Review Article

# Interactions between micro(nano)plastics and natural organic matter: implications for toxicity mitigation in aquatic species

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## Abstract

Plastics have significantly contributed to modern conveniences owing to their ease of use, stability, and adaptability. However, the fragmentation of plastics into microplastics (MPs) and nanoplastics (NPs) poses significant environmental risks. These micro(nano)plastics (MNPs) can adsorb various pollutants and pathogens, potentially posing significant ecological risks. This review critically examines the natural organic matter (NOM) in mitigating the toxicity of MNPs in both marine and freshwater species. Evidence suggests that NOM facilitates the formation of an eco-corona (EC) on MNPs, thereby reducing toxicity. Reduced toxicity attributed to EC formation has been observed in various freshwater species, such as *Danio rerio* and *Daphnia magna*, as well as marine species, including sea urchins, European sea bass, and marine algae. The presence of natural organic matter (NOM), particularly fulvic acid (FA) and humic acid (HA), significantly mitigates the toxic effects of MNPs, with HA exhibiting a strong protective effect. The interactions between MNPs and NOM, including the formation of the EC, which encompasses a protein corona component, are pivotal in understanding toxicity mitigation in aquatic environments. This review highlights the need for further research to elucidate the interactions between MNPs and NOM, and their role in mitigating toxicity across marine and freshwater ecosystems.



**Keywords:** Microplastics, Nanoplastics, Natural Organic Matter, Eco-corona, Aquatic Species, Toxicity Mitigation

## Introduction

The quality of human life has been significantly enhanced by the development and widespread use of plastics due to their low cost, lightweight properties, high adaptability, and stability. Numerous products utilize plastics, which are composed of several semi-synthetic or synthetic organic polymers (Allen et al., 2022). In addition to direct emissions from industrial and domestic sources, plastics fragment into microplastics (MPs, typically 1 μm to < 5 mm) and nanoplastics (NPs, <1000 nm) through environmental aging processes. These microplastics and nanoplastics (MNPs) have attracted considerable scientific attention due to their propensity to accumulate and transport various pollutants and pathogens, leading to complex and potentially enhanced toxicity in organisms. MNPs are emerging contaminants found in several environmental and biological matrices, including the human body (Ragusa et al., 2022). These particles can adsorb and transport coexisting toxic pollutants due to their surface charge and hydrophobicity, influencing the environmental fate, transport, bioavailability, and ecotoxicity of both the MNPs and the associated pollutants (Ali et al., 2022). Consequently, MNPs can act as vectors for pollutants and microbial pathogens (Ali et al., 2022).

Furthermore, natural organic matter (NOM) is ubiquitous in the environment and consists of a diverse array of organic compounds, differing in chemical structure, molecular weight, and physicochemical characteristics (Levchuk et al., 2018). Allochthonous NOM, including cellulose, alginate, humic acid (HA), and fulvic acid (FA), interacts with MNPs. The distinctive physicochemical properties of both MNPs and NOM, such as size, shape, mass, surface charge, and functionality, are crucial in determining these interactions (Chen et al., 2018).

While NOM is widely recognized as a critical modulator of MNP behavior, existing research has predominantly focused on HA and FA, leaving other ecologically relevant NOM components, such as extracellular polymeric substances (EPS), comparatively underexplored. HA and FA, which are derived through operational chemical extractions and standardized by sources like the International Humic Substances Society, possess well-defined solubility and functional group characteristics that enable reproducible mechanistic studies. FA, characterized by its lower molecular weight and high abundance of carboxyl and hydroxyl groups, stabilizes MNP suspensions and reduces metal ion release, thereby attenuating toxicity (Murbach et al., 2020). HA, with its higher aromaticity and hydrophobic domains, promotes aggregation and complexation of metal ions, often facilitating sedimentation and reduced nanoparticle mobility (Gunsolus et al., 2015). However, these fractions only represent a portion of environmental NOM complexity and may not accurately reflect native interactions occurring in situ.

EPS, a diverse matrix of biopolymers produced by microbial communities, contributes substantially to particle immobilization, aggregation, and altered reactivity in biofilm-dominated environments. (Hamid et al., 2022). Its role in nanoparticle sequestration remains insufficiently characterized, largely due to the variability in its composition and lack of standardized reference materials (Deng et al., 2019). Furthermore, most MNP–NOM studies have been conducted in freshwater systems, despite the pronounced physicochemical contrasts observed in marine environments. Elevated salinity, ionic strength, and sulfate concentrations in seawater induce heteroaggregation, modify surface charge distributions, and affect NOM conformational flexibility mechanisms that diverge considerably from those in freshwater settings (Govindarajan, 2025). For instance, sulfur- and nitrogen-enriched FA variants, such as those derived from microbial sources, provide enhanced colloidal stability and reduce $Ag^{+}$ ion release from silver nanoparticles,

suggesting environmental source-specific mitigation effects (Gunsolus et al., 2015). In contrast, HA's stronger hydrophobic interactions are less effective under high-salinity conditions, leading to increased agglomeration and altered nanoparticle transport. Environmental conditions such as ionic strength, pH, and salinity further modulate NOM functionality, with marine systems introducing elevated sulfate levels that accelerate aggregation and shift nanoparticle surface charge behavior (Govindarajan, 2025).

Taken together, the literature shows a bias toward studying FA and HA in simplified freshwater models, while overlooking the mechanistic diversity offered by EPS and marine-derived NOM. This gap impedes comprehensive understanding of MNP fate across aquatic systems and underscores the need for inclusion of structurally diverse and ecologically representative NOM fractions in future investigations.

In environmental and biological systems, MNPs acquire a dynamic coating of biomolecules upon exposure, known as the *corona*, which fundamentally alters their identity and interaction profiles. The protein corona, refers to the adsorption of host-derived proteins such as albumin, immunoglobulins, and fibrinogen onto NPs in biological fluids like blood or cell culture media. This corona governs MNPs behavior including biodistribution, cellular uptake, and toxicity (Bashiri et al., 2023). In contrast, the eco-corona emerges when MNPs encounter complex environmental matrices. It comprises macromolecules such as humic substances, extracellular polymeric substances (EPS), and organism-secreted proteins that bind to NPs in aquatic ecosystems. Eco-corona formation modifies nanoparticle aggregation, mobility, and bioavailability, often enhancing or mitigating their ecotoxicity depending on the specific biomolecular composition (Nasser & Lynch, 2016; Fadare et al., 2020). For example, humic acid

interacts strongly with nanoplastics through electrostatic and hydrophobic forces, stabilizing the particles and reducing their bioaccumulation and oxidative stress potential in species such as *Daphnia magna* (Yang et al., 2025). Unlike the protein corona's relevance to mammalian nanotoxicology, the eco-corona is crucial for understanding nanoparticle fate under realistic environmental exposure scenarios. Its formation reflects adaptive organismal responses and alters NP retention and feeding behavior in filter-feeding species, necessitating refined ecotoxicological assessment protocols (Nasser & Lynch, 2016).

Microplastics possess hydrophobic, smooth, and initially uncharged surfaces, which rapidly transform in aquatic systems due to adsorption of organic and inorganic substances. (Ragusa et al., 2022). In marine environments, natural organic matter (NOM), including humic substances, exopolymeric particles, and secretory biomolecules, binds to these surfaces forming an eco-corona analogous to the protein corona observed in biomedical nanomaterials. This adsorbed layer significantly influences the physicochemical behavior, bioavailability, and toxicological profile of micro/nanoplastics.

In biological fluids, nanoparticles acquire a protein corona comprising selectively bound proteins arranged in hard and soft layers, which regulate cellular interactions, internalization, and immunogenicity (Murbach et al., 2020). Similarly, NOM components interact with microplastic surfaces in layered structures, which can persist across environmental compartments and resemble biological corona mechanisms. Eco-coronas may enhance microplastic retention in organisms and modulate uptake by filter feeders. Their role in contaminant transport supports the "Trojan Horse" hypothesis, wherein absorbed pollutants become more bioavailable (Hayat Davoudi, 2023). Empirical evidence, such as reduced silver bioavailability in zebrafish when bound to plastic, substantiates this mechanism. Humic acids and exopolymeric substances influence particle charge,

dispersal, and aggregation, shaping sedimentation and ingestion dynamics (Bashiri et al., 2023). Moreover, NOM contains biologically active molecules infochemicals like dimethylsulfide that impart functional traits to plastics, triggering foraging or predator avoidance behaviors across trophic levels. These corona-mediated effects help explain widespread microplastic ingestion by aquatic and avian species (Li et al., 2020). Studies have documented that MNPs can interact with NOM to form an "eco-corona (EC)" or "protein corona" (Fadare et al., 2020). These complex interactions critically influence the accumulation, mobility, bioreactivity, and ecological impacts of plastic particles (Nasser and Lynch, 2016). The surface characteristics of MNPs play a crucial role in biogenic aggregates or ECs within ecosystems (Ali et al., 2024). Surface modifications can differentially influence the interactions with diverse types of allochthonous NOM during the formation of extracellular polymeric substances (EPS) or biogenic aggregates (Li et al., 2020). Such interactions play a critical role in determining the transport, dispersion, and fate of both MNPs and NOM (Wu et al., 2021a; Wu et al., 2021b). Previously, the prevalence of allochthonous NOM has been shown to suppress the adsorption while promoting the desorption of co-existing pollutants from MNPs (Zhang et al., 2021). This effect can be determined by the physicochemical characteristics of MNPs, NOM, and co-existing pollutants (Nguyen et al., 2021). Parameters including ionic strength, salinity, temperature, and pH can substantially affect the interactions between MNPs and allochthonous NOM (Pradel et al., 2021). The properties of NOM govern the transport of MNPs, the formation of biogenic aggregates (Chen et al., 2018), and the release of additives during MNPs aging, particularly in the presence of FA and HA (Yan et al., 2021a).

Currently, the interactions between MNPs with NOM have been explored in a limited number of review studies. Several studies have documented the interactions between MNPs and dissolved organic matter (DOM), providing valuable insights into the adsorption and desorption

processes, as well as the environmental fate of MNPs (Atugoda et al., 2021; Binda et al., 2021; Brewer et al., 2020; Sharma et al., 2021a). In contrast, some researchers have studied the interactions of MNPs with extracellular biomolecules in aquatic environments, focusing on EC formation and the factors influencing these processes (Hamid et al., 2022). These reviews have provided valuable insights but have not comprehensively addressed the interactions of a broader range of NOM types with MNPs and implications for toxicity mitigation in aquatic species.

The evaluation of MNPs' interactions with NOM in the environment is crucial for predicting their harmful effects and overall fate within ecosystems. (Fadare et al., 2020). However, due to the complexity of interactions in natural environments, it is essential to investigate the implications of NOM formation, characterization, and biologically mediated effects of MNPs for toxicity mitigation in aquatic organisms. (Zhang et al., 2022a). In this review, the EC formation process and characterization methods for toxicity mitigation in aquatic species in the presence of NOM along with MNPs are summarized. Notably, the factors that influence implications for toxicity mitigation in aquatic species are discussed, and research gaps in implications for NOM-facilitated toxicity mitigation in aquatic species and the resulting fate of MNPs in aquatic environments are proposed.

## 2.0 Bibliometric analysis

This meta-analysis comprises 28 studies published between early 2020 and 2024, focusing on NOM-mediated MNPs toxicity mitigation in aquatic species. The primary search engine used was Scopus, supplemented by Google Scholar and Web of Science. The main keywords, such as "microplastics," "nanoplastics," "toxicity mitigation," "natural organic matter," and "humic acid" were combined with other keywords like "aquatic species", "*Daphnia magna*" and "algae". The relevant research papers obtained were utilized for a comprehensive bibliometric analysis using

VOSviewer (version 1.6.1.7) developed by Walyman *et al*. (Waltman et al., 2010). The data were extracted by the software, and the co-occurrence of keywords was selected for the analysis. The least number of term occurrences was selected as '5'. The connecting lines between the circles explicate the degree of closeness among the keywords, the different font sizes of the terms show the co-occurring frequency of keywords, the arches between the nodes elucidate the rate of recurrence in the publication, and the distances among two nodes explain the co-occurrences of more than two terms within the publication. Keywords within the same cluster indicate strong thematic associations, reflecting their frequent co-occurrence in related research articles. A total of 54 items are grouped into four clusters, characterized by four different colors, with 2023 links formed with a total link strength of 3729 (**Figure 1a**). Cluster 1 (red) represents studies focusing on the general toxicity and environmental impact of microplastics and polymers in aquatic environments, including topics such as toxicity, microplastics, aquatic environments, plastics, and polymers. Cluster 2 (green) represents studies focusing on the interaction between nanoparticles and algae, including toxicity testing and the NOM-like HA in mitigating these effects, with topics such as nanoparticles, algae, toxicity testing, humic acid, photosynthesis, and chlorophyll a. Cluster 3 (blue) represents studies focusing on the environmental impact and fate of metal ions and nanotechnology, including their bioavailability and potential risks, with topics such as metal ions, environmental impact, bioavailability, nanotechnology, and environmental fate. Cluster 4 (yellow) represents studies emphasizing the broader ecological and biogeochemical impacts of nanomaterials on aquatic species and ecosystems, with topics such as aquatic species, ecosystems, nanomaterials, phytoplankton, and biogeochemistry.

The overlay visualization (**Figure 1b**) illustrates the evolutionary pattern of studies related to interactions between MNPs and NOM and their implications for toxicity mitigation in aquatic

199 species over the past two decades. The overlay visualization uses a color gradient to represent the
200 focal point in different studies at different times, specifically covering the period from 2020 to
201 2024. Studies conducted before and during 2020 covered the toxicity of MPs, metal ions, and
202 NOM in aquatic ecosystems, primarily featuring aquatic species such as crustaceans. From 2021
203 to 2022, the focus shifted to NPs' toxicity in freshwater aquatic species, such as algae and
204 phytoplankton, with studies highlighting the role of NOM in toxicity mitigation. By 2023, research
205 had primarily focused on the toxicity of MNPs, particularly polystyrene, with a focus on algae and
206 *Daphnia magna*. In 2024, the research emphasis was on the environmental exposure of polystyrene
207 MNPs in aquatic ecosystems and the toxicity mitigation potential of NOM forms, such as humic
208 acid and dissolved organic matter (DOM). This visualization provides a clear and concise overview
209 of the evolving research trends in the field of interactions between MNPs and NOM and their
210 implications for toxicity mitigation in aquatic species. It helps researchers and policymakers to
211 understand the focus areas over time and identify emerging topics in the rapidly developing field.

212 **3.0 Natural organic matter**

213 Generally, NOM is categorized into dissolved organic matter (DOM) and particulate organic
214 matter (POM). The complex structure of DOM makes its complete molecular characterization
215 challenging, although bulk parameters like dissolved organic carbon (DOC) concentration can be
216 readily measured (Pan et al., 2016). DOM often contains a significant fraction of humic substances,
217 such as humic acid (HA) and fulvic acid (FA), which are typically rich in aromatic content (Sharma
218 et al., 2021a). Being primarily hydrophobic, NOM can interact with the surfaces of MNPs,
219 influencing their behavior towards hydrophobic organic pollutants and heavy metals (Cao et al.,
220 2022; Velzeboer et al., 2014). Based on its origin, NOM is classified into three primary categories:
221 (1) Allochthonous NOM, derived from terrestrial sources and composed of FA, humin and HA;

(2) Autochthonous NOM, produced within the aquatic environment, encompassing extracellular polymeric substances (EPS) released by algae, bacteria, and other microorganisms; and (3) Anthropogenic NOM, originating from human activities, such as wastewater treatment plant effluents, domestic and agricultural runoff, and industrial discharges (Ali et al., 2022). These interactions between NOM components and MNPs can lead to the formation of complex aggregates, influenced by various abiotic factors.

### 3.1 Eco-corona complex formation

NOM is a ubiquitous constituent in water and soil matrices and is associated with MNPs through various mechanisms, including chemical bonding and physical interactions. Adsorption of NOM onto MNPs can modify their size, reduce surface hydrophobicity, and alter their surface charge and interaction potential. The interaction between NOM and MNPs can lead to the formation of layers of biomolecules adsorbed onto the MNP surface, commonly referred to as an eco-corona (EC) (Liu et al., 2022). The term "eco-corona" (EC) is defined as the layer of biomolecules and environmental constituents (composed of NOM components, proteins, and other organic matter) that forms on the surface of MNPs upon their release into the environment. The EC is primarily stabilized by hydrogen bonding, hydrophobic interactions, and van der Waals forces (Johnson et al., 2009). The EC formed on MNPs can be described as comprising "hard" and "soft" corona layers (Junaid and Wang, 2021). The "hard" corona refers to a closely bound single layer of molecules that bind to the MNP surface. In contrast, "soft" corona is defined by a loosely bound, dynamic layer of biomolecules that associates with the outer surface of the more stable and tightly bound "hard" corona. The composition of the "soft" corona is dynamic and readily exchangeable with new molecules, unlike the more stable and persistent "hard" corona (Liu et al., 2022) (**Figure 2**).

NOM adsorbs onto both primary and secondary MNPs, often competing for binding sites during EC formation. Cedervall *et al*. first described the formation of a (protein) corona (Cedervall et al., 2007), wherein interactions between nanoparticles and biomolecules in a biological environment create a layer of adsorbed proteins on the nanoparticle surface. Previously, several biomolecules, such as HA, FA, sodium alginate, and EPS, were utilized to determine the formation and fate of EC (Canesi et al., 2017). Nasser and Lynch (2016) observed that EC protein complexes formed by *Daphnia magna* neonates after 6 hours of exposure to carboxyl-modified polystyrene nanoplastics (COOH-PSNPs) and $NH_2$-PSNPs. The EC formation on amino-modified nanoplastics $NH_2$-PSNPs (100-120 nm) with HA and FA using *Daphnia magna* was also reported by Fadare *et al*. (Fadare et al., 2020). Likewise, the EC complexes were formed in the presence of HA and FA after 6 hours of exposure of COOH and $NH_2$ PS-NPs to *Daphnia magna* neonates (Zhang et al., 2022a). Extracellular polymeric substances (EPS) were extracted from the microalgae *Scenedesmus obliquus* and found a strong EC layer on COOH-PSNPs and $NH_2$-PSNPs (Das et al., 2023). Another study reported the EPS isolation from an algal suspension of *Chlorella pyrenoidosa* and found that the EC layer (18 μm) on polystyrene microplastics (PSMPs) was facilitated by $Ca^{2+}$ ions, bridging the EPS via carboxyl groups (Xiong et al., 2023). Notably, high molecular weight protein bands typically > 150 KDa were observed on PSNPs and COOH-PSNPs extracted from EPS. This phenomenon occurred in the presence of elevated $Cl^-$ and $SO_4^{2-}$ levels in marine water (Harris, 2020).

## 4.0 MNPs and NOM interaction and factors influencing EC formation

Upon entering aquatic environments, MNPs undergo various transformations that affect their physicochemical state, bioavailability, and toxicity to aquatic organisms (Alimi et al., 2018; Andrady, 2011). The association between NOM and MNPs is governed by both intrinsic and

extrinsic properties, mediated through intermolecular forces such as electrostatic and hydrophobic interactions. These interactions are largely dependent on the MNPs properties including particle size, surface chemistry, functional groups, the characteristics of NOM (e.g., molecular weight, aromaticity, functional groups), and the medium conditions (e.g., salinity, temperature, pH, light intensity, ionic strength) (Bhargava et al., 2018; Khan et al., 2015; Wang et al., 2015; Yin et al., 2020). Additionally, the chemical composition of the MNPs (polymer type, additives) significantly influences their interaction with NOM and consequently affects their toxicity to aquatic species (Wang et al., 2021b).

### 4.1 Polymer type, particle size, and ionic strength

MNPs-NOM interactions are strongly influenced by MNP physicochemical properties, such as particle size, density, and polymer type (Zhang et al., 2022b). NOM can adhere to the MNP surface through several interactive forces, such as hydrophobic interactions, electrostatic interactions, π-π interactions, hydrogen bonding, and van der Waals forces (Ali et al., 2022). Additionally, the polymer type and its crystallinity can exert significant effects due to their distinct structures and surface properties. Particle size, ionic strength, and surface properties of MNPs greatly influence their binding potential with NOM (Junaid et al., 2024). Previous studies have observed that smaller particles generally exhibit a greater tendency to form aggregates of larger size compared to their initial dimensions, relative to larger particles (Sharma et al., 2021b). For instance, smaller particles, particularly those below a certain size threshold (e.g., < 0.2 μm), typically exhibit a greater propensity for aggregation compared to larger microplastic particles, primarily due to their higher surface-area-to-volume ratio, which enhances interfacial interactions (Wang et al., 2021a; Yan et al., 2021b). A study highlighted that 50 nm NPs formed larger aggregates with EPS than 100-500 nm NPs in the presence of HA (Summers et al., 2018). Furthermore, Liu *et al*. suggested that

aggregate formation is likely enhanced with divalent cations (e.g., $Ca^{2+}$, $Mg^{2+}$) in the medium (Liu et al., 2019a). These cations can compress the electrical double layer surrounding the particles, reducing electrostatic repulsion and promoting aggregation. Meng *et al*. found that smaller PS-NPs (20 nm and 40 nm) exhibited more adverse effects compared to larger particles (60 nm and 100 nm) in crustacean species (Meng et al., 2023).

PSNPs functionalized with a single surface group (e.g., -COOH or $-NH_2$) maintained stable surface charges (positive or negative) across a varied pH range, with a high surface area available for adsorption (Pochelon et al., 2021). In addition, the availability of organic matter, primarily NOM and alginate, can significantly impact the stability of these PSNPs more profoundly than inorganic colloids, ultimately influencing their toxicity (Pradel et al., 2021). Saavedra *et al*. revealed that positively charged $NH_2$-PSNPs formed aggregates more rapidly with negatively charged HA and sodium alginate than negatively charged COOH-PSNPs did (Saavedra et al., 2019). Likewise, positively charged aminated PS formed strong aggregates with HA (Meng et al., 2023). The surface functionalization of MNPs can significantly influence the aggregation process, either enhancing or inhibiting it depending on the functional group and environmental conditions (Lowry et al., 2012). According to a previous report (Wegner et al., 2012), COOH-PSNPs with an initial size of 30 nm readily aggregated to sizes exceeding 1000 nm within 30 minutes in salt water.

Sulfate-functionalized PS also exhibited comparable behavior in different monovalent electrolytes, NaCl and KCl, at pH 4 (Montes Ruiz-Cabello et al., 2015). Although research on plastic aggregation with NOM is expanding, the effects are often complex and context-dependent, making broad generalizations challenging. Walker and Bob (2001) found that the presence of polysaccharides, FA, and HA reduced PSNP aggregation; nevertheless, more studies are required to fully understand the influence of NOM components on MNP stability. Additionally, Li *et al.* (Li

et al., 2019) demonstrated that HA can attenuate the settling rate of PSNPs in aquatic environments. This reduction is attributed to steric hindrance and enhanced electrostatic repulsion resulting from HA adsorption onto NPs via π-π interactions. Zhang (2017) suggested that MPs can bind with both organic and inorganic particles, resulting in an elevation of their size and density. This process may enhance their deposition onto benthic sediments and subsequently influence their bioavailability and toxicity. Furthermore, Nguyen *et al*. (Nguyen et al., 2020) demonstrated that microbial colonization can lead to the formation of aggregates incorporating MPs (**Table 1**). The adsorption of HA onto MNPs typically results in an increase in hydrodynamic size, a reduction in surface hydrophobicity, and an alteration of surface charge (often becoming more negative). Subsequently, the adsorbed HA layer creates steric hindrance and electrostatic repulsion between the NPs and negatively charged bacterial membrane components (e.g., lipopolysaccharides), thereby inhibiting NP binding to bacteria (Li et al., 2021b). Kansara *et al*. (Kansara et al., 2020) also observed that in systems containing HA, clay, and $TiO_2$ NPs, the zeta potential increased from -19 mV to -24 mV over 4 to 48 hours, indicating strong interactions between these components. The formation of these complexes contributed significantly to the mitigation of $TiO_2$ NPs toxicity in zebrafish embryos.

### 4.2 Particle concentration, pH, and temperature

Particle concentration, pH, and temperature also influence the interactions between MNPs and NOM (or other environmental constituents), and these interactions may in turn affect MNP toxicity. A study reported that higher temperatures decrease the Critical Coagulation Concentration (CCC) value, suggesting that elevated temperatures may destabilize PSNPs and promote aggregation in aqueous environments (Singh et al., 2019). Nevertheless, there is a lack of available data, especially in natural environments (Cai et al., 2018; Singh et al., 2019). Li et al. (Li et al.,

2019) highlighted that exposure to FA (0.5 mg/L) or HA (5 mg/L) in combination with aminated ($-NH_2$) or carboxylated (-COOH) PSNPs elevated reactive oxygen species (ROS) levels in [specify test organism/system]. In contrast, at a lower MNP concentration (1 μg/L), both types of functionalized PSNPs reduced ROS production in conjunction with NOM. Notably, at low NOM levels relative to PSNPs, NOM may partially cover the PSNP surface through electrostatic attraction, potentially reducing its toxicity (Li et al., 2021b). Lower NOM concentrations (e.g., 10 mg/L) exert minimal influence on the size of pre-formed large $TiO_2$ nanoparticle aggregates but can nonetheless significantly attenuate their toxicity (Kansara et al., 2020). For instance, negligible ROS production was observed in zebrafish after exposure to $TiO_2$ NPs alone or in combination with HA or HA+clay (Kansara et al., 2020).

Environmental conditions, such as pH, the presence of NOM, and multivalent ions, can significantly affect the colloidal stability and aggregation of NPs in the aquatic environment (Alimi et al., 2018; Cai et al., 2018; Zhou and Chu, 1991). Meng et al. (Meng et al., 2023) found that in lake water (pH 8.1), containing various ions and negatively charged NOM. When PSNPs interact with these components over a 48-hour test period, the zeta potential of PSNPs becomes significantly more negative, leading to increased aggregation and reduced toxicity to *Daphnia magna.* Previous studies have demonstrated that the solubility of HA is limited under strongly acidic conditions ($pH < 2$) and progressively increases with rising pH, especially above neutral pH (Haus et al., 2021). Further investigations into the binding behavior of HA under various pH conditions revealed that HA strongly adsorbs COOH-PSNPs, likely through interactions involving the COOH groups of HA and OH groups on the PSNP surface (Jayalath et al., 2018). In summary, the available literature indicates that smaller MNPs, MNPs with surface charges complementary to NOM (e.g., positively charged MNPs interacting with negatively charged NOM), and longer

aging times generally promote the formation of EC aggregates with NOM components like EPS. This aggregation process is a key factor in modulating MNP toxicity.

### 4.3 MNPs aging

DOM significantly influences the aging of MNPs under both UV light and dark conditions. During these processes, DOM can facilitate electron transfer, which may in turn promote the generation of ROS. This dual role of DOM under varying light conditions highlights its critical impact on the environmental transformation and degradation of MNPs (Junaid et al., 2024). The detection of elevated DOM levels during UV irradiation of MNPs can indicate the release of intermediate degradation products, some of which may undergo further mineralization (Ouyang et al., 2022). Aging of MPs, particularly through processes like photo-oxidation, often leads to a coarser surface texture and an increase in oxygen-containing functional groups (e.g., COOH, OH), which can enhance their sorption capacity for certain pollutants. At lower HA concentrations (< 10 mg/L), HA potentially increases the release of additives like bisphenol S (BPS) from MPs under light irradiation (Li et al., 2022). Natarajan *et al.* further observed that the propensity for EC formation and aggregation increased with the duration of exposure (or aging time) (Natarajan et al., 2020). For instance, the size of COOH-PSNPs increased from >282 nm to 512 nm after 12-48 hours of aging. In contrast, Ali *et al*. (Ali et al., 2022) suggested that aging processes (e.g., photo-oxidation) might reduce NOM adsorption on MNPs. This reduction could be due to aging-induced changes such as surface charge reversal and increased hydrophilicity, which in turn affect EC formation and toxicity.

Furthermore, oxidation index values, derived from FTIR spectra, offer a reliable measure of photo-induced chemical modifications, particularly the formation of carbonyl and hydroxyl groups (Fotopoulou and Karapanagioti, 2012). Similarly, surface functional group density (e.g., mmol/g

383 of –COOH or –OH) provides insight into the sorption potential of aged MNPs, especially in
384 relation to NOM binding (Liu et al., 2022). Changes in zeta potential can reflect surface charge
385 reversal, which influences electrostatic interactions and eco-corona formation (Ali et al., 2022).
386 Moreover, contact angle measurements serve as indicators of hydrophilicity shifts, with aged
387 particles typically exhibiting reduced angles due to increased polarity (Natarajan et al., 2020). In
388 biologically aged MNPs, microbial colonization can be quantified through EPS thickness and
389 biochemical composition, such as protein or polysaccharide content per unit area, which modulate
390 surface reactivity and steric hindrance (Ventura et al., 2024). Incorporating these metrics allows
391 for a more nuanced and mechanistic understanding of how aging influences NOM adsorption and
392 subsequent environmental behavior.

393 Biological aging of MNPs involves microbial colonization and biofilm formation, which
394 significantly alters surface chemistry and modulates interactions with natural organic matter
395 (NOM). Microorganisms such as bacteria, fungi, and algae adhere to MNP surfaces and secrete
396 extracellular polymeric substances (EPS), forming a hydrated matrix rich in proteins,
397 polysaccharides, and nucleic acids (Ghosh et al., 2019; Liaqat et al., 2019). This biofilm layer
398 introduces steric hindrance and modifies surface charge, often increasing hydrophilicity and
399 reducing the availability of active binding sites for NOM adsorption (Ventura et al., 2024).
400 Additionally, EPS components may compete with NOM for sorption sites or mask functional
401 groups critical for eco-corona formation (Ghosh et al., 2019) Biofilm-mediated degradation can
402 also lead to fragmentation and the release of additives or oligomers, further influencing surface
403 reactivity and NOM affinity (Wang et al., 2024). Unlike photoaging, which typically increases
404 oxygen-containing groups (e.g., –COOH, –OH), biological aging may suppress NOM adsorption
405 due to EPS shielding and altered interfacial chemistry. (Ghosh et al., 2019). These microbial

transformations affect aggregation behavior, vertical transport, and toxicity profiles, underscoring the need to distinguish biological aging pathways when evaluating MNP-NOM interactions in aquatic systems.

## 5.0 Role of NOM in MNPs toxicity mitigation

NOM adsorbs onto MNPs, forming an eco-corona that alters their surface properties and biological interactions. This modification reduces the bioavailability and toxicity of MNPs in aquatic organisms such as *Daphnia magna*. (Ijaz et al., 2025). Specifically, NOM-coated MNPs activate the Nrf2/ARE antioxidant pathway, enhancing the expression of detoxifying enzymes like catalase (CAT), superoxide dismutase (SOD), and glutathione S-transferase (GST), which collectively mitigate oxidative stress and inhibit apoptosis (Xue et al., 2020). Concurrently, NOM suppresses the NF-κB inflammatory pathway, reducing the expression of pro-inflammatory cytokines. These dual regulatory effects activation of Nrf2 and inhibition of NF-κB highlight NOM's role as a natural buffer against plastic-induced toxicity in freshwater ecosystems (Wang et al., 2022). These mechanisms are illustrated in Figure 5, which depicts the molecular pathways modulated by NOM-coated MNPs. (Ijaz et al., 2025).

### 5.1 Freshwater species

In most studies, NOM acts to mitigate MNP toxicity, primarily by adsorbing onto the MNP surface. This adsorption alters the biological reactivity and environmental fate of MNPs, thereby decreasing their toxic effects. Although elucidating the precise mechanisms of NOM-facilitated toxicity mitigation remains challenging, and the range of model organisms studied needs expansion, this review aims to address these gaps. By examining MNP-NOM interactions and their

implications for toxicity reduction in aquatic species, we aim to enhance our understanding of MNP fate and behavior in aquatic ecosystems.

Evidence suggests that PS-MNPs at environmentally relevant concentrations exhibit lower toxicological effects on aquatic species (Chen et al., 2011; Chen and Elimelech, 2006; Gao et al., 2009) (**Table 2**). Surface functionalization of MNPs, combined with the presence of natural organic matter (NOM), can alter their interactions with cellular membranes (and potentially intracellular organelles upon uptake), leading to variations in toxicity. The development of an EC on NPs decreases their toxicity, likely by passivating the particle surfaces through associations with organic molecules (Schultz et al., 2021). Saavedra *et al*. (Saavedra et al., 2019) exposed *Thamnocephalus platyurus* larvae*, Daphnia magna*, and *Brachionus calyciflorus* rotifers to COOH-PSNPs and $NH_2$-PSNPs (100 nm) with and without NOM for 24-96 hours. Higher $EC_{50}$ values (indicating lower toxicity) were observed in the presence of NOM, suggesting that EC formation reduced MNP toxicity. Fadare *et al*. (Fadare et al., 2020) explored the interactions between PS-NPs and three types of OM (NOM, FA, and HA) and their effects on *Daphnia magna*. Results showed that 7 days of exposure to individual NPs upregulated the genes linked with oxidative stress and endocrine disruption. However, the presence of NOM or HA markedly reduced nanoparticle-induced upregulation, while FA significantly amplified the upregulation of all the target genes. Furthermore, FA promoted enhanced protein adsorption onto NPs both in the *Daphnia magna* culture medium, facilitating EC formation, and in tissue homogenates, driving the establishment of a protein corona. In contrast, less protein adsorption occurred in media containing HA (Fadare et al., 2020). Shiu et al. [72] found that PS-MNPs of sizes 1 μm, 6 μm, and 55 nm exhibited reduced toxicity to the growth of phytoplankton species *Phaeodactylum tricornutum*, *Dunaliella tertiolecta, Thalassiosira pseudonana*, and *Skeletonema* sp. in the presence of NOM

(Shiu et al., 2020). Similarly, at a higher exposure level (100 mg $L^{-1}$) of PS-NPs, *Microcystis aeruginosa* growth decreases. However, this inhibition was followed by increased microcystin release and subsequent rapid growth after the initial phase. This phenomenon was attributed to the formation of a microcystin-corona (MC-corona), which may reduce direct MNP exposure (Zheng et al., 2021).

Wu et al. (Wu et al., 2019) reported that PSNPs with various functional groups (PS-COOH, n-PS-$NH_2$, p-PS-$NH_2$) exhibited dose-dependent acute toxicity to *Daphnia magna*. However, co-exposure with HA significantly mitigated this toxicity, increasing survival rates from 15% (in MNP-only groups) to 45-95%. Fadare *et al*. Fadare et al. (2019) investigated the toxicological effects of PS-MPs and PS-NPs on *Daphnia magna* neonates under conditions both with and without HA. The expression of stress response and detoxification biomarker genes (*cat*, *gst*, *hsp70*, and *pgp*) was upregulated in a dose-dependent manner, particularly without HA. Notably, HA at 50 mg/L mitigated the toxicity of a high dose of PS-NPs (400 mg/L), demonstrating its protective role. Lin et al. (Lin et al., 2020) observed that HA or a mixture of HA and PSMPs formed a layer that influenced the transfer of pollutants from the surrounding environment to the lipids in *Daphnia magna* gut after 36 hours of exposure. This interaction significantly reduced toxicity in most treatment groups.

It is noteworthy that the toxicity of MNPs is greatly influenced by the particle size, the absence or presence of NOM, and surface charges. For example, Liu et al. (Liu et al., 2019b) assessed the toxic effects of five differently sized PSMPs, with and without HA, on *Scenedesmus obliquus*. They revealed that particle size was a critical determinant of toxicity: larger particles did not markedly inhibit growth, while smaller particles induced oxidative stress. Furthermore, HA substantially mitigated the toxic effects of the smaller PSMPs. Scanning electron microscopy

images and ROS assays highlighted the role of HA in corona formation on the MNP surface. This corona formation reduces the affinity of MNPs for microalgae and mitigates their adverse effects (Liu et al., 2019b). Liu *et al*. (Liu et al., 2019b) also reported that co-exposure of *Danio rerio* to PS-NPs and natural acidic organic polymer (likely analogous to FA/HA) at low levels (1 µg/L and 1 mg/L) for 96 hours induced significant oxidative stress (**Figure 3I**). The particle size, surface charge, and aggregation behavior of MNPs, often modified by NOM, are critical factors influencing their toxicity (Meng et al., 2023). Supporting the role of EC, Giri, and Mukherjee [79] demonstrated that EC formation significantly mitigated the harmful effects of charged PSNPs ($NH_2$-PSNPs and COOH-PSNPs; 12.5-50 mg/L) on onion (*Allium cepa*) root cells.

### 5.2 Marine species

The available literature on the toxicological effects of MNPs in marine species in the presence of NOM is relatively limited compared to freshwater studies. Marques-Santos et al. (Marques-Santos et al., 2018) investigated the $NH_2$-PSNPs impacts after being combined with EDTA on immune cells of the sea urchin *Paracentrotus lividus* at low concentrations (1-25 µg/mL). It was found that EDTA mitigated $NH_2$-PSNP toxicity by decreasing apoptosis. This mitigation was facilitated by the protein corona formation dominated by the toposome precursor protein (TPP). Brandts et al. (Brandts et al., 2021b) highlighted the immunomodulatory effects of HA-coated PSNPs (0.02 and 20 mg/L) in European sea bass (Dicentrarchus labrax). Key biomarker genes related to steroidogenic stress were upregulated in most treatment groups; however, this upregulation was absent or attenuated in groups exposed to HA-coated PS-NPs. The development of an EC modulated the transcription of anti-inflammatory cytokine genes (e.g., *il10*, *tgfb*) and stress-related genes in kidney tissues (e.g., *mc2r* and *gr1*) (Brandts et al., 2021b). Similarly, Marques-Santos *et al*. (Marques-Santos et al., 2018) showed that protein corona

formation on $NH_2$-PSNPs increased nuclear alterations and decreased lysosomal membrane stability in sea urchin (*Paracentrotus lividus*) immune cells (coelomocytes). These effects were prevented by EDTA, indicating that the protein corona mediates the contact between $NH_2$-PSNPs and coelomocytes, facilitating NP uptake and toxicity. These findings suggest that the protein corona promotes NP recognition and internalization by cells, triggering toxic effects. In another study, Natarajan *et al*. (Natarajan et al., 2024) reported that EPS-mediated EC formation on PSNPs significantly reduced their toxicity to the marine alga *Chlorella* sp. Specifically, EC formation lessened the reduction in photosynthetic yield and helped maintain cell viability and membrane integrity. The degree of toxicity attenuation was influenced by the surface charge of the NP and their aging duration in the EPS medium. In contrast, Grassi et al. (Grassi et al., 2020) observed no significant toxicity from PS-COOH exposure (1-100 mg/L) to the marine diatom *Phaeodactylum tricornutum*, regardless of EPS presence. However, exogenous EPS facilitated EC formation, which reduced ROS production. This suggests that the EPS-corona may possess antioxidant scavenging activity.

## 6.0 Eco-corona formation with co-occurring pollutants

The development of an EC on MNPs can significantly alter their capacity to adsorb co-existing organic pollutants, thereby influencing the overall toxicity profile (Wu et al., 2022). While studies are emerging, the combined effects of HA, MNPs, and other co-contaminants on toxicity mitigation in aquatic species require further characterization to fully understand the complex interactions. Among the available studies, benzo[a]pyrene (BaP), a polycyclic aromatic hydrocarbon, adsorbs onto PSNPs primarily via hydrophobic interactions. The presence of HA significantly hindered BaP adsorption onto anionic NPs, likely due to competitive binding for adsorption sites (Feng et al., 2022). Similarly, in systems containing HA, 40 nm PSNPs, or

519 PVCNPs, and ciprofloxacin (CIP), the sorption capacity for CIP increased with HA concentration
520 [85]. The observed enhancement was primarily driven by strengthened electrostatic interactions
521 between protonated CIP and negatively charged nanoparticles or HA under acidic conditions, with
522 HA potentially modulating this interaction. The rapidly formed HA layer may also limit the
523 bioavailability of CIP (Yan et al., 2020). In contrast, the sorption capacity of CIP onto polyethylene
524 (PE) MPs was diminished in the presence of HA (Atugoda et al., 2021). This decrease was
525 attributed to the strong hydrogen bonding complexes between HA and CIP, which subsequently
526 decreased CIP bioavailability and toxicity. Li *et al*. (Li et al., 2021a) found that HA reduced the
527 binding affinity of tetrabromobisphenol-A (TBBPA) onto four types of MNPs (PS, PP, PE, PVC).
528 This decrease was attributed to competitive binding between TBBPA and HA for adsorption sites
529 on the MNP surfaces.

530 Khoshnamvand et al. (Khoshnamvand et al., 2024a) further revealed that the acute toxicity
531 (96 h) of combined $NH_2$-PSNPs and atrazine (ATZ) (0.5-2 mg/L) to *C. vulgaris* was reduced in
532 the presence of 5 mg/L HA than treatments without HA. Exposure to HA at an environmentally
533 relevant concentration (ERC) significantly reduced toxicity to *C. vulgaris*, demonstrating an
534 antagonistic interaction between the toxicants. This mitigation is likely due to EC formation,
535 resulting in the entrapment (adsorption/complexation) of both ATZ and NP particles by HA
536 (**Figure 3II**). Khoshnamvand *et al*. (Khoshnamvand et al., 2024a) investigated the chronic toxicity
537 of co-exposed aminated polystyrene ($NH_2$-PSNPs) and atrazine (ATZ) to *Chlorella vulgaris*, with
538 or without HA. The results demonstrated that co-exposure to $NH_2$-PSNPs and ATZ produced a
539 synergistic effect, significantly inhibiting algal growth. Conversely, HA markedly decreases the
540 toxicity, likely due to EC formation on the particle surfaces (Khoshnamvand et al., 2024a) (**Figure**
541 **4I**). Tong *et al*. (Tong et al., 2020) investigated the impact of tetracycline (TC) (0.5-10 mg/L) on

the microalga *Coelastrella* sp. in the context of HA exposure. Notably, the toxicity of TC decreased significantly with increasing HA concentration. Notably, TC-induced toxicity declined markedly with increasing HA concentrations. This attenuation was reflected by enhanced algal biomass, elevated chlorophyll-a and total protein levels, and a reduction in oxidative stress within the cells. Similarly, HA also decreased TC toxicity in *E. coli*, reducing the genetic expression of antibiotic-resistance genes (Chen et al., 2015).

Kansara *et al*. (Kansara et al., 2020) assessed the toxicity of $TiO_2$ NPs to *Danio rerio* embryos when co-exposed with humic acid (HA) and clay minerals. While $TiO_2$ NPs exposure upregulated genes related to the dorsoventral axis and neural network development, the HA alone or HA+clay demonstrated a shielding effect on embryonic development and mitigated $TiO_2$ NP toxicity. Li *et al*. (Li et al., 2022) reported that high DOM levels can decrease the adsorption of hydrophobic organic pollutants onto MNPs. For example, specific DOM components or mixtures reduced the adsorption of tannic acid onto polystyrene microplastics by 20-48%. In contrast, transcriptomic analysis by Qiao *et al*. (Qiao et al., 2019) indicated that the presence of PSMPs enhanced copper (Cu) adsorption (likely by providing additional surfaces or facilitating EC formation containing Cu). This interaction led to increased oxidative stress and elevated Cu bioaccumulation in the zebrafish liver. Lin *et al*. (Lin et al., 2020) used modeling to show that PSMPs coated with HA had a negligible effect on PAH uptake in the *Daphnia magna* intestine. Experimentally, they found that HA or a mixture of HA and PSMPs limited the uptake of PAHs from the environment into the lipid accumulation of *Daphnia magna*. Similarly, Yu *et al*. (Yu et al., 2022) observed a negligible impact of NOM on the combined toxicity of CuNPs and ZnONPs in *Daphnia magna.* Li *et al*. (Li et al., 2024) studied the antimony (Sb) toxicity effects to *Daphnia magna* at ERC in the presence of FA, HA, and cations ($Ca^{2+}$, $Mg^{2+}$, $Na^{+}$). The $EC_{50}$ for Sb alone

565 decreased from 90 mg/L at 24 h to 63 mg/L at 48 h, indicating increased toxicity over time. Notably,
566 both FA and HA, as well as the cations, provided significant protection against Sb toxicity,
567 increasing survival (**Figure 4II**).

568 While NOM demonstrates a protective role against MNP toxicity in both freshwater and
569 marine ecosystems, the underlying mechanisms and contextual modifiers differ significantly. In
570 freshwater systems, HA and FA often facilitate robust eco-corona (EC) formation on MNPs,
571 leading to reduced oxidative stress, suppression of stress-inducible genes, and enhanced organism
572 survival (Fadare et al., 2020). These effects are influenced by particle size, surface charge, and
573 NOM concentration. In contrast, the relatively high salinity and ionic strength in marine
574 environments may affect NOM solubility and corona stability, thereby modulating its efficacy.
575 Marine studies although fewer, highlight the role of protein-rich coronas (e.g., toposome,
576 exopolysaccharides) in reducing apoptosis and immunotoxicity in sea urchins and sea bass
577 (Brandts et al., 2021a). However, inconsistent outcomes, such as minimal toxicity mitigation by
578 EPS on PS-COOH NPs in diatoms. Bellingeri et al. (2020), suggest that marine toxicity attenuation
579 may be more variable and species-specific. These inter-ecosystem contrasts underscore the
580 importance of considering environmental parameters such as salinity, NOM type, and particle
581 aging in predicting MNP fate and biological impact.

582 **7.0 Research gaps and future recommendations**

583 Current understanding of natural organic matter (NOM)-MNPs interactions and their role
584 in mitigating aquatic toxicity remains constrained by critical knowledge gaps. To advance
585 mechanistic predictions and ecological risk assessment, future research must prioritize several key
586 directions.

587 Despite substantial progress using transcriptomics and proteomics to investigate NOM-
588 mediated modulation of MNP toxicity, key knowledge gaps remain that limit comprehensive
589 mechanistic insight. Current omics datasets are largely restricted to a narrow range of aquatic
590 species, undermining the ecological validity and cross-species extrapolation of DEG and protein
591 expression profiles (Recio-Vega et al., 2023). Moreover, the compositional variability of NOM
592 such as differences in humic and fulvic content is rarely characterized or standardized across
593 studies, complicating comparative omics workflows (Steen et al., 2020). Proteomic studies often
594 omit spatiotemporal resolution or translational modifications (PTM) dynamics, which are critical
595 for modeling real-time changes in antioxidant responses, membrane integrity, and mitochondrial
596 function under MNP–NOM co-exposure. (Steen et al., 2020). To address these limitations, future
597 investigations should incorporate high-resolution omics platforms such as single-cell RNA-seq
598 and spatial proteomics, enabling tissue-specific insights into NOM–MNP interactions. Enhanced
599 bioinformatics tools are also needed to support signaling network reconstruction and design risk
600 analysis modeling based on genomic regions that control gene expression and molecular
601 phenotypes. (Recio-Vega et al., 2023). Integrating these technologies will refine environmental
602 risk assessment and inform targeted mitigation strategies for freshwater and marine ecosystems.

603 Molecular-scale mechanisms governing NOM adsorption dynamics and environmental
604 corona (EC) formation on MNPs require rigorous elucidation. A key focus should be
605 understanding how these mechanisms precisely control MNP bioavailability and intracellular
606 toxicity pathways. This necessitates differentiating the behavior of structurally distinct NOM
607 fractions (e.g., fulvic acids, humic acids, extracellular polymeric substances) during interactions,
608 as their type-specific effects on EC formation and resultant toxicity modulation are poorly resolved.

Beyond adsorption studies, significant unknowns persist in the bioaccumulation and trophic transfer of NOM-MNP complexes across diverse aquatic species. Research must expand to quantify uptake kinetics, tissue distribution, and transgenerational impacts, especially under realistic environmental scenarios involving co-existing stressors such as heavy metals, antibiotics, and per- and polyfluoroalkyl substances (PFAS). Concurrently, the dual role of NOM in regulating contaminant vector potential demands clarification: mechanistic conditions under which NOM either inhibits or enhances MNP sorption of organic pollutants, dependent on MNP physicochemical properties, pollutant nature, and NOM characteristics, must be systematically defined.

The inherent heterogeneity of MNPs represents another fundamental gap. Current studies disproportionately focus on limited size ranges (e.g., MPs: 0.2–280 μm; NPs: 20–100 nm) and polymer types, neglecting particle-specific toxicokinetics. Investigations should extend to broader size spectra and environmentally prevalent polymers. Furthermore, the transformation of MNPs via aging processes (e.g., UV exposure, oxidation) critically alters surface properties and NOM affinity, yet its long-term consequences for EC evolution, complex stability, and ecotoxicity are minimally explored.

Environmental realism in experimental design is essential but often lacking. The stability and toxicity of NOM-MNP complexes exhibit high sensitivity to fluctuating conditions (pH, salinity, temperature, and NOM composition). Consequently, studies must systematically evaluate these parameters under dynamic, field-relevant settings. Long-term fate assessments are equally imperative to understand the persistence, transformation, and time-dependent toxicity of complexes in natural hydrosystems, particularly under seasonal variations in hydrological and biogeochemical cycles.

Methodological limitations also impede progress. Advanced analytical tools are urgently needed for in situ characterization of NOM-MNP complex properties within environmental matrices and biological systems, enabling accurate quantification of interactions and bioeffects. Finally, ecological relevance must be strengthened by expanding test species diversity mainly marine species across trophic levels and life stages, establishing whether observed protective effects of NOM scale to population and community-level impacts.

Addressing these interconnected gaps will transform fragmented knowledge into a predictive framework, clarifying how NOM modulates MNP ecotoxicity under environmental complexity. This is foundational for developing evidence-based risk mitigation strategies for plastic pollution in aquatic ecosystems.

## 8.0 Conclusion

This review comprehensively evaluates evidence on the toxicity mitigation potential of NOM towards aquatic species exposed to MNPs. Collectively, the reviewed studies highlight the significant role of NOM in modulating the toxicity of MNPs in aquatic environments. NOM, including HA, FA, and EPS, forms an eco-corona on the surface of MNPs, reducing their biological reactivity and toxicity by passivating their surfaces and altering their interactions with cellular membranes and organelles. The presence of NOM significantly reduces the toxic effects of MNPs on various aquatic species, including crustaceans, algae, and fish, as evidenced by decreased oxidative stress, lower ROS production, and improved survival rates. NOM can also modulate the expression of genes related to detoxification, oxidative stress, and endocrine activity, often mitigating the upregulation induced by MNP exposure. The toxicity of MNPs is influenced by their particle size and surface charge, with smaller particles and specific surface functionalization exhibiting higher toxicity, which can be mitigated by NOM. These findings highlight the critical

need to consider environmentally relevant exposure conditions and the widespread presence of NOM in assessing the ecological risks of MNPs. Collectively, the evidence demonstrates that NOM holds significant potential to mitigate the toxicity and environmental impact of MNPs in aquatic ecosystems.

## Acknowledgments

The authors would like to acknowledge the funding support from the Ministry of Higher Education Malaysia under the Talent and Publication Enhancement Research Grant, TAPE-RG vote number 55448 to N.H, Chongqing Technology Innovation and Application Development Sichuan-Chongqing Special Key Project (CSTB2024TIAD-CYKJCXX0017), High-level Talents Project of Chongqing Medical University (No. R4014), and Chongqing Postdoctoral Innovation Mentor Studio (X7928 D.S.P.).

## Conflicts of interest

The authors declare no conflict of interest.

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**Table 1** Influencing factors of MNPs aggregation

| Factors | Main findings | Reference |
|---|---|---|
| Temperature, Particle size, river water and seawater | In artificial saltwater and coastal seawater, where the ionic strength is higher, NPs can aggregate up to 2000 nm from 70 nm, and this aggregation is enhanced by temperature and particle concentration. | (Lee and Fang, 2022) |
| Electrolyte concentrations | Before reaching a maximum value at the diffusion-limited regime, the aggregation rates of PS NPs rose with an increase in electrolyte concentrations throughout a wide range of electrolytes. | (Kim et al., 2022) |
| Stability ratio | With rising electrolyte concentrations i.e., NaCl, $CaCl_2$, and $LaCl_3$, the stability ratios dropped until they reached unity. | (Kim et al., 2022) |
| Ionic Strength | Because ionic strength screens out electrostatic repulsion, it affects the stability of nanoplastics. In a broad variety of IS found in the aquatic environment, NPs exhibit great stability. | (Singh et al., 2019) |
| Salinity, Humic Acid | The aggregation of four different NPs (PS, PS-COOH, n-PS-$NH_2$, and p-PS-$NH_2$) with varied functional groups and charges was greatly enhanced by salinity, whereas HA mostly stabilized the three negatively charged NPs. The positively charged p-PS-$NH_2$, on the other hand, first accumulated considerably but then stabilized with the increased HA concentration. | (Wu et al., 2020) |

**Table 2 *In vivo* toxicity modulation in the presence of NOM and MNPs observed in aquatic species**

| Toxicity model | MNP type & size) | NOM type &dose | MNPs exposure dose | Exposure time | Modulation Toxicity endpoints | Reference |
|---|---|---|---|---|---|---|
| **Freshwater species** | | | | | | |
| *Scenedesmus obliquus* | PS, PS-$NH_2$ (0.1, 0.5, 1, & 2 μm) | Humic acid-HA:1–15 mg/L | 0–100 mg/L | - | The addition of HA significantly alleviated the toxicity of smaller-size MPs, but not of the larger ones, indicating modulating toxicity. | (Liu et al., 2019a) |
| *Chlorella vulgaris* | PS-$NH_2$ (200 nm) | HA: 300 mg/L | 5-10 mg/L | 72 h | HA significantly mitigated PS-$NH_2$ toxicity to *C. vulgaris* biomass and chlorophyll α end-points | (Hanachi et al., 2022) |
| *Chlorella vulgaris* | PS–$NH_2$ (100 nm) | HA: 1 mg/L | 0, 0.05, 0.1, 0.2, 0.3 and 0.4 mg/L | 21 days | The exposure of PS–$NH_2$+ATZ treatments to the HA could remarkably reduce their toxicity. In addition, HA was able to decrease the changes in the expression of genes related to oxidative stress | (Khoshnamvand et al., 2024a) |
| *Chlorella vulgaris* | PS–$NH_2$ (100 nm) | HA: 5 mg/L | 0.5, 1, and 2 mg/L | 96 h | The addition of environment-relevant concentration of HA significantly alleviated its toxicity to *C. vulgaris,* indicating an antagonistic effect due to the emergence of an eco-corona, and entrapment and sedimentation of PS-$NH_2$+ATZ particles by HA. | (Khoshnamvand et al., 2024b) |
| *Daphnia magna* | ZnO-NPs + $TiO_2$-NPs (25 nm) | NOM: 20 mg/L | 100 mg/L | 48 h | NOM alleviated the $TiO_2$NPs toxicity in all testing scenarios. In contrast, after the addition of NOM, the ZnONPs did not decrease toxicity. | (Cupi et al., 2015) |
| *Daphnia magna* | PS-$NH_2$ (60 nm) | HA:1–50 mg/L | 1–400 mg/L | 96 h | NPs were much more toxic than MPs after 10 mg/L exposure showing 70% | (Fadare et al., 2019) |

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|---|---|---|---|---|---|---|
| | | | | | mortality in 96 h but MPPs (as high as 400 mg/L) caused no mortality in all samples. In addition, HA played a protective role against NPs toxicity at environment-relevant levels. | |
| *Daphnia magna* | PS(-$CNH_2NH^{2+}$), PS (-$COO^-$) (0.2 μm) | HA: 2 mg/L | 5 mg/L | 24 h | Humic acid reduced significantly the toxicity of both amidine and carboxyl PS nanoplastics to the *daphnia magna* | (Saavedra et al., 2019) |
| *Daphnia magna* | Polystyrene latex nanoparticles-PLNPs (50–100 nm) | FA and DOM: 5 mg/L | 10 mg/L | 3 and 24 h | Toxicity test indicated the PLNPs exhibited acute toxicity and physical damage to Daphnia magna. However, the presence of FA and DOM formed a bridge and hence helped to mitigate the toxicity. | (Zhang et al., 2019) |
| *Daphnia magna* | PS, PS-$NH_2$ (100 nm) | HA: 5–50 mg/L | 20-30 mg/L | 48 h | The presence of HA effectively alleviated the toxicity of PS and p-PS single bond $NH_2$, as the survival rates increased from 15% to 45%, 95%, and 100% | (Wu et al., 2019) |
| *Daphnia magna* | PS, (100 nm), PAHs | HA: 100 mg/L | 1 mg/L | 36 h | The HA or the HA-PS matrix would formulate a layer and the mass transfer of PAHs from the matrix to lipids in the gut. However, the decrease in toxicity was profound in most of the samples. | (Lin et al., 2020) |
| *Daphnia magna* | PS-$NH_2$ (60 nm) | HA & FA: 10 mg/L | 50 mg/L | 7 days | NPs increased the upregulation of all genes related to detoxification, oxidative stress, and endocrine activity after exposure. Interestingly, the presence of NOM mainly HA resulted in the mitigation of gene expression, whereas significantly higher upregulation of all of the genes was observed with FA. | (Fadare et al., 2020) |

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| *Daphnia magna* | CuNPs + ZnONPs (25 nm) | NOM: 1, 10 and 20 mg/L | 1, 10, 20 mg/L | 48 h | NOM had no significant impact on the joint toxicity of CuNPs + ZnONPs in daphnia magna. | (Yu et al., 2022) |
| *Daphnia magna* | PS-NH-$NH_2^+$ (20-100 nm) | NOM | 0.5-20 mg/L | 24 h | The surface charge and aggregation behavior of NOM are the most important in reducing the toxicity of PS-NPs | (Meng et al., 2023) |
| *Caenorhabditis elegans* | PS (100 nm) | OM: 1.7 mg/L | 2-200 mg/L | - | The surface functionalization along with the OM may change the nature of NPs interactions with cell membranes leading to variations in toxicity. Eco-corona formation reduced the toxicity of all nanoplastics indicating that organic molecule associations may passivate surfaces. | (Schultz et al., 2021) |
| *Zebrafish (Danio rerio)* | PS-COOH, PS-$NH_2$ (50-100 nm) | FA & HA: (0.5 mg/L and 5 mg/L) | 1 µg/L & 1 mg/L | 96 h | The FA and HA combined with the NPs showed oxidative stress responses in *D. rerio*. However, the toxicity decreases on the concentration and types of both NPs particle size and NOM interaction. | (Liu et al., 2019b) |
| **Marine species** | | | | | | |
| Sea urchin *(Paracentrotus lividus)* | PS–$NH_2$ (50 nm) | Ethylenediamin etetraacetic acid (EDTA) | 1, 5, 10, and 25 µg/mL | 48 h | In the presence of EDTA, these toxic effects of PS-NPs mainly apoptosis were eliminated, indicating the involvement of NOM and EDTA in facilitating the interaction between PS–$NH_2$ and coelomocytes. | (Marques-Santos et al., 2018) |

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|---|---|---|---|---|---|---|
| *Dicentrarchus labrax* | PS-MPs (115 nm) | HA (1 mg/L) | 0.02 and 20 mg/L | 96 h | PSNPs and HA elicited an immuno-modulatory response, with an activation of steroidogenic stress-related pathways. In addition, An upregulation of anti-inflammatory cytokine (*il10, tgfb*) and stress-related (*mc2r, gr1*) transcripts were observed after individual and joint exposure of HA and PSNPs invivo. | (Brandts et al., 2021b) |

**Figure captions**

**Figure 1.** Meta-Analysis of studies related to microplastics/nanoplastics toxicity mitigation utilizing natural organic matter in aqueous species based on co-occurrences of keywords, such as "microplastics," "nanoplastics," "toxicity mitigation," "natural organic matter," "humic acid" and "aqueous species". Font size denotes the recurrence frequency of individual keywords across the selected publications. Node diameter is quantitatively scaled to reflect keyword co-occurrence frequency, with larger nodes representing more frequent co-occurrences. Curved edges connecting nodes indicate co-occurrences within the same publication, and the spatial proximity between nodes is inversely proportional to their co-occurrence count closer nodes co-occur more frequently (a) Network visualization and (b) Overlay visualization of studies over the past four years.

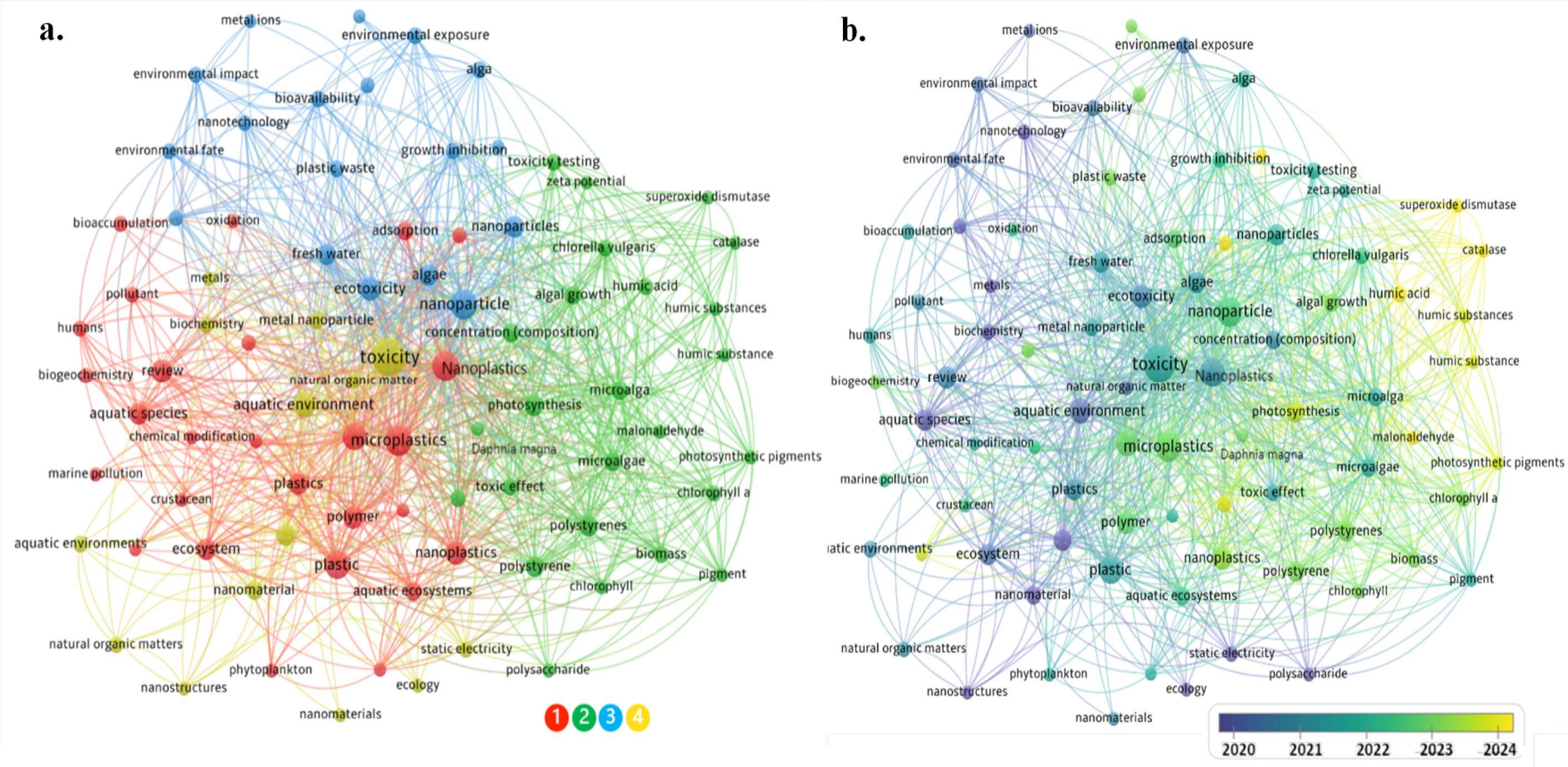
**Figure 2.** Illustration showing the eco-corona formation and the factors affecting the toxicity modulation in aquatic species. Created with BioRender (www.biorender.com).

**Figure 3.** (I) Reactive oxygen species (ROS) production and accumulation were observed after NPs (1 mg/L) exposure with the presence and absence of HA and FA in zebrafish. Reprinted with permission from the publisher (Liu et al., 2019b). (II) Genetic expression of the GR, SOD, and CAT genes after 96 h PS-$NH_2$ + ATZ with HA exposure in *C. vulgaris*. Images reproduced with the permission (Khoshnamvand et al., 2024b).

**Figure 4.** (I) SEM images displaying mitigating toxicity in *C. vulgaris* by showing healthy algal cells, compared to the individual NPs and NPs+ATZ exposure. Reproduced after permission (Khoshnamvand et al., 2024a). (II) Effective concentration ($EC_{50}$) values show reduced toxicity of Antimony (Sb) after joint exposure to HA and FA in *Daphnia magna* (Li et al., 2024).

**Figure 5**. Illustration of cellular-level toxicity mechanisms induced by MNPs in aquatic organisms, and the mitigating role of NOM. Adapted from Ijaz et al, 2025.

**Figure 1**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humic substances
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bioaccumulation
oxidation
adsorption
nanoparticles
chlorella vulgaris
catalase
fresh water
metals
algae
ecotoxicity
humic acid
pollutant
nanoparticle
algal growth
humic substances
humans
biochemistry
metal nanoparticle
concentration (composition)
toxicity
Nanoplastics
humic substance
biogeochemistry
review
natural organic matter
microalga
aquatic species
aquatic environment
photosynthesis
chemical modification
microplastics
malonaldehyde
Daphnia magna
photosynthetic pigments
marine pollution
microalgae
plastics
toxic effect
crustacean
chlorophyll a
polymer
polystyrenes
ecosystem
nanoplastics
biomass
plastic
polystyrene
pigment
nanomaterial
aquatic ecosystems
chlorophyll
natural organic matters
static electricity
phytoplankton
polysaccharide
nanostructures
ecology
nanomaterials
2020
2021
2022
2023
2024

**Figure 2**

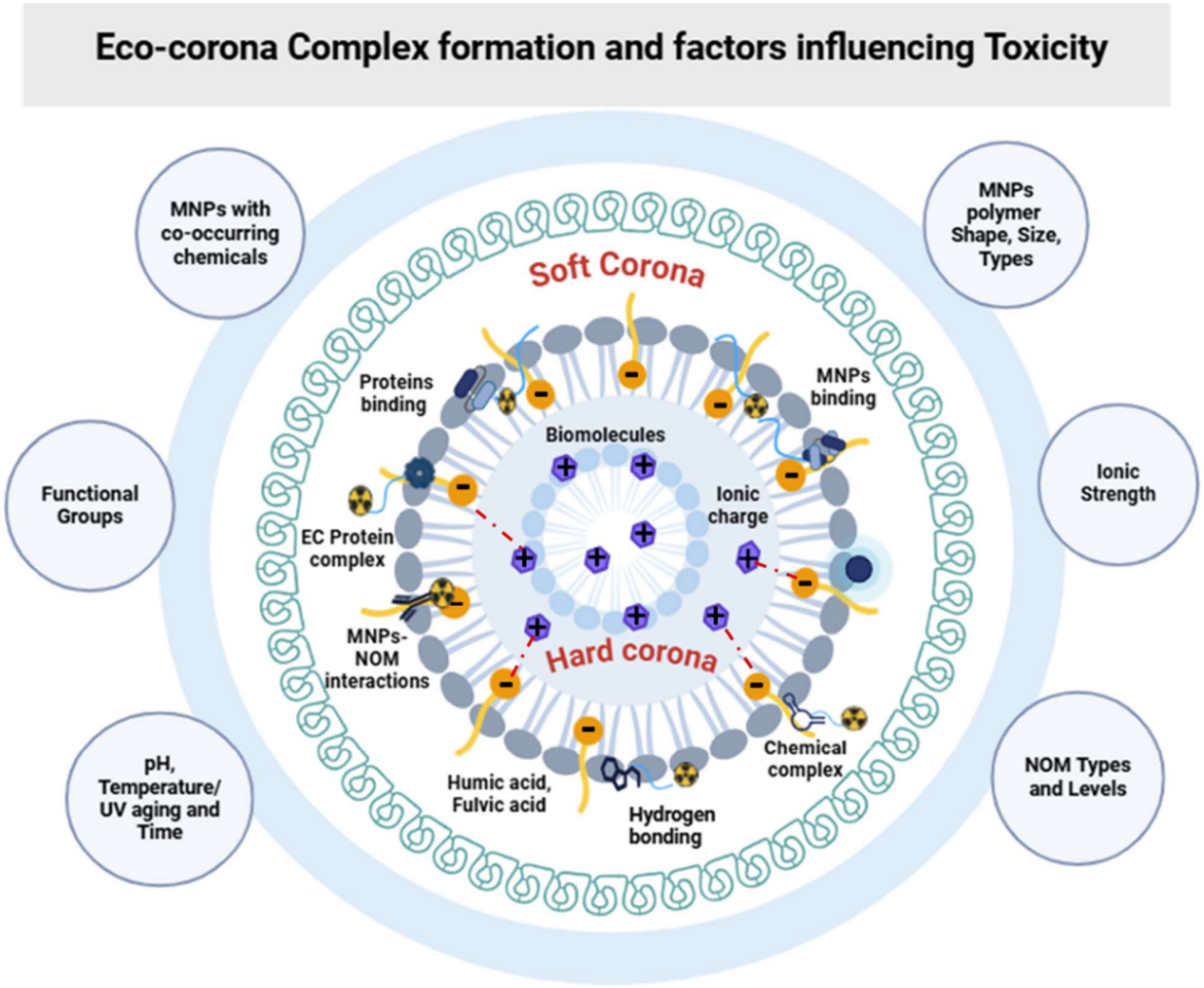

Eco-corona Complex formation and factors influencing Toxicity
MNPs with co-occurring chemicals
MNPs polymer Shape, Size, Types
Functional Groups
Ionic Strength
pH, Temperature/ UV aging and Time
NOM Types and Levels
Soft Corona
Hard corona
Biomolecules
Proteins binding
MNPs binding
Ionic charge
EC Protein complex
MNPs-NOM interactions
Humic acid, Fulvic acid
Hydrogen bonding
Chemical complex

**Figure 3**

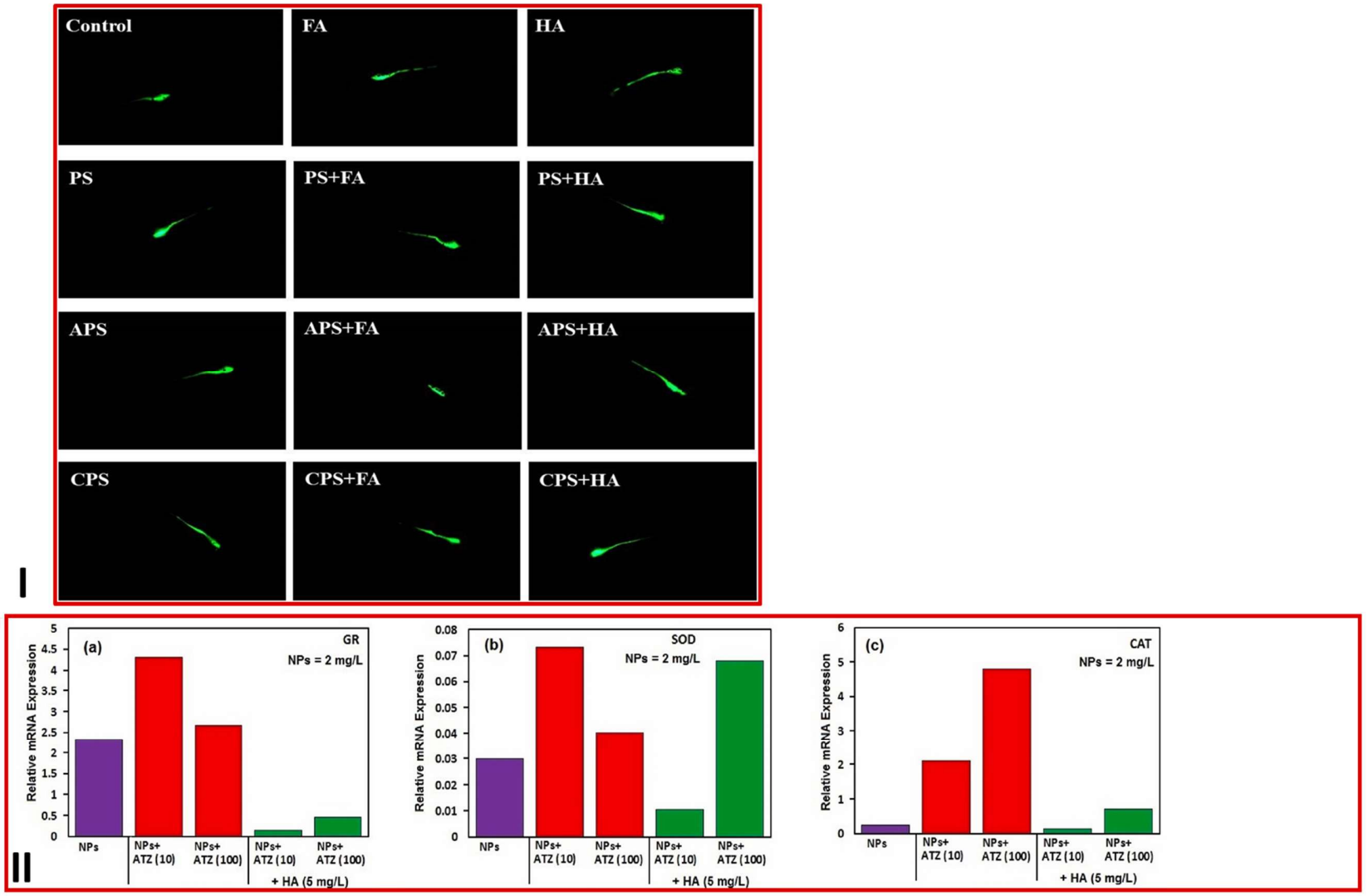

Control
FA
HA
PS
PS+FA
PS+HA
APS
APS+FA
APS+HA
CPS
CPS+FA
CPS+HA
I
II
(a)
GR
NPs = 2 mg/L
Relative mRNA Expression
(b)
SOD
NPs = 2 mg/L
(c)
CAT
NPs = 2 mg/L
NPs
NPs+ ATZ (10)
NPs+ ATZ (100)
+ HA (5 mg/L)

**Figure 4**

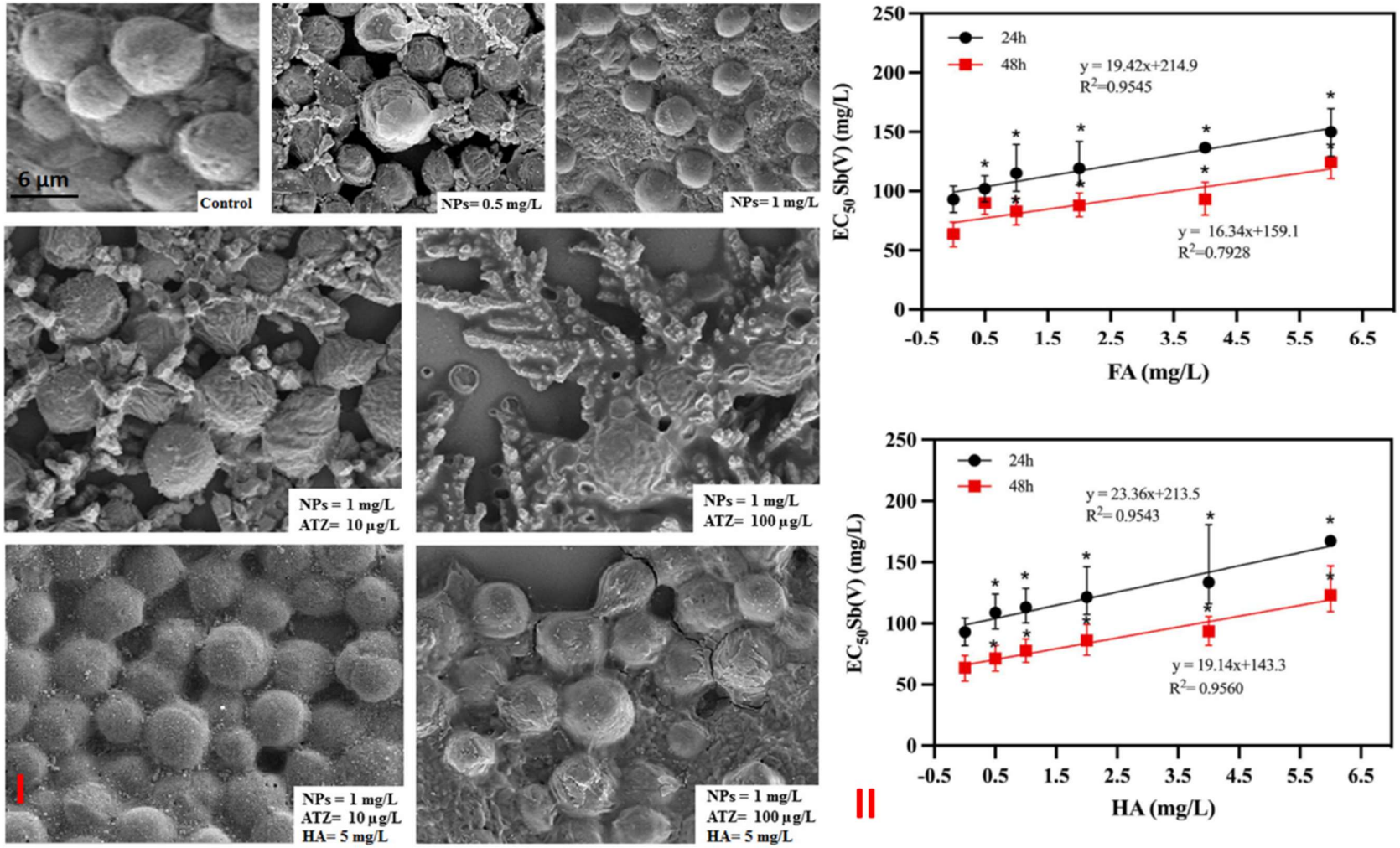
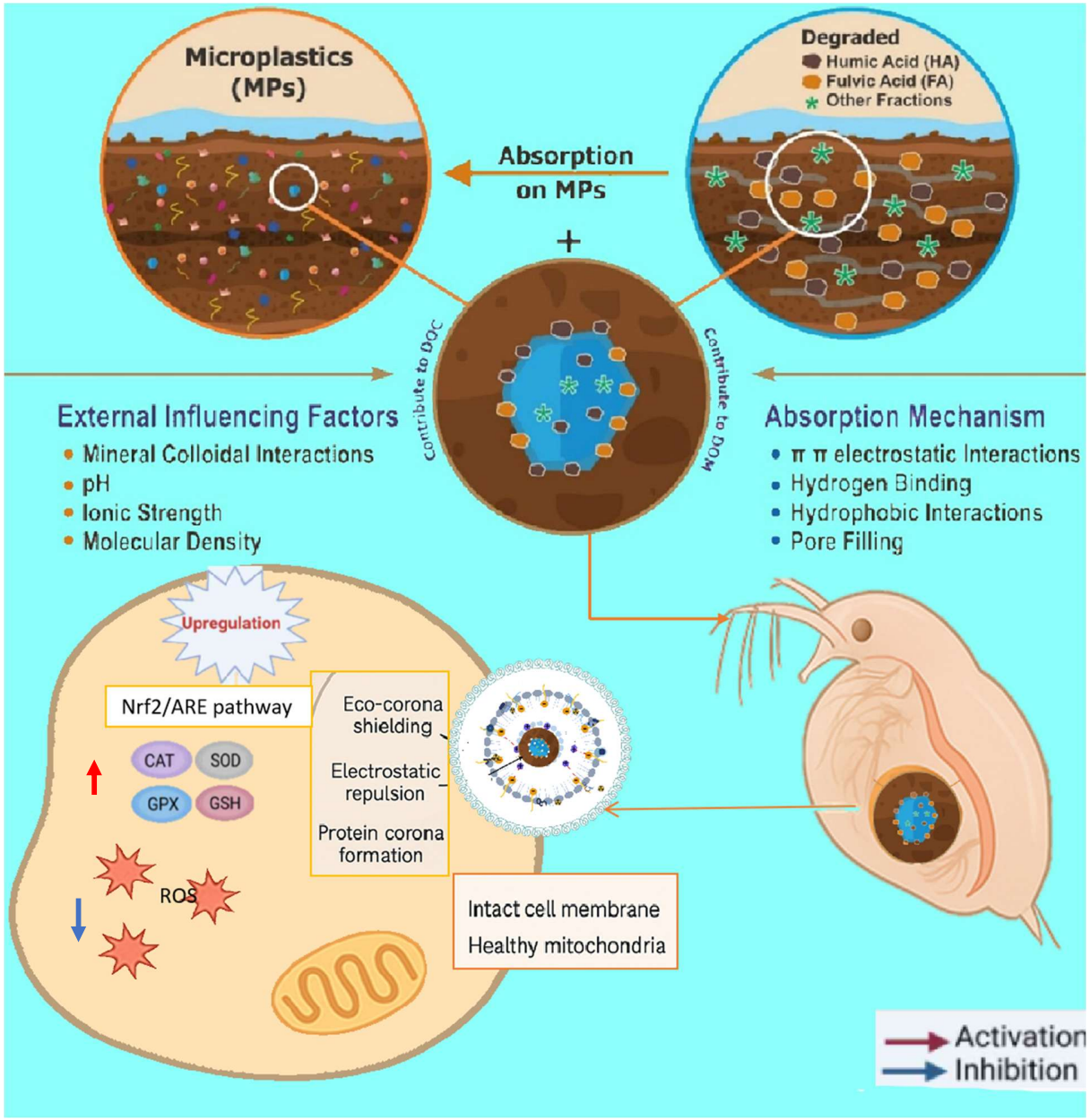

6 µm
Control
NPs= 0.5 mg/L
NPs= 1 mg/L
NPs = 1 mg/L
ATZ= 10 µg/L
NPs = 1 mg/L
ATZ= 100 µg/L
NPs = 1 mg/L
ATZ= 10 µg/L
HA= 5 mg/L
NPs = 1 mg/L
ATZ= 100 µg/L
HA= 5 mg/L
I
24h
48h
y = 19.42x+214.9
R2=0.9545
y = 16.34x+159.1
R2=0.7928
EC50 Sb(V) (mg/L)
FA (mg/L)
II
24h
48h
y = 23.36x+213.5
R2= 0.9543
y = 19.14x+143.3
R2= 0.9560
EC50 Sb(V) (mg/L)
HA (mg/L)

**Figure 5**


Microplastics
(MPs)
Degraded
Humic Acid (HA)
Fulvic Acid (FA)
Other Fractions
Absorption
on MPs
+
Contribute to DOC
Contribute to DOM
External Influencing Factors
Mineral Colloidal Interactions
pH
Ionic Strength
Molecular Density
Absorption Mechanism
π π electrostatic Interactions
Hydrogen Binding
Hydrophobic Interactions
Pore Filling
Upregulation
Nrf2/ARE pathway
CAT
SOD
GPX
GSH
ROS
Eco-corona shielding
Electrostatic repulsion
Protein corona formation
Intact cell membrane
Healthy mitochondria
Activation
Inhibition