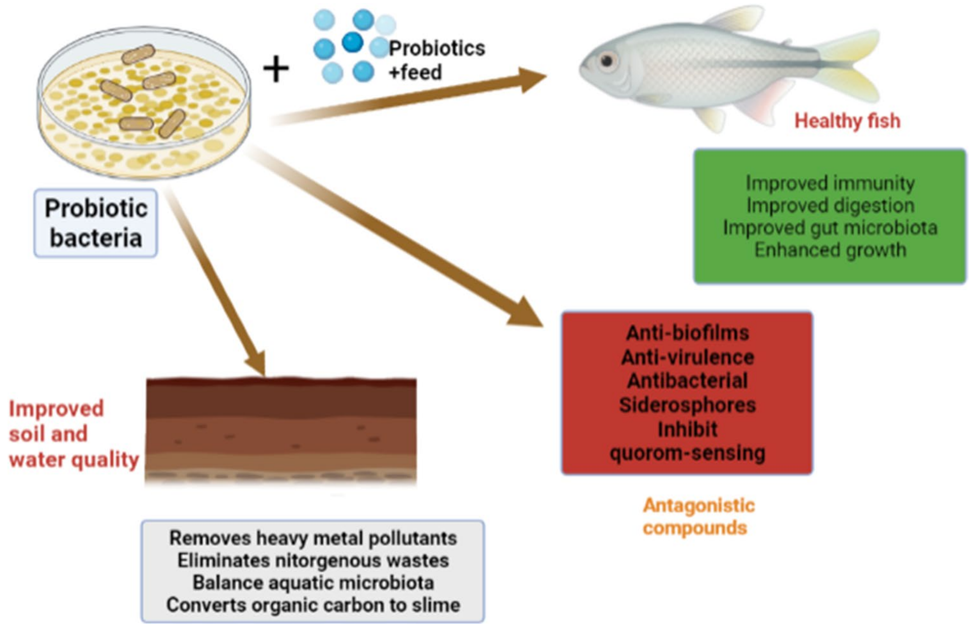

Fig. 4 Beneficial action of probiotics to aquatic animals/ecosystems

significantly improved red blood cells, hemoglobin, serum superoxide dismutase activity, white blood cells, survival, protease, and intestinal α-amylase activities. Field trials using these bacteria combined further showed their potential as a trusted dietary probiotic with various benefits (Saravanan et al. 2021). Conversely, a few nano-derived probiotic studies showed these formulations' antioxidant and antimicrobial potentials, which can be applied to aquaculture with desirable outcomes (Table 7). There is a need for more specific studies on applying nano-derived probiotics in aquaculture and aquatic ecosystems, particularly in overcoming the uprise of antibiotic pollution and resistance.

Nanosensors/detectors for estimating the level of antibiotic pollution

Detection of antibiotics and antimicrobial resistance microbes is an initial step to prevent or manage their widespread in aquaculture or aquatic ecosystems. Nanotechnology has been valuable in developing very sensitive biosensors for detecting antibiotics and antibiotic resistance in recent years. Zeng et al. (2022) reported nanobiosensors as parts of the advanced approach for antibiotic detection. Various nanoparticles have shown good precision when adapted to various colorimetric, fluorimetric, and electrochemical biosensors.

Colorimetric biosensors are nanosensitive detectors that show visible color changes on detection and color gradients based on the concentration of antibiotics in aquaculture or aquatic ecosystem. Due to the strong affinity of tetracycline (TCs) to Fe(II) and Fe(III), Fe_3O_4 magnetic nanoparticles (MNPs) have been applied in the fabrication of TCs colorimetric biosensors. If TCs is present in a solution, a TC-Fe_3O_4 complex is formed, which fosters the oxidation of 3,3′,5,5′-tetramethylbenzidine (TMB) by H_2O_2 to produce a dark visible solution. UV spectroscopy can quantify TCs and their derivatives in the medium, with a limit of detection (LOD) between 12 and 48 nM. A recent and similar study used carbon quantum dots as the probes for fluorescence detection of TCs-Fe_3O_4 complex rather than the TMB in the colorimetric detection system. Moreover, the LOD was therefore improved to 9.5 nM. Other antibiotics biosensors have been developed in recent times. Examples are streptomycin colorimetric sensors (LOD 86 nM), ampicillin fluorescence sensors developed from gold nanoparticles, ampicillin, and oxytetracycline fluorescence detection on nanographene oxide hydrogel. Finally, nanoparticles also find applications as electrodes in electrochemical biosensors for detecting antibiotics in aquacultures.

Nanosystems for some remediation of antibiotics pollution and antimicrobial resistance in aquaculture and aquatic ecosystem

This section presents an overview of some recent nanosystem for managing the widespread antibiotic pollution in aquaculture/aquatic environments. This remediative nanosystem includes nanofiltration, nanoadsorbent, advanced nanooxidation process, magnetic nanoparticles, nanocatalyst/nanodegrader, and engineering microbial biofilms.

Table 7 Potential application of nano-derived probiotics in aquaculture

Probiotics	Sources	Nanoparticles	Shape	Size	Potential application in aquaculture	Ref
Lactobacillus delbrueckii	Probiotic curd	Ag-NPs	Spherical	54.3–112.7 nm	Antimicrobial	(Saravanan et al. 2011)
Lactobacillus sporogens	N/a	ZnO NPs	Hexagonal	145.70	Antimicrobial	(Mishra et al. 2013)
Lactobacillus kimchicus DCY51T	Korean kimchi	AuNPs	Spherical	5–30 nm	Antioxidant	(Markus et al. 2016)
Lactobacillus casei ATCC 393	N/A	Selenium NPs	Spherical	50–80 nm	Antimicrobial, increase intestinal cell proliferation, and antioxidant	(Xu et al. 2018a, b)
Lactobacillus casei subsp. *casei*	N/A	CuO NPs	Spherical	30 -75 nm	Antimicrobial	(Kouhkan et al. 2019)

Nanofiltration

Nanofilter is very valuable in removing antibiotics from aquaculture and the aquatic environment. Nanofiltration technologies apply a moderate pressure-driven membrane separation process to separate different organics and pharmaceuticals from water. Its general principles and operational standing occupy the midpoint between ultrafiltration and reverse osmosis. While reverse osmosis rejects or prevents the passage of most organic and salts, ultrafiltration membranes freely allow their passage. On the other hand, nanofiltration captures or restricts the passage of organics that could usually go through an ultrafilter, except for deficient molecular weight compounds. Hence, nanofilters are also called "loose reverse osmosis membranes" or "tight ultrafiltration membranes". This use of nanofillers to remove antibiotics in aquaculture is more economical than reverse osmosis membrane because a lower operating pressure is needed to drive water permeability. It was reported that most commercially available nanofiltration membranes have a nominal molecular weight cutoff (MWCO) range between 100 and 1000 Da, and most antibiotics have their molecular weights within this range. The MWCO is a range of molecular weights of organics at which the nanofilter optimally operates. In many recent studies, the use of nanofiller achieved more than 90% removal of antibiotics from aquaculture or wastewater or even in several aquatic environments.

Moreover, incorporating nanoparticles in the nanofiller membrane overcomes the significant biofouling limitations, makes familiar with convectional nanofilters, and fosters the improved flux movement for an enhanced separation. Nanoparticle incorporation ensures that the membrane filter is easily adaptable to several properties in the nanofilter membrane. Standard nanoparticles used in membrane filters are metal oxides (TiO_2), carbon nanotubules (CNT), and zeolites. A study by Liu et al. (2017) reported the potential of a hybrid carbon membrane with a tiny pore (between 3 and 10 nm) for effectively removing tetracycline antibiotics from water. The nanomaterial composition of the hybrid membrane was thick graphene oxide and activated carbon (15 µm thickness), and about 99% of tetracycline was separate via vacuum filtration. Moreover, the hybridized nanomembrane showed better adsorption efficiency than the nanofilter membrane from single nanomaterials such as graphene oxide, activated carbon, and CNTs. Carbon nanotube singled walled membrane was successfully applied to remove antibiotics—tetracycline, sulfamethoxazole, and trimethoprim—from water through adsorption, filtration, and protraction process. The CNTs were fabricated with hydrophobic and hydrophilic layers on a single wall, and the pore sizes were modulated by adding a SiO_2 (743 to 1218 mm^3/g). It was reported that the modified CNTs eliminated the 98.8% sulfamethozole, 95.5% trimethoprim, and 87.0% tetracycline within 2.3 s of filtration and 5 h of adsorption.

Nanoadsorbents

The nanoadsorption separation techniques have recently gained more attention because of their lower cost, easy operation, and availability of nanoadsorbent. Several nanomaterials of different sorts have been adapted to function as nanoadsorbent for antibiotics and pharmaceuticals in aquaculture and aquatic ecosystems. The large surface area of nanoparticles confers more advantages as adsorbents than other convectional and bulky particles (natural clay, zeolites, and other polymeric substance), which is also less selective and has a smaller surface area. Nanoadsorbents can also be organic or inorganic, with excellent catalytic potential, reactivity, specificity, and adaptability. Examples of nanosorbents include nanoactivated carbon, graphene and graphene oxides, biochar, carbon nanotubes, nanozeolites, molybdenum disulfide nanosheets, boron nitride, silica, and others. Antibiotics from aquaculture and the aquatic ecosystem get trapped in the pore space and surfaces of the adsorbents due to several intermolecular and atomistic interactions. Common interactions reported in numerous studies are π-π interaction, electrostatic and hydrophobic interaction, and hydrogen bonding. Other studies have reported the occurrence of surface complexation and covalent interaction, especially for carbon-based nanoparticles. The surfaces of nanomaterials are adaptable with functional groups or high-affinity compounds to enhance the effectiveness of the adsorption process. In a new study by Wahab et al. (2019), a novel composite nanoadsorbent system was designed to remove ofloxacin antibiotics from industrial liquid waste. The nanoadsorbents composed of magnetic carbon-nanocomposite prepared from waste biomass (Dalbergia sissoo sawdust) showed a retention/adsorption efficiency of ofloxacin between 57.8 and 99.57%. Similarly, Vu et al. (2020) reported an 88% efficiency in removing tetracycline from wastewater with a nanocomposite fabricated from polyanion-modified laterite. In the study, the adsorption system was optimum at a pH of 4.0, contact time of 180 min, and a solid–liquid ratio of 5 mg/mL.

Nanocatalytic oxidation processes

Antibiotic contamination of aquaculture and aquatic ecosystem, as well as other organic, can be eliminated by oxidative degradation to more minor toxic metabolites, usually CO_2 and water. Catalytic ozonation and photocatalytic degradations are the primary alternative route for the nanocatalytic oxidation process (Chen et al. 2021). Nanomaterials are the preferable catalyst in these processes because of their large surface area, easy modification, more reactive surfaces, and enhanced mass transfer, which cumulatively improves the overall reaction kinetics (Chankhanittha et al. 2021). Nanometal oxides, CNTs, and graphene oxides have been very popular in recent studies on the catalytic ozonation or photocatalytic degradation of pharmaceuticals and antibiotics (Sukidpaneenid et al. 2023). Advance studies have shown enhanced remediation effects arising from the synergistic coupling of photocatalysis and ozonation on nanosurfaces to eliminate pharmaceuticals from aquacultures (Table 8).

The application of nanoparticles in aquaculture and aquatic organisms

The application of nanotechnology has studded recent biotechnological advancements in aquaculture, providing more efficient disinfection technologies than traditional chemical substances (Hjorth et al. 2017). The utilization of nanotechnology for drug delivery, nutrient transport, and remediation of resistant antibiotics amongst others provides very promising prospects in aquatic ecosystem sustainability. Nanoenabled techniques have also been applied to the removal of organic pollutants and other contaminants in the aquatic ecosystem (Dar et al. 2019). TiO_2 and TiO_2–SiO_2 nanocomposites were found to exhibit great potential for aquaculture purification after significantly absorbing up to 94.3 mg/g of fluoride from an aqueous solution (Zeng et al. 2017). AgNPs synthesized from the cell filtrate of *Streptomyces* sp. reportedly decontaminate 1log10 CFU hazardous *Bacillus* endospores within around 20 min (Gopinath et al. 2015). In another study, AgNPs were immobilized on silica beads in a water filter column against *Vibrio* sp. It was discovered that the filtered seawater used for rearing the post-larval stage of *P. vannamei* not only enhanced their survival rate but also improved their growth performance (Sarkheil et al. 2016). Hesni et al. (2020) investigated the simultaneous use of iron oxide nanoparticles and microalgae in the purification of aquaculture effluents in a constructed bioreactor, significant percentage reduction of nitrite, nitrates, ammonium, and phosphates at 89.3, 92.23, 93.67, and 89.25%, respectively, was achieved in comparison to other parameters at the end of the study period. Purification and treatment of aquaculture is considered a major factor in its sustainability, and the emergence of nanotechnology provides promising potentials with novel nanotools for its actualization.

Disease outbreak is one of the main problems in aquaculture systems (Fajardo et al. 2022), and vaccination has become an effective means to boast immunity against infections. Three main routes of aquaculture drugs delivery have been stipulated. The first is through bath or immersion, which although is the more applicable method, requires large drug amounts and often leads to unavoidable fish stress. The second and easiest method is the in-feed formulation administered orally through normal feeding at no extra cost or stress; and the third is by injection, which seems unachievable for fishes (Rather et al. 2021). In the aquaculture industry, DNA strands within nanocapsules have been used to stimulate the immune response in fishes (Fajardo et al. 2022). Poly-lactide-coglycolide acid and chitosan have been developed and used extensively as carriers for oral DNA vaccines against viral and bacterial diseases in shrimps. Their water-solubility, biodegradability, and nontoxic properties make them highly effective in these applications (Chalamcherla 2015). The emergence of different encapsulation techniques has resulted in the use of alginate particles as preliminary candidates for the oral delivery of vaccines to aquatic animals (Shah and Mraz 2020). Several studies have reported the successful use of nanoencapsulated vaccines against bacterial and viral

Table 8 Some selected studies on nanophotocatalytic degradation of antibiotics in aquatic ecosystem or waste water

Photocatalyst	Irradiation source(s) and time	Target PhACs	Degradation rate (%)	Refs
Graphitic carbon nitride/mesoporous nanosilica ($g\text{-}C_3N_4$/KCC-1)	UV radiation (120 min) pH 7.0; dosage 0.6 g/L	Penicillin G (PG)	93.98%	(Esmati et al. 2021)
$CoP/ZnSnO_3$	Visible light (60 min) Dosage: 2%	Tetracycline (TC)	96.44%	(Chen et al. 2021)
$g\text{-}C_3N_4/Bi_4NbO_8Cl$ nanocomposite	Visible light (60 min) Dosage: 20%	Oxytetracycline (OTC)	87.0%	(Majumdar et al. 2021)
Recyclable magnetic titania (MT) photocatalyst	Visible light (63 min) Dosage = 195 mg/L	Gentamicin (GMC)	94.7%	(Shirazinejad et al. 2021)
Nano-α-Fe_2O_3-MOF	UV/H_2O_2 Dosage-catalyst = 150 mg/L and H_2O_2 = 5 ppm	Cefazolin (CFZ)	85.88%	(Blourfrosh and Mahanpoor 2021)
Ag-ZnO	UV light (sunlight 5%) (80 min)	Ofloxacin	100%	(Chankhanittha et al. 2021)
Ti_3C_2 MXene-TiO2	UVA irradiation (5 h)	Enrofloxacin (ENR)	62.8–93.4%	(Sukidpaneenid et al. 2023)
ZnO/CdS-SDS nanocomposite	Visible light	Ofloxacin	73%	(Senasu et al. 2021)
CdS/Bi_2MoO_6/BiOBr	Visible light	Tetracycline hydrochloride (TC)	94.41%	(Wang et al. 2021b)
Ce^{3+}/TiO_2	UV-A radiations (2 h) pH 6.0	Amoxicillin (AMX) and tetracycline (TC)	AMX 67% TC 61%	(Lalliansanga et al. 2022)
Zn-MOC–[Zn(meso-{5,10,15,20-tetrakis(4-cyanophenyl) porphyrin}) (H_2O)]0.3DMF	Visible light (50 min) Dosage 1.0 g/L pH 7.3 Initial TC conc 5.0 mg/L	Tetracycline (TC)	95.5%	(Jafarizadeh et al. 2021)
TiO_2-Rgo	Sunlight, 180 min	Sulfamethoxazole (SMX), Erythromycin (ERY) Clarithromycin (CLA) AMR *E. coli* Resistance gene (*ampC* and *ecfX*)	SMX, 87 ± 4% ERY, 84 ± 2% CLA, 86 ± 5% AMR *E. coli*—Inactivation *ampC* 100% *ecfX* reduction	(Karaolia et al. 2018)
Hap-ZnO	UV irradiation, 20 min and 60 min	Ciprofloxacin (CIP) Ofloxacin (OFL)	CIP (20 min), ≈ 99% OFL (60 min), ≈ 99%	(Bekkali et al. 2018)
Ce-doped $Lu_3Al_5O_{12}$/ZnO	UV–Visible, 90 min Visible, 300 min	Sulfathiazole	100%	(Zammouri et al. 2018)
CuO	UV-C lamps (8, 15, and 30 W), 60 min	Ciprofloxacin (CIP)	CIP(8 W), 82.23 ± 1.23% CIP (15 W), 92.96 ± 1.47% CIP (30 W), 96.58 ± 1.04%	(Khoshnamvand et al. 2018)
Iodine, potassium co-doped-C_3N_4	Visible light irradiation, 45 min	Sulfamethoxazole (SMX)	99%	(Paragas et al. 2018)

diseases in fishes (Bhattacharyya et al. 2015; Ogunkalu 2019).

Several kinds of literature have reported the application of nanotechnology in the delivery of dietary supplements in aquaculture. Abd El-Naby et al. (2020) evaluated the effect of chitosan nanoparticle (ChNP) and/or thymol (THY) supplementation on growth, whole-body composition, and other parameters on Nile tilapia (*Oreochromis niloticus*). It was observed that even though the co-addition had the best performance, the individual application of THY or ChNP to the fish diet significantly improved growth performance indicators, feed utilization, erythrogram profile, oxidative stress parameters, lipase enzyme activity, and lipid sedimentation. Another study conducted on Siberian sturgeon (*Acipenser baerii*) using *Aloe vera* NPs at three different levels (0.5, 1, and 1.5%) of fish diet, reported a significant improvement in the fish growth in the diet supplemented with 1% *Aloe vera* NPs (Rohani and Moghaddam 2017). Naiel et al. (2020) highlighted the antioxidative and immunity roles of diets supplemented with ChNP and vitamin C on *Oreochromis niloticus* against sublethal imidacloprid (IMID) toxicity. The mixture of vitamin C with chitosan nanoparticles alleviated the toxicological stress caused by exposure to the pesticide and also improved the fish growth. The antioxidant defense system and growth of common carp (*Cyprinus carpio*) were significantly improved after its feed was supplemented with selenium nanoparticles (Ashouri et al. 2015). Similarly, a fish diet supplemented with a probiotic (*Lactobacillus caseias*) and iron NPs significantly enhanced the growth parameters in rainbow trout (*Oncorhynchus mykiss*) (Mohammadi and Tukmechi 2015). A strong relationship between the emergence of antibiotic-resistant bacteria and excessive antibiotic administration has been observed (Shaalan et al. 2016), necessitating the application of nanotechnology to the remediation of antibiotic resistance in aquaculture. A survey conducted on the usage of antimicrobials in fish farms in 25 countries, revealed tetracycline to be the most used antibiotic agent in fish farms (Tuševljak et al. 2013). Metal-based nanoparticles having both antibacterial and antifungal activities have been successfully applied to combat the fish pathogens in aquaculture. Lima et al. (2013) found that gold nanoparticles (Au-NPs) supported on zeolite demonstrated bactericidal effects against *Escherichia coli* and *Salmonella typhi*. Ahmad et al. (2013) and Wani and Ahmad (2013) also reported the antifungicidal activity of Au-NPs against *Candida* species, noting that their high efficacy was size-dependent.

Ag-NPs have been documented as the most investigated nanoantibacterial agent in the research literature (Shaalan et al. 2016). Ag-NPs have demonstrated high antibacterial efficacy against multi-drug resistant bacterial isolates (Prakash et al. 2013). Several reports on the use of Ag-NPs against fungi species such as dermatophytes and *Candida* species have been documented (Kim et al. 2009; Sanjenbam et al. 2014; Mallmann et al. 2015), even comparing its efficacy to other commercial antifungal agents. Other metal-based nanoparticles such as zinc oxide (ZnO), copper oxide (CuO), silver-doped titanium dioxide ($Ag–TiO_2$), and titanium dioxide nanoparticles (TiO_2-NPs) have also drawn much attention due to their antibacterial and antifungal effects. For instance, Zn and ZnO reportedly showed antifungal activity against fungi Penicillium and other Mucor species, while CuO, ZnO, and silver-doped titanium dioxide ($Ag–TiO_2$) showed broad-spectrum antibacterial activity (Swain et al. 2014). On the other hand, combined TiO_2-NPs and magnetic Fe_3O_4-NPs activated by visible light were used to decontaminate water by binding the fish pathogens to the nanoparticles, and further extracted from water using a magnet (Cheng et al. 2009, 2011). These metal nanoparticles have shown high antimicrobial activity against bacteria, fungi and viruses in fish medicine**.**

Pathogen detection in fish

There has been recent progress in the application of NPs in pathogen diagnosis in aquaculture, particularly in fishes and it has been proven to be a sensitive and rapid approach. For example, gold nanoparticles are one of the most extensively utilized nanoparticles in pathogen diagnosis, and they can be used in a variety of ways (Saleh et al. 2015). Nanobiosensor devices are now being developed to detect extremely low levels of parasites, viruses, and bacteria concentrations, as well as contaminating substances in the aquatic ecosystem (Chen et al. 2015). This is highly relevant in outbreaks affecting commercial aquaculture systems because it can take too long for the causative agents to produce an impact and be detected, delaying pathogen control treatments and causing significant economic losses. In this aspect, nanotechnology can solve this problem by detecting and eradicating pathogens early. The use of gold nanoparticles also showed significant positive results in the detection of pathogens in fish using *A. salmonicida* antibody-gold nanoparticles conjugated for the specific immunodiagnosis of furunculosis tissues of fish (Saleh et al. 2011). An electrochemical DNA biosensor based on the coupling with Au-NPs with a DNA reporter probe for the detection of *Aphanomyces invadans* in fish (Kuan et al. 2013), compared to PCR, this assay could identify fungi at a lower level.

There was a successful detection of a single viral particle using an electric biosensor (Patolsky et al. 2004). A recent report shows that immunoglobulin G-capped gold nanoparticles were developed to specifically bind to antibodies generated against *S. aureus*, *S. pyrogenes*, etc. (Roy, et al. 2012). There are recent reports on the application of nanosensors in the clearing of fishponds and stock inspection especially those based on carbon nanotubes due to their high sensitivity for detecting traces of viruses, bacteria, parasites, as well as other heavy metals in both water and food. Nanosensors are also used for fishpond cleaning and stock scrutinies, such as those based on carbon nanotubes, which are highly sensitive for the detection of traces of pathogens like viruses, parasites, and bacteria, and also, heavy metals, both from food and water (Dar et al. 2019). Through the application of big data analysis technology, tracking nanosensors with trackers that convey information concerning the location and health status of fish have been reported, allowing the control of individual fish or the development of intelligent cage systems (Singh Sekhon 2014; Dar et al. 2019). A chip that had incorporated a nanoscale radio circuit linked to an embedded identification code, called nanobarcode, has been reported as an individual tracking device, in such a way that the information held in the tags can be scanned from the distance to identify them automatically. Such tags could be used as a tracking device, monitoring swimming patterns, feeding behavior, and the metabolism of animals (Singh Sekhon 2014). Processing industries and exporters benefit from the use of nanobarcoding since it allows them to track the source of a product as well as the delivery status. These nanosensors, when combined with synthetic DNA labeled with color-coded probes, could be utilized to identify viruses, monitor leakages, change in temperature, and other parameters, thereby improving the quality of the product (Rather et al. 2011).

A rapid, specific, and highly sensitive method that combines an AuNPs colorimetric assay with loop-mediated isothermal amplification (LAMP) to visually detect the yellow head virus in shrimp (Jaroenram et al. 2012). Another specific and sensitive nanocombination of DNA-functionalized AuNPs with loop-mediated isothermal amplification which is suitable for field application was recently developed for white spot syndrome virus detection in shrimp (Seetang-Nun et al. 2013). A cost-effective method capable of detecting nervous necrosis virus (NNV) using Au-nanoparticle-based biosensor for detecting the nucleic acids of the virus after amplification with qRT-PCR (Toubanaki et al. 2015). A magnetic nanoparticle coated with rabbit anti-NNV antibody to develop an immunomagnetic reduction test for nervous necrosis virus in grouper fish. Immunodiagnosis was based on the movement of magnetic NPs when an external magnetic field was applied: if the antibody-coated nanoparticles adhered to the viral antigen, they formed clusters that reduced their motility (Yang et al. 2012). A magnetic immunoassay analyzer was used to calculate the viral titer.

Nano-based fish vaccines

The use of nanoparticles in vaccine formulations is a promising medical research area. Polymeric nanoparticles have received the greatest attention because they have various advantages as vaccine delivery vehicles, including the capacity to maintain the stability of antigen against enzyme degradation, preserve immunogenicity, and provide long-term vaccine release (Myhr and Myskja 2011; Zhao et al. 2014). Nanovaccines have been utilized as immunostimulant adjuvants or as a delivery mechanism for targeted antigen delivery, both with gradual antigen release (Zhao et al. 2014). Fish vaccines have been developed using chitosan nanoparticles, such as the inactivated virus vaccine against infectious salmon anemia virus (ISAV), which includes the DNA coding for ISAV replicase as an adjuvant. This vaccination exhibited protection rates > 77% against ISAV (Rivas-Aravena et al. 2015). Chitosan and chitosan/tripolyphosphate NP was used to develop an oral DNA vaccine against *Vibrio anguillarum* in an Asian *Lates calcarifer* (Vimal et al. 2012). Although the pathogen was only moderately protected by the nanovaccine.

The outer membrane protein K (ompK) gene of *Vibrio parahemolyticus* was loaded onto chitosan-NPs to develop an oral DNA vaccine. In black seabream (*Acanthopagrus schlegelii*), a protective immune response was elicited by the recombinant nanovaccine against *Vibrio parahemolyticus* (Li et al. 2013). The ability of recombinant DNA-chitosan-NPs to protect shrimps from the white spot syndrome virus (WSSV) was studied. The vaccine was proven to boost shrimp immunity and provide a protective response against WSSV when given orally (Singh Sekhon 2014). PLGA nanoparticles have been shown to be effective as a DNA vaccination carrier and adjuvant (Hølvold et al. 2014). The application of PLGA nanoparticles in fisheries has been limited thus far. The Japanese flounder (*Paralichthys olivaceus*) was given an oral DNA vaccine against the lymphocystis disease virus (LCDV) (Tian and Yu 2011). In a separate investigation, rainbow trout were immunized with an orally delivered DNA vaccine against the infectious hematopoietic necrosis virus, and immune response was found (Adomako et al. 2012). Other nanoparticle employed as a delivery system for vaccines includes; immunostimulant complex, liposomes, virus-like particles, polymeric nanoparticles, and metal nanoparticles (Gregory et al. 2013; Zhao et al. 2014). Technical problems in creating nanovaccines with stable qualities, their possible toxicity, and a lack of understanding regarding their distribution within biosystems have all been raised as concerns about nanovaccines (Gregory et al. 2013). PLGA and polymeric chitosan and nanoparticles have been the most studied nanoparticles in fish vaccination research so far.

Seafood processing

To prolong the shelf-life of seafood products has become necessary and such nanotechnology can be applied in the marketing of seafood as well as in aquaculture species production. The application of nanomaterials in the food packaging sector has significantly enhanced research efforts because they can offer additional benefits such as reduced enzyme activity, and product degradation, oxygen depletion, reduced antimicrobial and antifungal activities, improved stability of product, and toxin detection (Adomako et al. 2012; Kuswandi 2016; Luis et al. 2019; Kumar et al. 2020). A broad range of nanostructures including nanostructures, nanofibers, and nanoemulsions have recorded tremendous success in delaying food decay, thereby maintaining the food quality and other sensory properties like flavor and color (Ozogul et al. 2017). A large body of evidence shows that application of essential oils encapsulated in different nanostructures such as nanotubes, polymeric nanoparticles, zein nanoparticles, cyclic oligosaccharides, and other biodegradable nanoparticles (da Rosa et al. 2015; Abarca et al. 2016; Kim et al. 2016; Liakos et al. 2016; Chifiriuc et al. 2017; Pavela et al. 2017) in seafood processing has also recorded positive results. The use of chitosan as a preservative agent for seafood like *Oreochromis* sp. (Tapilatu et al. 2016).

Natural biopolymers such as proteins, polysaccharides, and lipids are used to make nanocomposites films. These alternative packaging materials are rapidly being used to replace petrochemically produced plastics due to their environmentally friendly nature, anti-carcinogenic nature, and edibility (Ogunkalu 2019). Nanocomposite films made from chitosan NPs and gelatin, with oregano essential oil added, exhibited high antimicrobial activity against four notable food pathogens *Listeria monocytogenes*, *Salmonella enteritidis*, *E. coli*, and *S. aureus* (Hosseini et al. 2016). The use of nanoemulsions for the preparation of edible films is gaining global attention. Alginate films containing essential oil-loaded nanoemulsions have been produced to enhance water dispersion and prevent essential oil degradation (Acevedo-Fani et al. 2015). Recent reports show that nanoemulsion manufactured with essential oil with some antibacterial activities and thyme essential oil exhibited the growth of *E. coli* (Otoni et al. 2014). Recently, lecithin nanoliposomes were shown to be able to encapsulate essential oils (Valencia-Sullca et al. 2016). The encapsulation of orange essential oil with the help of soy lecithin and rapeseed resulted in extraordinarily stable nanoliposomes, which were then integrated into caseinate starch films (Jiménez et al. 2014).

Potential human health risks and toxicities associated with nanotechnology and its mitigation measures

Nanotechnology-based products and materials have been shown to exert a harmful impact on the environment and human health despite their fundamental relevance in the development and sustainability of aquaculture (Shah and Mraz 2020). The potential toxicity of nano-based products and materials has raised global concerns. Nanoparticles can transverse across cell membranes inducing genotoxicity due to their incredibly small size. Because of their inherent chemical reactivity, nanomaterials produce more reactive oxygen species and free radicals, which is one of the nanoparticles' principal toxicity mechanisms resulting in inflammation, oxidative stress, protein, and DNA damage (Vicari et al. 2018; Meghani et al. 2020). The toxic effects of nanomaterial on aquatic organisms have been extensively studied and reported by many researchers (Sendra et al. 2017a, b, 2018a, b; Volland et al. 2018; Aouini et al. 2018; Naguib et al. 2020; Sayed et al. 2020). ZnO NPs triggered an oxidative stress-related response in the fish liver after 10 days of administration probably hindering the activities of cytochrome P450 (Connolly et al. 2016). Organ pathological studies shows that *Oreochromis niloticus* exposure to 10–30 nm ZnO NPs ameliorated various pathological conditions in the organs of study (Kaya et al. 2016). AgNPs altered the brain antioxidant system in *Tilapia zillii* and *Oreochromis niloticus* (Afifi et al. 2016). Similarly, AgNPs showed a significant adverse effect on *Carassius auratus and Rutilus* (Yalsuyi and Vajargah 2017). AgNPs were also found to accumulate in the brain than in the gills and liver of juvenile *Piaractus mesopotamicus* resulting in a significant increase in lipid peroxidation and damage to the DNA (Bacchetta et al. 2017).

Nanotoxicology studies have been carried out to elucidate the regulatory aspects and biodistribution of these components and to assess their potential environmental dangers at the molecular level (Bello and Leong 2017). Despite this, there is still no globally harmonized legislation for manmade nanoparticles. To attain a sustainable application of nanotechnology in aquaculture, extensive study is required on the mechanism of accumulation and potential toxic effect of these materials on aquatic organisms and possible trophic level transfer to humans (Luis et al. 2019). More public participation is necessary to maintain public trust in nanotechnology, particularly in the areas of environmental, and food safety. Extensive risk analysis on the impact of long-term exposure effect of nano-based materials in both human and aquatic foods needs to be carried out. Recent studies have shown that nanoparticles bioaccumulate in fish tissues (Shaw and Handy 2011; Khosravi-Katuli et al. 2017), thereby raising concerns on potential risks to human health due to long-term consumption via trophic transfer.

Despite the risks associated with some nanoparticles, there still exists a certain level of benefits. The assessment of risks, advantages, and ethical issues is based on several criteria, including nanomaterial composition, the specific application area, deployment methods, and overall aim. Over the last few decades, a great deal of attention has been devoted to legislation, which has been thoroughly reviewed by different researchers who conclusively stated that to produce regulatory rules that can leverage the maximum potential of nanotechnology, experimental methods should be devised to help assess the prospective impacts for a specific substance prior to its application in food, agriculture, and the environment (Jain et al. 2017; Kaphle et al. 2017). It is quite sad that despite the growing concerns, no standard regulatory legislation governing the use of nanotechnology in the food and agriculture industries has yet been enacted. As a result, comprehensive policies and guidelines are required for the industry's safe use of nanoparticles. As a result of these constraints, actual legislation is still in its early stages of development, addressing only broad strategies to nanotechnology and nanomaterials. Because of the complexity of nanomaterials and the case-by-case legislative procedures, there is limited regulation of nanofood (He et al. 2019). The varying levels of toxicity, impacts, and dangers associated with different categories of nanomaterials contribute to the dearth of understanding (Deng et al. 2018). The Scientific Committee on Emerging and Newly Identified Health Risks, EU, and FDA, USA, are the two major organizations in charge of food nanotechnology legislation and regulation. Food products containing nanomaterials should undergo safety checks, according to EU regulations, to ensure that they are safe for human consumption (Tinkle et al. 2014). The EFSA Scientific Network of Risk Assessment of Nanotechnologies in Food and Feed celebrates 2020 its 10th anniversary and seeks to establish new guidelines for the regulation and risk assessment of nanomaterial in food, agricultural, and feed products (EFSA 2021). There is a need for the Asian continent particularly Japan and China to develop sustainable frameworks and guidelines for the usage and disposal of nanomaterial-containing products (Nile et al. 2020). However, the Taiwan FDA has announced regulatory guidelines for food packaging nanomaterials safety assessment and pre-market approval.

Conclusion and perspectives

The hazardous impact of antimicrobial resistance in the environment particularly the aquatic ecosystem is a global concern. The following recommendations if adhered to will improve the management of releases into the environment that could contribute to the emergence and spread of antibiotic resistance. Nanotechnology undoubtedly plays an important role in the growth and long-term sustainability of aquaculture. Various nanotechnology-based solutions have been used to enhance the major pillars of aquaculture and fishing so far. However, there is rising worry in this field concerning the toxicity of NPs, as well as the overuse of antibiotics and other synthetic substances. As a result, the use of safe and environmentally friendly methods is unavoidable. In this regard, natural bioactive chemicals have recently received a lot of interest, particularly curcumin, which has been found to play a significant role in fisheries. Currently, the majority of these applications are in the early stages of development, with high costs identified as the primary impediment to their widespread adoption. A careful analysis of the life cycle and shelf life of new nanomaterials, as well as an evaluation of possible environmental and health risks, such as exposure, release, and deposition, will be required to ensure the sustainable development and management of nanotechnology in the aquaculture industries and aquatic ecosystem in general. Such concerns, however, must not deter us from attempting to apply nanotechnological applications in the aquaculture industry, which should be linked to strict monitoring and controlled use, encouraging efforts to limit risks while maximizing benefits.

However, there are numerous limitations in nanotechnology in fish medicine. Nanoparticles in various forms, such as liposomes, nanocapsules, nanotubes, and dendrimers could theoretically be useful in the study of fish diseases. Antifungal and antiviral and antifungal properties of NPs against fish infections are yet to be investigated. If nanotechnological technologies are to be extensively used, more research into vaccine development in fish is required. Only a few research have looked into the use of nanoparticles in aquaculture for diagnosing bacterial and mycotic infections. Considering the proven potential of NPs, there is a necessity for more focused research into their use in a variety of fish healthcare research subjects in order to promote more efficient fish diseases diagnostics and therapeutics and address the ever-increasing demand for aquatic animal health. In the future, nanoparticle production procedures such as biological methods, which are defined as easy and generate nontoxic, ecologically friendly, and economical products, will be required. All categories of aquaculture farmers would be able to gain from nanotechnology in this manner. Overall, nanotechnology could play a significant role in the long-term sustainability of aquaculture.

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Declarations

Conflict of interest The authors declare no competing interests.

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