Toxicology Reports 14 (2025) 102013

Contents lists available at ScienceDirect

Toxicology Reports

journal homepage: www.elsevier.com/locate/toxrep

Review of mechanisms and impacts of nanoplastic toxicity in aquatic organisms and potential impacts on human health

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ARTICLE INFO

Keywords:
Nanoplastics
Bioavailability
Toxicity Exposure
Microplastics

ABSTRACT

The harmful environmental impact of plastic waste has justifiably received substantial attention from the scientific community. In contrast, the toxicological effects of nanoplastics (NP) on aquatic organisms, as well as the potential implications for human health, remain largely unexplored and poorly understood. Despite the growing awareness of plastic pollution, the risks associated with the ubiquitous presence of nanoplastics in our food and beverages are not yet fully recognized. NPs, which are smaller than 1 μm, along with a mixture of MPs and plastic fragments, can find their way into water bodies through various sources and may easily be taken up by aquatic organisms. This paper summarizes the existing literature on NPs bioavailability, their accumulation patterns within the tissues of fish, shellfish, and zooplankton, as well as the influence of biological and environmental factors on NPs absorption from water and diet. Study indicated that the NPs pose significant risks to both aquatic ecosystems and human health due to their ability to bioaccumulate in marine organisms and biomagnify through the food web. It highlighted that various aquatic species can ingest NPs, leading to their distribution across different tissues, which may result in toxic effects such as oxidative stress, DNA damage, and inflammation, as well as impacts on growth and reproduction. The identified critical gaps in current research, particularly regarding the long-term effects of low-dose NP exposure and the need for standardized testing methodologies to ensure comparability across studies. Furthermore, the necessity for further research to understand the pathways through which humans may be exposed to NPs, their toxicokinetics, and the potential implications for chronic health issues. Therefore, more studies are required which employ rigorous and uniform methodologies to fully address NPs as an emerging threat within aquatic ecosystems and food chains; accurately assess related risks with human health together with cumulative toxicity perhaps when combined with other pollutants.

1. Introduction

Due to the long-lasting and ubiquitous nature of plastic waste in land and water, plastic pollution is now a crucial environmental problem. It is estimated that 4.8 and 12.7 million metric tonnes of plastic debris enter the oceans from different sources on land annually [1]. While large macroplastics remains a risk of entanglement or ingestion for wildlife, a relatively new concern is surrounding environmental presence along with impacts related to microplastics (MPs) and nanoplastics (NPs). MPs are defined as plastic particles found in marine habitats, classified based on size: less than 1 μm to 1000 μm for MPs, 1 mm to 10 mm for mesoplastics, and more than 1 cm for macroplastics., freshwater and terrestrial habitats worldwide [2]. NPs fall within the range of 1–1000 nm size thus are considered as one component among many when it comes to

Abbreviations: MP, Microplastic; NPS, Nanoplastics; Nm, nanometer; ROS, reactive oxygen species; ADMET, Absorption, Distribution, Metabolism, Excretion, and Toxicity; BPA, bisphenol A; DNA, deoxyribonucleic acid; TNF-α, tumor necrosis factor alpha; PS, polystyrene; PE, polyethylene; PP, polypropylene; PAHs, Polycyclic aromatic hydrocarbons; OECD, Organisation for Economic Co-operation and Development; ISO, International Organization for Standardization.

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https://doi.org/10.1016/j.toxrep.2025.102013
Received 22 December 2024; Received in revised form 17 March 2025; Accepted 25 March 2025
Available online 28 March 2025

global aspects of plastic pollution yet their significance is not widely known [3].

NPs emerge as a result of a variety of natural and industrial processes, such as disintegration and decay of bigger molecules by physical, chemical and biological weathering. These can occur in the primary form during processing and application of nanoscale polymers within sectors like personal care products industry, paints production, medical supplies or as accidental outcomes from synthetic textile washing, tire wear, and marine anti-fouling paints [4]. However, atmospheric emission and the mechanical and weathering breakdown of macro- and MPs are considered major transport pathways introducing nanometer-sized plastic debris into natural environments. Due to their enhanced surface area to volume ratio, NPs may display different physicochemical properties than larger plastic items influencing environmental fate, reactivity, and biological interactions [5].

Once NPs enter aquatic systems, have been found to be easily distributed through water flows and movement of sediments. Their tiny size enables them to penetrate biological tissues and cells by different routes including internalization via endocytic pathways, cell adhesion and passive diffusion across membranes with high surface energy [6,7]. Their translocation within food webs presents additional complexity as investigations demonstrate plastics accumulation in guts and body parts of animals from different phyla such as zooplankton, fish, shellfishes and seabirds [8,9]. Although there is ongoing research on the toxicological aspects concerning NPs, their toxicity mechanisms remain poorly understood; however possible adverse outcomes include oxidative stress, inflammation responses to genotoxicity and endocrine disruption, respiratory burst as well as impaired enzyme activity due to reactive oxygen species (ROS) production and intracellular interactions. The transfer of bioaccumulated NPs through trophic levels in aquatic organisms also implies that seafood consumers may be at risk from this source of exposure [10,11].

While providing economic and nutritional benefits, commercial fisheries and aquaculture operations have been linked to inadvertent MP pollution emissions. Coastal communities involved in fishing and fish farming are thus at risk from increased environmental NPs concentrations through occupationally-intensive activities. Although data assessing NPs concentrations in harvested seafood intended for human diets are still limited, the feasibility of translocating nano-sized plastics across biological membranes, particularly the epithelial lining of the gastrointestinal tract, implies a possible route of entry into human circulation [12]. However, extrapolating toxicity knowledge from aquatic ecological models to human health scenarios presents challenges from differences in plastic biodistribution, toxicokinetics, and species sensitivities [12,13]. Hence, additional toxicological investigations considering physiologically-relevant exposure scenarios are warranted to holistically estimate NPs implications for both ecosystems and public health (Fig. 1).

This review aims to summarize the state of literature on NPs in aquatic environments and associated ecological hazards. The most up-to-date findings on NPs sources, distribution patterns, uptake mechanisms, and toxicity outcomes observed in aquatic organisms were highlighted. Potential effects for upper-level consumers including humans were also be discussed based on current understanding of exposure pathways and implications from aquatic toxicity data. Critical research gaps necessary to more comprehensively measure NPs risks are identified, alongside recommendations for integrating ecotoxicological, analytical, and human health perspectives to strengthen risk characterization. Overall, a better-founded toxicological analysis of NPs in aquatic organisms and consequent impacts for environmental and public health is advanced.

2. Nanoplastics uptake and toxicokinetics in aquatic organisms

2.1. Nanoplastics bioavailability and bioaccumulation

NPs introduced into aquatic environments have considerable potential to bioaccumulate in resident organisms through multiple exposure pathways. Upon release, physicochemical characteristics of NPs direct bioavailability for uptake [14]. NPs, with smaller sizes below 100 nm more readily interact with organisms as they can adsorb to gills, penetrate cell membranes, ingest through filtration or ingestion of contaminated water and prey items [15].

Hydrophobic particles are highly likely to accumulate in fatty tissues while surface charge is known to influence cellular adhesion. Laboratory studies have shown that nanoparticle concentrations increase over time in the tissues of exposed fish models, with NPs being transported to organs such as the liver where the metabolism and processing of accumulated contaminants takes place. The other group includes bivalves which feed continuously and also concentrate their NPs within a few hours of uptake. NPs have been proven to be transferred from primary producers into zooplankton and small fish, which can result in biomagnification through aquatic food webs, a possibility supported by discoveries of MPs samples could result into high trophic marine predators [16]. Field investigations sampling filter feeding bivalves and ocean quahogs near wastewater outflows correlating to elevated MPs and NPs further corroborate bioconcentration occurs in natural environments receiving plastic pollution. Overall, multiple lines of evidence

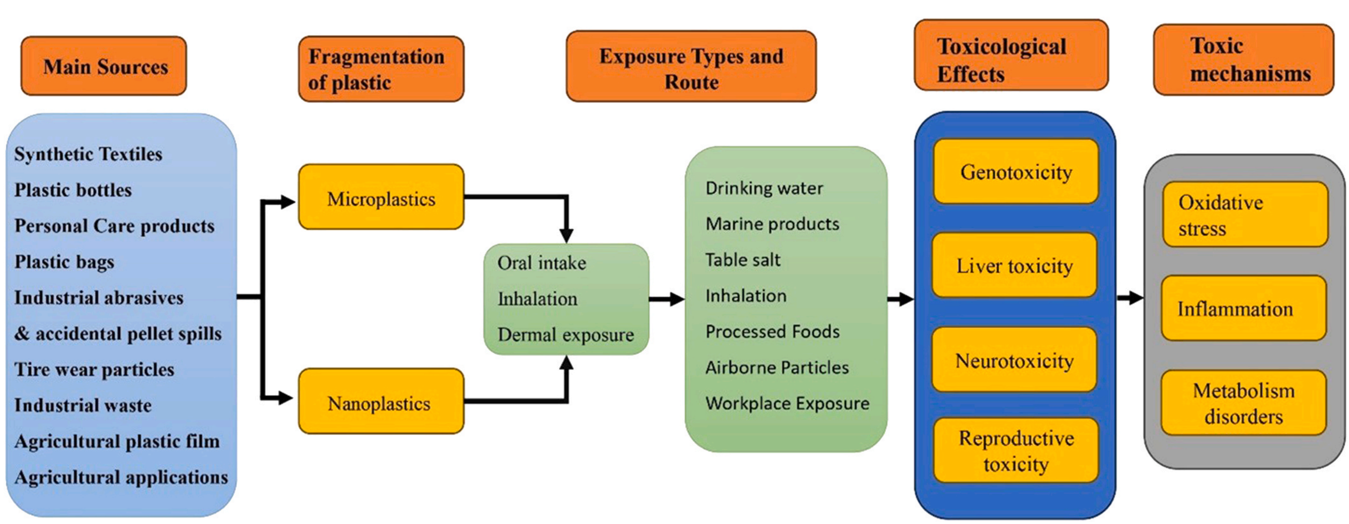

Fig. 1. Main sources and exposure routes of microplastics and their potential toxicological effects.

from controlled lab exposures to field monitoring elucidate the propensity for NPs to bioaccumulate in aquatic life which has serious imlications for health of fisheries and consumer safety if plastic contaminants progress up the filial web [17]. (Table 1)

2.2. Tissue distribution and elimination

Once nanoplastics enter aquatic organisms, they are subjected to complex toxicokinetic pathways that determine biological fate and influence toxicity potential. Recent studies have provided insights into 'Nanoplastics' ADMET profile [18]. Upon cellular internalization, NPs specially enter lysosomes for attempted breakdown however plastics resist catabolism and overwhelm the organelle, triggering stress responses. Yet some particles avoid lysosomes to persist cytosolically and transfer between tissues. Distribution experiments observe accumulation preferentially in liver and other metabolic organs like intestine and gills that process absorbed contaminants. The hepatobiliary system plays a central excretory role in shunting ingested NPs from the gastrointestinal tract to bile and faeces. Intravenous exposures find uptake predominantly by immune cells of the reticuloendothelial system prior to redistribution to other tissues such as intestine, highlighting clearance mechanisms from circulation [19]. However, depuration kinetics assessments note NPs can remain in tissues for weeks, with potential for longer retention suggested by MPs retrieved from wildlife [20]. Both physicochemical attributes of NPs governing biopersistence along with organismal metabolic competence for recognizing and removing foreign materials impact elimination rate. The pharmacokinetic profile elucidated by multiple approaches collectively shows NPs, do not simply excrete from exposed organisms and instead follow convoluted trafficking pathways that can potentially concentrate, and store particles long-term with unknown consequences [21].

Table 1
Summary of studies on the distribution of engineered nanoplastics (ENPs) in different organisms upon exposure. The details of the test species, type and size of ENP used, exposure concentration and duration, tissues/organs showing ENP accumulation. The studies reported ENP accumulation in various tissues like gills, gut, liver, brain, etc. post exposure through water or diet. This table provides an overview of ENP distribution in aquatic and terrestrial organisms [35,36,37,38].

S. No	Species	MNP size & type	Location
1.	oysters	6.9 ± 3.84 items/individual and 0.81 ± 0.45 items/g Polyethylene (PE) and polypropylene (PP) fibers	Tuticorin coast in Gulf of Mannar in Southeast India
2.	pelagic fish (MP in muscle and skin) and inedible (gill and viscera) tissues	0.07 ± 0.26 items/fish (i.e., 0.005 ± 0.02 items/g)	Kerala, India
3.	Perna viridis meretrix meretrix	1.8 ± 0.54 microplastics/g 0.18 ± 0.04 microplastics/g	Ariyankuppam, Panithittu, and Chunnambar in Pondicherry, India
4.	Channa punctatus Labeorohita Labeo bata Salmostomabacaila Puntius amphibius	7.86 ± 2.0 items/individual (4.17 ± 0.6 items/individual) a (3.03 ± 0.4 items/individual); 0.83 ± 0.13 0.77 ± 0.2	Fibre-type MP Cyprinidae and Channidae family, caught in wild conditions from a local fish market in Lucknow, Uttar Pradesh
5.	Rastrelligerkanagurta, Leiognathusruconius, Sardinella gibbosa, and Megalops cyprinoide	polyethylene terephthalate and polypropylene ~30 % of fish contained MP	fish samples from seven locations along the eastern coast of India, including New Digha in West Bengal, Chandipur, Puri, and Gopalpur in Odisha, and Vizag, Manginapudi, and Mypadu in Andhra Pradesh

2.3. Factors influencing uptake

Many intrinsic and extrinsic factors across biological scales govern NPs uptake and toxicokinetic in aquatic organisms. At the level of individual organisms, feeding strategy and trophic position play a crucial role in exposure potential. For example, higher-level predators that biomagnify plastics via prey and filter feeding benthic invertebrates are continuously concentrating particles from large water volumes resulting in high internal NPs burdens. Uptake is affected by physiological traits such as gill characteristics which serve as a major site for the entrance of waterborne NPs into circulatory systems of an organism [22]. The diffusion capacities are determined by surface area, mucus production as well as vascularisation of gills; hence, species like eels having thin highly vascularised gills have optimized their oxygen absorption in hypoxic zones to enhance absorption [23]. Surface properties facilitate interactions at the cellular scale with major uptake routes involved in endocytic mechanisms. Negatively charged functional groups promote electrostatic attachment and receptor-mediated endocytosis while small hydrophobic NPs directly penetrate lipid bilayers [24]. Once internalized, however, sub cellular trafficking is dictated by properties such as those of hydrophilic NPs which trigger stress once they get into lysosomes from catabolic failure but passing through cytosol or escaping from lysosomes to persist between tissues. Smaller spheres (<100 nm) actively penetrate tissues and cells more than NPs do while irregular shapes experience less ineffective uptake and for surface modifications like PEGylation that serves to camouflage hydrophobicity thereby reducing protein/cellular interactions. A comprehensive understanding of these multiscale determinants from organismal traits and physiological variations down to nanoparticle physicochemistry enables predictive modelling of uptake and informs mitigation efforts [25].

3. Toxicological effects in aquatic organisms

The toxic effects of nanoplastic pollution have been demonstrated in numerous aquatic organisms. Plastics of nano-size are able to enter aquatic species through alternative channels such as ingestion, inhalation and dermal exposure. In an organism, NPs may cause physical damage to tissues or induce biological responses [13]. Researchers have revealed that fish, bivalve and zooplankton species can develop gastrointestinal tract obstruction or perforations after being fed with NPs. Also, ingestible NPs might concern individuals because they release additional compounds like bisphenol A (BPA) and phthalates into living tissues that never encounter those substances before [26]. NPs are another source of oxidative stress in aquatic animals since their small size enables them easy penetration into cells causing interruptions in normal biochemical processes via reactive oxygen species formation [25]. The mechanisms through which NPs exposure affects aquatic life are diverse and threaten individuals, populations, and entire ecosystems [13,25,26]. (S1)

3.1. Mechanisms of nanoplastic toxicity

3.1.1. Oxidative stress

Oxidative stress is one of the main toxicological impacts observed in aquatic organisms exposed to NPs. Due to their small size, NPs can easily translocate through the cell and tissue barriers following ingestion or absorption. Once inside biological systems, NPs generate reactive oxygen species (ROS) through several methods. NPs possesses a large surface area-to-volume ratio which enables them to act as substrates for ROS formation by catalytic reactions. Also, during biodegradation, additives could be released from NPs capable of redox cycling and continuously generating ROS [27]. Other intra-cellular mechanisms have also been reported to impair antioxidant defence system in aquatic animals by lowering such endogenous antioxidants like superoxide dismutase, glutathione and catalase that regulate ROS levels in a normal animal [27]. Oxidative stress is initiated by an imbalance arising from excessive ROS production and antioxidant capacity. In aquatic life, there are different toxic effects of excess ROS production resulting from the use of NPs materials [28]. It damages biomolecules including proteins, lipids and DNA by oxidation that alter normal cellular functions. Cellular signalling as well as gene expression pathways are also disrupted by oxidative stress. Many studies have reported elevated oxidative stress markers such as lipid peroxidation, protein oxidation, and DNA damage in various fish, shellfish and zooplankton exposed to NPs. Such effects raise metabolic costs in organisms that need to counteract heightened ROS levels while repairing oxidative damage through antioxidant synthesis [26,29]. Persistent oxidative stress ultimately overwhelms repair mechanisms and leads to toxicity, affecting aquatic species at individual and population levels over long term NPs exposures.

3.1.2. Genotoxicity

Genotoxicity is an important toxicological effect of NPs that can cause damage to genetic material such as DNA in aquatic lives. Whereby, NPs are small enough to move across cell membranes and into the nucleus where they easily interact closely with genetic material. Several studies have been conducted, both in vitro and in vivo, showing how different species of animals can have their genomes damaged by NPs [27,30]. Genotoxicity tests can include comet assays for examining DNA strand breaks, micronucleus tests for chromosomal aberrations, and gene mutation assays for mutations. Studies involving zebrafish, medaka fish, oysters and mussels exposed to various sizes of NPs, have shown significant increases in DNA damage as well as micronucleus formation and mutant frequencies with dose-dependent manner. The underlying mechanisms contributing to NPs-associated genotoxicity are manifold. NPs generate reactive oxygen species as discussed previously which can directly attack DNA bases and backbone phosphate links yielding single and double strand breaks as well as DNA–protein cross-links [31]. Further, certain plastic additives like bisphenol A leaching from NPs are endocrine disrupting chemicals shown to damage DNA and diminish DNA repair capacity. Also, chromosomal anomalies can also be caused by these NPs adhering to DNA or hampering mitotic checkpoints. A major concern is that DNA mutations and other lesions caused by NPs may get inherited trans-generationally, since they can induce heritable changes at the genome level [32]. This can lead to long-term genomic instability and mutations that would seriously impede normal growth and development among aqua-biotic species as well as impair population dynamics through reduced reproduction ability and reduced heritability over generations exposed to NPs pollution. Such genotoxic risks warrant more investigation given the critical roles DNA plays in regulating all cellular functions and inheritance of traits [21,33].

3.1.3. Inflammation

Nanoplastics exposure has been demonstrated to trigger inflammatory responses in various aquatic species. Inflammation is a complex biological response of vascular tissues and immune cells to various forms of harmful stimuli such as pathogens, infections or poisons. Once NPs invade an aquatic organism, they cause direct physical and chemical damage to the cells and tissues. The damage in cells and tissues sets up various pathways for the inflammatory mediators. Study results have shown increased levels of important inflammatory cytokines in fish, crustaceans and mussels like tumour necrosis factor alpha (TNF-α), C-reactive protein and interleukins such as IL-1β, IL-6, IL-8 respectively following exposure to NPs particles [34,35]. These inflammatory mediators increase vascular permeability by causing leakage at site of inflammation leading to recruitment of inflammatory cell from vessels to affected sites. Examples include infiltration of macrophages, neutrophils and lymphocytes into lungs, gills intestines or other organs when triggered by nano-plastic materials in aquatic organisms. Persistent inflammation arises from the chronic presence of NPs inside biological systems triggering prolonged tissue infiltration of immune cells producing ROS, cytotoxic enzymes and inflammatory signalling molecules in a hyper activated state [26]. This disrupts normal redox homeostasis locally and also systemically. Over time, both localized inflammation, which is spread over a small area at the body level, and systemic inflammation which affects the entire body tend to cause harmful side effects on biomolecules together with tissues that alter their functions resulting in organ-level abnormalities [35]. For example, histopathological lesions involving respiratory epithelia have been associated with NPs induced inflammatory responses that affect intestines and hepatocytes thereby compromising integrity as well as functionality of organs in aquatic organisms. Additionally, chronic inflammatory conditions require significant metabolic energy resources thus impeding growth along with reproduction. The prolonged dysregulation of immune reactions caused by NPs is a major toxic process that impairs aquatic health [26,35,36].

3.2. Organ-specific toxicity (e.g. liver, gut)

NPs exposure leads to identifiable organ-specific toxicity in various vital organs of aquatic species through diverse pathophysiological mechanisms [37]. This is why the liver and gastrointestinal tract are vulnerable, considering their roles in xenobiotic metabolism and nutrient absorption. Studies have demonstrated that hepatocyte damage, fatty changes, and inflammation occur in the livers of fish, mussels and shrimp exposed to NPs. Moreover, NPs are small enough to translocate from intestines into hepatocytes where they probably induce oxidative stress leading to impaired metabolic as well as detoxification functions [38]. Aquatic animals suffer prolonged liver injury caused by NPs which makes them prone to pathological states like steatosis and fibrosis. Similarly, NPs have also been found sticking to gut epithelial cells causing penetration into intestines and sloughing off essential micro-ridges for absorption purposes [39]. Another experiment on intestines of NPs-exposed aquatic animals indicated different lesions ranging from submucosal edema, epithelial lifting/erosion up to villi deformation or mucosal thickening impairing normal digestion. Furthermore, within gastrointestinal environments NPs may also leach out harmful chemicals which interfere with intestinal physiology [40]. Even respiratory systems are not spared, where NPs deposit in gills causing pathological changes like fusion of lamellae, clubbing and aneurysm formations that hamper respiration. Moreover, adverse effects of NPs on reproductive organs include impaired gametogenesis, hormonal imbalance and teratogenicity during early development. Furthermore, such crucial organ malfunctions leave the victims weak with reduced abilities to survive, grow, reproduce and metabolically fit in their environment. In addition to that, tissue reservoirs for NPs like liver lead to more damage at the organ-level in aquatic species with detrimental population-level implications.

4. Potential human health impacts

Given the ubiquitous presence of NPs in aquatic ecosystems and seafood, human exposure through ingestion is considered inevitable. Whereas there are limited possibilities of direct inhalation or dermal routes, eating contaminated fish and other seafood on a regular basis could lead to the accumulation of NPs in the human body over time [41]. The toxicity will depend on individual's health status and consumption patterns as well as types and properties of the NPs involved. Some groups including children and pregnant women who consume more seafood are at more risk [42]. Once inside an organism body, nano-sized plastics can pass through cellular membranes, tissues barriers, get distributed to other parts via blood circulation, and have an interaction with biomolecules among others. It disrupts normal metabolic pathways, causing oxidative damage or inflammatory reactions. In some studies apoptosis and fibrogenic signalling cascades have been seen activated in human intestinal cells lines, liver cells lines, respiratory cell lines once exposed to NPs material [43]. In vivo, nanoplastics may bio magnify up the food chain and higher doses transmitted maternally could impact foetal development [44]. Further, leachates from consumed plastics might have endocrine disrupting substances and persistent organic pollutants that can disrupt hormonal balance and increase cancer risk. Although there is no concrete proof of human bioaccumulation or bioconcentration of NPs, emerging information suggests that this may pose some concerns [37]. Regular biomonitoring of commonly consumed fish species could help assess human internal NPs levels over time and identify vulnerable groups. There is need for more research to understand the process by which humans take in oral doses of NPs, how toxicokinetics proceeds and implications for chronic non-communicable diseases, such as dose-effect relationships [44].

4.1. Dietary exposure from seafood consumption

Seafood consumption represents one of the major pathways for human exposure to NPS pollution. This is because large amounts of NPs are found in oceans and seas. Inhabitants of the ocean and seas, such as fish and shellfish, eat plankton and other particles with different sizes including those that are nano-sized, thereby taking in NPs found in their environment [19,25]. Studies utilizing simulated gastrointestinal juices have demonstrated the ability of fish toretain ingested NPs in their tissues post digestion [45]. Tuna and salmon are among top predators at the apex of the food chain thus accumulating more & more NPs overtime through bio-magnification processes. Through routine daily intake of popular types like shrimp, salmon, sardines could deliver a significant proportion of the recommended weekly intake of NPs for an average individual [17]. Important areas where risks increase include high volumes of sea-food; therefore, coastal communities relying mostly on fishing experience higher exposure levels than inland regions do due to moderately elevated consumption rates that differ between countries' populations. For example, average Asian intakes of NPs contaminated seafood are estimated 3–10 times higher than European and American intakes [46]. Further still processing techniques which involve steaming, boiling or even grilling cannot guarantee complete removal of these materials since they may be released into the water during cooking process by additives used their in. Even though reliable computations of the MPs intake through fish/seafood is viable, comparable NPs specific data are not yet available due to limitations in analysis. This is however an understatement as research on MPs and their transfer efficiencies into consumers has shown that typical consumers could be ingesting a minimum of tens of thousands up to millions of NPs annually that far exceed the baseline levels in the environment. The high-risk groups need special attention and mitigation measures aimed at reducing dietary exposures from polluted foods. More research is clearly needed to better characterize site-specific NPs burdens in commonly eaten varieties as baseline information for exposure assessment and regulation [47].

4.2. Occupational exposure

Inhalation and dermal exposure remain a significant pathway for workers in certain industries to be at risk to get significantly exposed to NPs. In this case, the laps of polymer extrusion and recycling processes such as injection moulding, involve handling of plastic powders, resin binders and additives which results in the release of airborne NPs fumes and particulates. Studies conducted within plastics manufacturing companies have found out that the concentrations of NPs are often orders of magnitude higher than those detected in background air or surface samples [11]. For example, nanofibers released by textile factories making synthetics during fabric manufacture are thermally stable and mechanical processes do not cause any defects in them. When handling sludge from domestic and industrial waste streams with high loads of nano and MPs, bioaerosols inhalation could occur among wastewater treatment plant operators [20]. NPs even have been found near landfills as well as waste incinerators in atmospheric fallout. Also, outdoor workers including plastic users in construction sites as well as garbage collectors are exposed too. It is strongly supported by evidence that inhalation of airborne NPs might result in their deposition deep into gas-exchange regions within the lung tissue where their extremely high surface area can promote oxidative stress and inflammatory cellular responses due to their reactivity [48]. Cardiovascular and respiratory diseases are well-known consequences of chronic inflammation of the lungs [49]. Additionally, absorption through the skin is another means by which individuals who have come into contact with plastic products could be exposed. As a result, resin additions can be observed as they move from plastic materials to sweat, creating a medium for systemic distribution. For this reason, it is vital that occupational health research takes into account disparate nano-specific exposures and biological effects in order to develop preventive measures aimed at protecting populations of vulnerable workers throughout the world.

4.3. Implications of NPs in aquatic food webs for human health

Nanoplastics released into aquatic ecosystems become incorporated into trophic food webs posing implications for human health through seafood consumption [16]. As primary producers and consumers, plankton readily ingest NPs and MPs including polystyrene (PS), polyethylene (PE) and polypropylene (PP) [40]. Some nanoplastics types may even be directly absorbed onto algal surfaces. Ingesting contaminant-laden plankton, filter-feeding bivalves and zooplankton accumulate NPs in their soft tissues. This first-level biomagnifications render shellfish and small fish important vectors for transferring NPs higher up the marine food chain. Larger predatory fish accumulate nanoplastics to a greater degree through the diet predominantly consisting of smaller contaminated fish [24]. Studies have demonstrated the preferential accumulation of NPs $<$ 300 nm in certain tissues of organisms spanning multiple trophic levels. However, effects of biomagnification to higher-level marine predators including seals, dolphins and whales regularly consumed are yet unknown. Humans, as top-level consumers, face magnified NPs exposure risks through regularly eating low-trophic fish and shellfish [50]. NPs may also act as 'vectors' transporting absorbed hydrophobic pollutants into human bodies. Chronic, low-dose effects of such biomagnified combination exposures on human health require careful investigation given the likelihood of bioaccumulation and difficulties of excretion. Considering threats, large-scale monitoring of NPs biomagnification in commercial fisheries is urgently needed to pin point risks for vulnerable coastal communities dependent on seafood (S2).

5. Knowledge gaps and future research directions

There are still many unknowns and areas that require further research regarding the potential toxicological impacts of NPs on aquatic organisms and humans. Even though some information has been obtained through research in relation to the effects that come with NPs' exposure, there are many knowledge gaps which prevent us from understanding fully about these risks. One major gap is understanding the fate as well as transport of NPs across various water environments [14]. It is important to investigate further how over time NPs degrade and transform when subjected to different environmental conditions such as UV radiation, temperature variations, interactions with other contaminants and biotic plus abiotic factors among others. This information is crucial for determining NPs exposure levels and routes that organisms may face. Furthermore, additional research are necessary so that more can be known about uptake, accumulation, and depuration of NPs by a greater variety of aquatic organisms at different trophic levels [30,51]. Although the existence of some data for a few model species, the impact of species-specific factors on NPs toxicity which is not yet fully characterized. Moreover, more longitudinal studies are required to investigate multi-generational and long term low-dose exposure effects that short term studies currently fail to capture [17,52]. Similarly, there is also a lack of consensus on appropriate dosimetry, exposure routes and relevant endpoints among scientists carrying out tests on NPs toxicity. There is need for standardized testing frameworks that would result in more robust and comparable data across different studies. From a human health perspective, more work still needs to be done to assess possible oral, dermal and inhalation exposures potentials to NPs through seafood consumption, recreational waters or employment involving plastic waste management. Furthermore, since smaller nano-sized particles can enter tissues and cross biological barriers more easily than bigger MPs do; their impacts on organs, tissues as well as cellular/molecular in humans also warrant deeper investigation. Finally, interdisciplinary collaboration with toxicologists, material scientists, chemists and environmental engineers is necessary to better characterize the hazards and risks posed by the wide diversity of polymer types that constitute particle sizes or shapes made from NPs pollution. Addressing these knowledge gaps through well-designed future studies will help obtain a more conclusive understanding of NPs hazards.

5.1. Complex ecotoxicology of nanoplastics

Understanding the impacts of NPs on aquatic organisms can be quite challenging because their ecotoxicology is too complex. Firstly, a variety of factors contribute to the diversity of NPs such as different manufacturing techniques, usage patterns, and environmental changes and this results in various polymer types, additives, surface properties, and degradation states. Some of the common contributors to NPs pollution include polystyrene polyethylene and polyvinyl chloride, but there could be hundreds of other formulations in the environment. Each type might elicit diverse toxicity which always depends on its chemical composition and physical characteristics. Moreover, NPs are not static objects but rather dynamic substances that undergo transformations [12]. For instance, additives may leach out of the NPs themselves or these particles may absorb pollutants from surrounding waters while being subjected to photo- and bio-degradation or aggregating into fragments via aquatic processes throughout time [52,53]. All these changes directly influence properties and potentially interactions with organisms. Importantly, NPs have high surface area to volume ratio thus enabling rapid adsorption of proteins toxins among other molecules bringing forth novel toxic modes of action [54]. Therefore, it is difficult to generalize about toxicity across studies using different NPs recipes meaning that it is always context dependent when it comes to toxicity implications of NPs.

Additionally, NPs' uptake, accumulation and related consequences are probably going to differ extensively between aquatic species due to biological factors. For instance, filter feeders and insects may face a higher ingestion risk compared with predatory fish because of their feeding mechanisms. Digestion efficiencies also vary among species whereas rates of metabolization and depuration mediate internal NPs doses for different types [30]. Likewise, within a single species larva vs adult stages might show diverse sensitivities towards NPs toxicity depending on the developmental physiological periods involved [48]. At sub-organismal levels, cellular and molecular toxicokinetic differences at sub-organismal levels such as clearance by the immune system further introduce inter-individual variability. Moreover, most recent studies deal with acute or short-term NPs exposures, however environmental exposures are chronic and multi-generational [55,56]. Long-term low-level impacts such as bioaccumulation, epigenetic toxicity and effects of maternal transfer have not been explored in depth. Lastly, there is little information on how NPs behave in the environment (natural ecosystems) compared to their behaviour under controlled lab conditions. Field conditions encompass greater variation due to diverse co-existing species' trophic interactions and continuous multimedia exposure pathways, unlike simple single-species laboratory experiments. Controlled experiments help to isolate mechanisms but have no ecological realism. This calls for interdisciplinary research that bridges toxicology, material characterization, analytical chemistry, exposure modeling and mesocosm experimentation to complement laboratory findings and develop realistic risk assessments of NPs pollution in aquatic environments and communities. the complicated ecotoxicology of NPs continually presents daunting challenges as well as promises new insights through imaginative multifaceted future research designs [57].

5.2. Interactions with other pollutants

NPs in the aquatic environment do not exist in isolation and frequently interact and combine with other pollutants present. For instance, the water bodies may become polluted by different kinds of pollutants including MPs and other plastics; heavy metals especially mercury; hydrocarbon pollutants as well as nanoparticulate materials [48]. These interactions between NPs and these other pollutants have significant implications on environmental fate and biodegradability of all substances involved. Heavy metals are primarily considered as environmental contaminants that mainly arise due to industrial, mining or agricultural activities. Globally most coastal and freshwater system contain high levels of heavy metals such as cadmium, lead, mercury, copper, zinc and chromium [58]. When surrounded by water these particles can absorb heavy metals present because they possess a large surface area compared to its volume [57]. Several studies have shown that NPs effectively adsorb and accumulate various toxic heavy metals on their outer surface. This facilitates transport of normally insoluble heavy metals into living organisms. It has also been noted that some polystyrene NPs showed higher adsorption rates for cadmium, lead and mercury thereby increasing their bioavailability in terms of toxicity towards living organisms [48,57,59]. The absorbed metals can then be ingested by aquatic life along with plastic particles and introduce heavy metal toxicity issues in addition to plastic pollution effects.

Pesticides are another common aquatic pollutant that comes from runoff due to agriculture. Their environmental fate, transport and toxicity may be affected by their interaction with NPs [14]. A study examining interaction of atrazine, a widely used herbicide, with polyethylene MPs and NPs found enhanced adsorption of atrazine onto NPs [42]. It enhances the mobility and bioavailability of atrazine. Pathogenic NPS containing absorbed pesticides can thus induce pesticide poisoning once they have been eaten by aquatic organisms. The others include hydrocarbon contaminants like polycyclic aromatic hydrocarbons (PAHs) which are released into water bodies through different industries' effluent systems. This is because these are large surface areas where PAHs such as phenanthrene and pyrene can sorb onto NPs based upon extensive research carried out on their sorption affinities for various pollutants including heavy metals and organic compounds [12,60]. This represents another toxic pollutant that can be readily transported and biomagnified in the food chain along with ingested NPs. The point here is, when taken together as complex mixtures of plastic particles plus other pollutants present in them, the combined effects of NPs and their associated adsorbed pollutants might turn out to be much worse than evaluating them independently.

5.3. Standardization of testing methods

Accurate assessment of the toxicity and determination of how it compares in different experiments is necessary for standardization of testing methods for NPs. Variations methodology used to characterize, expose and evaluate the ecotoxicity of NPs has many differences among studies. The characteristics, size, shape and concentration of test NPs all vary greatly between studies. Some studies use pristine NPs that are spheres with uniform size while other works have more realistic environmental NPs having irregular shapes and broad size distributions [57,61,62]. In addition, exposure media are diverse while conditions such as concentration levels and time durations also vary significantly from one study to another [57,63,64]. Furthermore, endpoints measured and analytical techniques used to identify and quantify them are inconsistent. This lack of uniformity makes it difficult to compare or reproduce already published findings.

Concerted efforts are needed to develop internationally recognized guidelines and protocols that will harmonize NPs testing methodologies. Some of the key aspects that need to be standardized include techniques used to determine critical parameters such as size, shape, polymers type and surface charge; exposure conditions which should mimic real environmental scenarios; and selection of representative indicator species from primary producers to higher trophic organisms. It is also important to agree on core endpoints to be evaluated such as uptake and internalization, oxidative stress, inflammation, histopathological effects, and impacts on growth, development and reproduction. This would enable comparability through ensuring that reference or certified reference NPs have known physico-chemical characteristics across studies. International organizations like OECD and ISO, which are dealing with international matters, must lead. This would enable them to build consensus through multi-stakeholder consultation processes and develop frameworks for standardized analysis of NPs. Robust risk assessment can be enabled if high quality comparable information about hazards and risks of NPs is made available through international organizations like OECD and ISO using methods recommended for performing standardized tests on nanoplastics.

6. Conclusion

While nanoplastics (NPs) are an issue of increasing concern due to their ability to enter aquatic ecosystems and accumulate within food webs, many questions remain about how much they really affect the environment as well as human health. Extensive research to date has demonstrated that various types of sea creatures from zooplankton to fish and shellfish can ingest NPs. In these organisms, nanoplastics have shown the ability to distributed throughout various tissues and organs with excretion being dependent on such factors as plastic size and chemistry. This bioaccumulation is risky since it leads to biomagnification of NPs through several trophic levels towards humans. However, numerous studies conducted using multiple aquatic species have indicated that exposure to nanoplastics can cause toxic effects such as oxidative stress, DNA damage, inflammation, liver- gastrointestinal tract harm among others. Such raises concerns as it may interfere with normal biological processes within individuals, populations, communities or even ecosystems.

Wastewater technicians, among the many other occupations of humans are at risk of direct inhalation, or ingestion for these plastics makers. Additionally, as fisheries and aquaculture have been major contributors to global food supplies, nanoplastics working their way up marine and freshwater food webs pose a threat of chronic dietary exposure for much of the population. Although there is limited epidemiological data, lab studies that provide mechanistic insights suggest that the risks could include metabolic disruption, developmental disruption, cardiovascular disease, immune system dysfunction and brain developmental problems if plastic-related pollutants can penetrate the human gut-blood barrier and accumulate in human tissues over a lifetime. Further complicating the issue are knowledge gaps regarding complex ecotoxicological interactions may occur when nanoplastics mix with other widely distributed contaminants such as heavy metals, pesticides and MPs. Additional research employing standardized methods is critically needed to better characterize dosage-dependent toxicokinetics within organisms, understand effects of chronic low-dose exposures, and assess human health impacts under real-world exposure scenarios to completely evaluate risks and inform regulatory policies aimed at curbing plastic pollution at the source. Overall, given their demonstrated ability to cause toxicity along with persistent uncertainty surrounding impacts, continued research on nanoplastics should be prioritized to safeguard against potential future threats to both environmental and human well-being.

Funding sources

This is a review type article and our institute didn't applied for any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

CRediT authorship contribution statement

Rana Sindhuprava: Writing – review & editing, Writing – original draft, Data curation, Conceptualization. **Tiwari Rajnarayan R:** Writing – review & editing, Formal analysis. **Jindal Neetesh:** Writing – review & editing, Formal analysis, Data curation. **Sahoo Ganesh Chandra:** Writing – review & editing, Data curation, Conceptualization. **Joshi Vibhor:** Writing – original draft, Methodology, Data curation. **Thakur Rahul:** Writing – review & editing, Writing – original draft, Formal analysis, Data curation, Conceptualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

The authors are happy to express their gratitude to Mrs. Grisma, and Dr. Dharma Raj for their invaluable suggestions and thoughtful feedback during the development of this work. Their encouragement and support were greatly motivating. This achievement would have been difficult to attain without their guidance and motivation.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.toxrep.2025.102013.

Data availability

Data already shared

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