Toxicity, bioaccumulation and trophic transfer of engineered nanoparticles in the aquatic environment

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Chapter 1

General Introduction

Nanomaterials (NMs) are defined as materials containing 50% or more particles with at least one dimension on the nanoscale level. The European Commission Regulation 2011/696/EU (Science for Environment Policy, 2017; The European Commission recommendations, 2010) has defined nanoscale between 1 and 100 nm. Nanoparticles (NPs) are NMs with all three external dimensions in the nanoscale (ISO, 2008; *Terminology for nanomaterials*, 2007). Nanotechnology is the use of matter at the nano scale and is an emerging technology. The development of nanotechnology not only brings the promise of radical technological development– for example, clean energy, highly effective medicines and lightweight products - but also brings its own safety challenges (Science for Environment Policy, 2017). In this thesis, ecological hazard risk of engineering nanoparticles (ENPs) in the aquatic environment was assessed.

1.1 Application and release of ENPs

The applications for ENPs are numerous, with use in cosmetics, fuel additives, electronics, pharmaceuticals, clothing, biomedicine, catalysis and materials, and environmental remediation (Ju-Nam and Lead, 2008; Keller and Lazareva, 2013; Thomas et al., 2013). The common use of ENPs relies on their nanoscale size and relative large surface area, which result in extraordinary and tuneable nature of optical, electrical, chemical, thermal, magnetic, and mechanical properties (Dolez, 2015; Ju-Nam and Lead, 2008; Rai et al., 2018).

The global nanomaterials market (GNM) size has been expanding rapidly. The Project on Emerging Nanotechnologies (PEN, 2013) reported that the number of products had a 25-fold growth between 2005 and 2010. The GNM value was estimated to be €20 billion (aroung 11 million tonnes NMs) in 2012 by European Commission Communication (European Commission, 2012). Furthermore, the GNM is expected to expand at a compound annual growth rate of more than 19% from 2022 to 2027 (Mordor Intelligence, 2022). In order to meet the growing market demand and potential applications, a number of ENPs are currently manufactured to arrange the size, shape, and crystal structure of NPs, as well as composition (single or mixture) (Peralta-Videa et al., 2011). Especially, more and more complex and functional ENPs such as gold-silica NPs for medical treatment and silicon–organic hybrid nanostructures for electro-optic nanomodulators, are predicted to dominate the market (Camboni et al., 2019; Wolf et al., 2018). **The complex nanomaterial systems are currently in short of risk assessment and evaluation under the REACH Regulation.**

Given the worldwide use and production of ENPs, their release into freshwater ecosystems is inevitable during their lifecycle (Bundschuh et al., 2016; Peng et al., 2017). Keller and Lazareva (2013) estimated the global mass flow of ENPs to be over 69,200 metric tons per year disposed or released into aquatic environments as of 2010. ENPs in freshwater ecosystems can interact with organisms due to their small size, which may lead to trophic transfer into food chains. To address this, it is essential to determine the fate and behavior of ENPs in the aqueous environment (Batley et al., 2013; Klaine et al., 2008; Williams et al., 2019).

1.2 Fate of ENPs in the aquatic environment

The stability and fate of ENPs in the aquatic environment are influenced by physical, chemical and biological processes (Lowry et al., 2012; Peijnenburg et al., 2015). Dwivedi et al. (2015) further proposed that physicochemical processes (comprising of aggregation, sedimentation, and dissolution of the particles) also play a vital role in affecting the behavior of ENPs in water as illustrated in Figure 1.1 (Rocha et al., 2016; Van Koetsem et al., 2015).

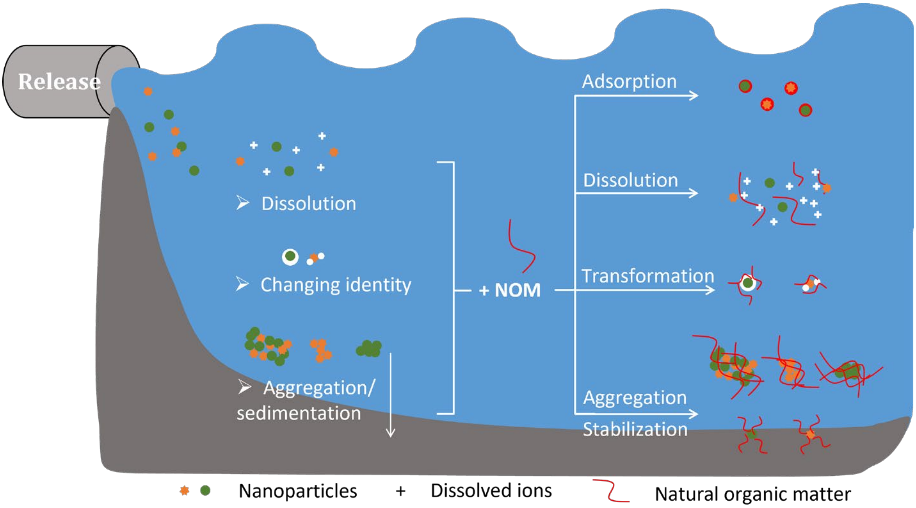

Figure 1.1 Schematic diagram showing the physicochemical transformation and the influence of natural organic matter (NOM) in the aquatic environment.

1.2.1 Aggregation and sedimentation

Aggregation describes the dynamics of nano-sized particles that bounded or fused together into larger clusters (Garner and Keller, 2014). Sedimentation occurs when the particles or aggregated particles have a higher density than the exposure medium (Alstrup Jensen et al., 2009). The degree of aggregation and the rate of sedimentation are determined by the properties and concentrations of the NPs, and the characteristics of the aqueous system (for example the presence of natural organic matter (NOM)) (Du et al., 2019; Dunphy Guzman et al., 2006; Farkas et al., 2010; Garner and Keller, 2014; Phenrat et al., 2007). The aggregation and sedimentation of NPs will dictate mobility and fate in the aquatic environment, and thus bioavailability and possible ecotoxicological effects (Liu and Cohen, 2014; Velzeboer et al., 2008).

1.2.2 Dissolution of soluble ENPs

Some ENPs can dissolve, e.g. ZnONPs and CuNPs, and as a result both ions as well as particles occur within exposure media influencing toxicological effects (Lowry et al., 2012; Van Koetsem et al., 2015; Williams et al., 2019). The rate and extent of dissolution mainly depends on the surface functionalization (e.g. surface to volume ratios and surface charge) (Peijnenburg et al., 2015; Quik et al., 2011). Dissolution is concentration dependent (Lead et al., 2018; Merrifield et al., 2017), and the dynamics are influenced by solubility, size and composition of particles as well as environmental conditions (for example pH, temperature and the concentrations of NOM) (Jiang et al., 2015; Levard et al., 2012; Peralta-Videa et al., 2011; Quik et al., 2011; Zhang et al., 2010).

1.2.3 Influence of NOM

Ubiquitous and abundant NOM can alter the aggregation, sedimentation and dissolution progresses of ENPs in the aquatic environment (Bo et al., 2017; Carapar et al., 2022; Grillo et al., 2015; Tortella et al., 2020; Wang et al., 2018, 2016).

The interactions between NOM and ENPs contain hydrophobic interactions, electrostatic interactions, steric interactions, hydrogen bonding, and bridging (Li et al., 2022). For example, on the one hand, the presence of NOM may inhibit the aggregation and enhance the stability of ENPs, as a reason of electrostatic and steric interactions (Baalousha et al., 2013; Bo et al., 2017; Mohd Omar et al., 2014; Wang et al., 2018). On the other hand, the presence of NOM, may promote the aggregation due to bridging interactions (Akaighe et al., 2012; Li et al., 2022). Moreover, the existence of NOM was reported to slow down the dissolution progress of AgNPs via sulfidation due to the formation of a passivating coat on the surface (Reinsch et al., 2012), or via making the surface charge more negatively charged (Fabrega et al., 2009).

Although several mechanisms of NOM-ENPs interactions have been investigated, up till now there is limited knowledge on realistic fresh water system containing the mixtures of ENPs, and the further interactions with water chemistry parameters that all may impact the ecotoxicity to organisms (Levard et al., 2012). The above statements highlight that the environmental behavior of ENPs in the aquatic ecosystem is quite complex (Carapar et al., 2022) and a challenging research topic.

1.3 Uptake, bioaccumulation and trophic transfer of ENPs

1.3.1 Uptake and bioaccumulation of ENPs from aquatic environment

Uptake routes embody direct ingestion and entry across surface epithelia such as gills and body walls (Moore, 2006). There are researchers reporting uptake and accumulation of different kinds of ENPs (e.g. metal-based NPs, metal oxide NPs and nanoplastics, etc.) into organisms in various trophic levels (Gupta et al., 2017; Mateos-Cárdenas et al., 2021; Nam et al., 2014; Nowack and Bucheli, 2007; Tortella et al., 2020; Wang et al., 2016).

Particles can be ingested or incorporated into organisms, e.g. the uptake of polystyrene nanoplastics in zebrafish embryos (Pakrashi et al., 2014; van Pomeren et al., 2017). Aggregates of particles are less mobile, yet ingestion by animals, like *Daphnia magna,* still occurred (Xiao et al., 2015). Moreover, filter-feeder, benthic, sediment-dwelling organisms have shown to be prone to uptake of ENPs (Carocci et al., 2015; Gupta et al., 2016; Nowack and Bucheli, 2007).

Uptake and accumulation of ENPs depend on the particle size and the presence of NOM (Bundschuh et al., 2016; Limbach et al., 2005; Mateos-Cárdenas et al., 2021; Nowack and Bucheli, 2007; Wang et al., 2016). Generally, the smaller the particle size is, the more uptake and accumulation of ENPs. However, an opposite finding was observed on the uptake of AuNPs, which increased along with an increasing particle size (Pan et al., 2012). This highlights that further investigations on size relations are needed. Likely, the relationship between the presence of NOM and uptake of ENPs is not elucidated, but several studies have found some impacts as summarized by Wang et al. (2016).

Previous studies mostly focused on the impact of particle size and NOM on a certain ENP or a certain organism. The conclusion from different studies were not consistent, highlighting the complex relationship and mechanisms between NOM and ENPs. Therefore, more research is needed.

1.3.2 Trophic transfer of ENPs

Evidence has been found on transfer of ENPs through aquatic food chains (Chae and An, 2016; Lee et al., 2015; Wang et al., 2017; Yan and Wang, 2021; Zhao et al., 2017; Zhu et al., 2010). To evaluate the environment risk of ENPs, trophic transfer is a crucial aspect, especially when biomagnification (tropic transfer factor > 1) occurs (Shi et al., 2020).

A series of factors can affect trophic transfer of ENPs through food chains in aquatic environments. As concluded by Dang et al. (2021) and Tangaa et al. (2016), the main factors include (1) the ENP characteristics, (2) prey and predator species, (3) the exposure route of the prey, (4) the uptake and internalization of ENPs in preys, and (5) the digestive physiology of predators and the subcellular fractionation of ENPs. To the best of our knowledge, few studies have looked at above five aspects. For instance, uptake of AgNPs in *D.*

magna depended on dietary exposure instead of aqueous exposure. In the case of the relationship between digestive physiology with trophic availability, experiments using soluble metals have shown that when bound to organelle particles were more readily available to predator than those partitioned to insoluble components (Chen et al., 2016). As is concluded by in previous studies (Chang and Reinfelder, 2000; Wallace et al., 1998), dissolved metals associated with organelles or cytosolic proteins are more easily solubilized by the digestive processes of predators. The position organisms in the food chains has shown to impact the magnitude of transfer, namely ENP concentration increased between the first and the second trophic level organism (Gupta et al. 2017). Whereas, the extent of transfer decreased to several fold from the second to the third trophic level organism To investigate the multistage trophic transfer of ENPs, research on a three-level food chain could provide more information compared with research on a two-level food chain (Shi et al., 2020), yet so far poorly studied. It remains also a question if the particulate or the ions of the ENPs transfer across organisms, and how the size and concentration alter this transfer. Ionic metal shedded from ENPs were found to move along food chains according to the total mass concentration (Bhuvaneshwari et al., 2017; Gambardella et al., 2014; Lammel et al., 2014; Wu et al., 2017).

For particle transfer the techniques are nowadays in their infancies and therefore limited information was found. Earlier reports showed measurements based on the total mass concentration including both the particles and the dissolved ions of ENPs in the biota (Baccaro et al., 2018; Chen et al., 2015; Lee et al., 2015; Yan and Wang, 2021). With the development of single particle inductively coupled plasma mass spectrometry (sp-ICP-MS) and single cell ICP-MS, the first attempts to quantify particulate ENPs are available. For example, Gray et al. (2013) successfully established and verified a method to determine the particle number concentration of gold nanoparticles (AuNPs) and AgNPs in *Daphnia magna* and *Lumbriculus variegatus* samples. Particle number-based assessment was also applied in the trophic transfer of AuNPs from algae to daphnia to fishes (Monikh et al., 2021). Despite the fact that these techniques are in their infancies, they have great potential for furthering this field of research.

1.4 Toxicity of ENPs

Although quite some toxicity tests with aquatic organisms have been executed and published (overview for instance in Chen et al (2015)), the majority of studies have focused on acute endpoints (Balraadjsing et al., 2022) using standard organisms (Chen et al., 2015). Understanding the processes at the interface of exposure, uptake, effects and trophic transfer requires more attention especially with considering the fate of metallic NPs that are in exposure media as ions and particles in suspension. To discuss these gaps, single and joint toxicity, as well as the influence of NOM on the toxicity are summarized as shown below.

1.4.1 Single toxicity

The toxic action of soluble and insoluble ENPs can be roughly described with three pathways or mechanisms (Besseling et al., 2019;

Brunner et al., 2006; Ma et al., 2013; Peng et al., 2017; Santschi et al., 2017): (1) surface interactions or internalization of particles, (2) shedding toxic ions from soluble ENPs (e.g. CuNPs and ZnONPs), and (3) oxidative stress caused by chemical radicals or reactive oxygen species (ROS).

These responses can be impacted by the surface functionality and surface charge (Garner and Keller, 2014). As described in section 1.2, the environmental behavior of ENPs (aggregation, sedimentation and dissolution) in the water column play an important role in determining the surface chemistry and stability of ENPs, and thus determine the bioavailability and potential ecotoxicological effects on aquatic organisms (Borm et al., 2006; Holden et al., 2016). The type of organisms used – which all have their own requirements related to exposure medium composition and the multiplicity of experimental methods and conditions will also affect the toxicity values reported (Libralato et al., 2017). Hence, different exposure conditions to different trophic level organisms should be considered in the studies of toxic effect.

Another key area of research is the contribution to toxicity of particles compared to the released/dissolved ions for soluble ENPs. It is debated that in nanotoxicity the total toxic effect generated from particulate part (ENPs themselves) and/or the ionic metal part released from metal-based or metal oxide-based ENPs both should be accounted for (Libralato et al., 2017; Ma et al., 2013; Malhotra et al., 2020). Several studies have demonstrated that the effects of soluble ENPs result not solely from dissolved ions or particles (Carocci et al., 2015; Griffitt et al., 2008; Wang and Wang, 2014). The contribution of particles versus ions might vary on the basis of the physicochemical processes especially the dissolution, and the exposure conditions such as the presentence of NOM (Malhotra et al., 2020; Saleh et al., 2014). Therefore, further studies are hence devoted to quantitative clarify the interaction and contribution of particles and ions, and to understand the mechanism of soluble ENPs toxicity under different parameters and conditions.

1.4.2 Joint toxicity

"*There is no such thing as a single chemical exposure*" (Yang et al., 1998). Aquatic organisms are mostly co-exposed to ENP mixtures in the real scenario due to the release of individual ENPs as introduced in front, and the emerging of hybrid nanoparticles consisted of multiple components (Deng et al., 2017; Maji et al., 2019; Pacheco et al., 2018). More knowledge is needed on the joint toxicity of multiple ENPs to provide basis to assess the risk of ENPs in the realistic and complex natural systems.

The behavior and toxicity of ENP mixtures may differ from exposure to single ENPs. Interactions of ENPs in a mixture can result in different toxic actions including increasing (synergistic) or decreasing (antagonistic) effects as compared with summed (additive) behavior (Altenburger et al., 2003). The existing literature on joint toxic actions of ENPs and the contribution of individual component to the joint effect is rather limited (Deng et al., 2017; Pacheco et al., 2018). Deng et al. (2017) reviewed the joint toxicity of NPs together with another contaminants involving organic medicals, metal ions, NPs. In this review, several cases for the joint toxicity of ENPs to bacteria and human cells are reported. Here, current literatures on the joint toxicity upon freshwater organisms' exposure to two types of NPs are collected and summarized in Table 1.1.

As shown in Table 1.1, the toxic actions of multiple ENP mixtures varied in different exposure systems. However, information on the mechanisms of action is an aspect that is still scarce in literature, especially for the soluble metal-based or metal oxide ENPs (Hernández-Moreno et al., 2019; Ogunsuyi et al., 2019). Note that the suspensions of soluble ENP mixtures are complicated due to the coexistence of different kinds of particulate and ionic ENPs. The interaction between multiple particles and released metal ions might alter the additive toxicity. It is, thus, necessary to unravel if one of the particulate or ionic components dominates the toxic action, or if the contribution to total toxicity depend on interactions of multiple components. Moreover, previous studies have investigated the joint toxicity of metal salts. It is important to elucidate if the toxic effect of metal-based or metal oxide ENP mixtures can be dealt with in a similar way as with the responses of biota to mixtures of metal salts.

Table 1.1 List of published studies (to date) conducted on joint toxicity of ENPs to organisms in freshwater

ENP mixture	Exposure species	Exposure time	Endpoint	Joint effect	References
CuNPs+CrNPs	Waterflea *Daphnia magna*	48 hours 7 days 21 days	survival, reproduction, growth, feeding behavior, four biomarkers	comparable to nCu on feeding behavior and biomarker responses.	(Lu et al., 2017)
AgNPs+hematite (HemNPs)	Alga *Chlamydomonas reinhardtii* and *Ochromonas danica*	24 hours	cell-specific growth rate	antagonistic 1) decreasing the bioavailability of Ag ions through adsorption 2) competitively inhibiting AgNP uptake.	(Huang et al., 2019)
AgNPs+polystyrene (PsNPs)	Alga *Chlamydomonas reinhardtii* and *Ochromonas danica*	24 hours	cell-specific growth rate	synergistic	(Huang et al., 2019)

AgNPs+CuONPs	African mud catfish *Clarias gariepinus*	28 days	oxidative stress analyses, biomarkers	antagonistic genotoxicity and oxidative damage	(Ogunsuyi et al., 2019)
ZnONPs+graphene oxide nanoplatelets (GO NPs)	Alga *Scenedesmus obliquus* Waterflea *Daphnia magna* Fish larva *Danio rerio*	96 hours 48 hours 96 hours	growth inhibition, lethality tests, Embryo–larval toxicity bioassays	additive to S. obliquus and D. magna antagonistic to D. rerio.	(Ye et al., 2018)
AuNPs+microplastics	Waterflea *Daphnia magna*	21 days	lethality tests, reproduction	High concentrations: synergistic Low concentrations: antagonistic	(Pacheco et al., 2018)
CuNPs+ZnONPs	rainbow trout	96 hours	behaviour, lethality tests, oxidative stress, accumulation	CuNPs increase the uptake of Zn. Co-exposure alters of the GST activity and GSH/GSSG ratio in gill and liver.	(Hernández-Moreno et al., 2019)
30 combinations (CuONPs, ZnONPs, NiONPs, TiO_2NPs, Fe_2O_3NPs)	Alga *Chlorella vulgaris*	72 hours	growth inhibition (cell count and chlorophyll content)	additive (67%) antagonistic (16.5%) synergistic (16.5%)	(Ko et al., 2018)

1.4.3 Influence of NOM

Numerous studies have reported the influence of NOM on the single toxicity of ENPs (Farner et al., 2019; Wang et al., 2016, 2011). The presence of NOM mostly modulate the original toxic effect (Cerrillo et al., 2016; Saleh et al., 2014). For instance, Suwannee River NOM can alleviate the adverse effects of NPs on algal growth (Cerrillo et al., 2016). Deng et al. (2017) concluded that the mechanism of the impact of NOM on the availability and toxic action of ENPs accounts for altered electrostatic repulsion between ENPs and/or between ENPs and cells, scavenging of ENPs-induced reactive oxidative species, and the formation of complexes with released ions. However, the relationship between NOM influenced ENP single toxicity to different trophic level has not been clearly understood. In addition, there is a research gap on the impact of NOM on the joint toxicity of multiple ENPs and the alteration on the contributions of particulate/ionic components. To fill these gaps, more concern should be focused on the relationship of the presence of NOM and the single or joint toxic effect of ENPs. The exposure condition such as the presence of NOM is the key factor affecting the behavior and stability of ENPs, as well as a factor affecting the toxicity of ENPs.

1.5 Test organisms

In order to determine the bioaccumulation, trophic transfer, and toxicity of ENPs in aquatic organisms, different trophic level test species were selected as follows. Images of these species are shown in Figure 1.2.

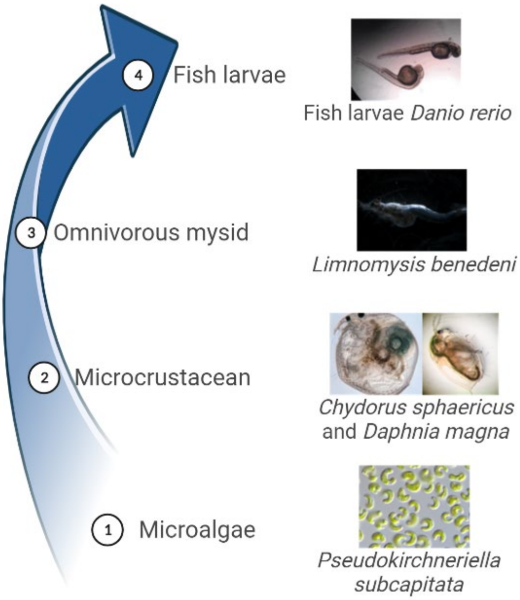

Figure 1.2 Images of test organisms in different trophic levels.

1.5.1 Microalgae *Pseudokirchneriella subcapitata*

As primary producers, microalgae contain species important to freshwater ecosystems and those that have potential applied usages (Suzuki et al., 2018). In particular, *Pseudokirchneriella subcapitata* (= *Raphidocelis subcapitata*), shown in the first image of Figure 1.2, is an unicellular, sickle-shaped, freshwater green microalga (Machado and Soares, 2014; Yamagishi et al., 2017). Compared with other algae, *P. subcapitata* has been widely and most frequently used for bioassays in toxicological risk assessments accounting for its high growth rate, sensitivity to toxicants, and good reproducibility (Yamagishi et al., 2017). Hence, *P. subcapitata* was recommended as an ecotoxicological bioindicator by the Organization for Economic

Cooperation and Development (OECD) (Andrews and Walsh, 2007; Suzuki et al., 2018). Here, *P. subcapitata* was selected as the first trophic level as the food for microcrustaceans and mysids.

1.5.2 Microcrustacean *Chydorus sphaericus* and *Daphnia magna*

Microcrustacean is composed of species that are important components of freshwater food webs. Two species of planktonic genera microcrustacean, *Chydorus sphaericus* and *Daphnia magna*, were used in the research presented in this thesis. They are vital components in food and energy relationships between primary produces and higher-level consumers, especially within lakes and ponds (de los Ríos-Escalante et al., 2011).

C. sphaericus is found worldwide in water bodies, from the equator to the Arctic Circle (Kotov et al., 2016). It is generally found in lakes or ponds with eutrophication and around the bottom sediments (Central Michigan University, n.d.). It can swim well for only short distances, but is most likely to be found clinging to various filamentous algae with its modified limbs (Central Michigan University, n.d.; Fryer. G, 1968). *C. sphaericus* is tolerant of a wide range of pH levels (from 3.4 to 9.5) and varying levels of dissolved oxygen, including very low levels of oxygen (Fryer. G, 1968).

D. magna is model species for toxicity test recommended by OECD guidelines 202 (OECD, 2004). It is widespread in a variety of freshwater systems from acidic swamps to lakes, ponds, and streams. The body of daphnia is usually 1–5 millimeters long, and is divided into segments, although this division is not visible. Daphnids are typically filter feeders, ingesting suspended particles (mainly unicellular algae) as large as 70 μm (Geller and Müller, 1981). Moreover, as a result of the high efficiency of filtering water, *D. magna* are sensitive to pollutants in aquatic environment.

As experimental organisms, *C. sphaericus* and *D. magna* are suitable to culture in the laboratory for their short generation time and strong adaptability to the environment. Furthermore, observation with the microscope is possible due to their transparency and small sizes. Thus, *C. sphaericus* and *D. magna* are good choice as test organisms to construct aquatic food chains and to determine the toxicity of ENPs (Baun et al., 2008). It is closely related to algae present which is one of its major food sources (i.e., Anabaena).

1.5.3 Omnivorous mysid *Limnomysis benedeni*

Limnomysis benedeni is a freshwater mysid originally located in the area of the Black Sea and the lower Danube river (Gergs et al., 2008). As an invasive species, it has spread in freshwater systems globally (Yohannes and Rothhaupt, 2017). *L. benedeni* is an omnivorous species ingesting both microalgae and microcrustaceans in the laboratory (Gergs et al., 2008). It is a perfect predator to construct a food chain with different food sources, and then to compare the trophic transfer of ENPs in these food chains. Meanwhile, it is a beneficiary food source for fish (Gergs et al., 2008; Kelleher et al., 1999). *L. benedeni* thus plays an important role as a bridge to connect the lower trophic levels to the higher trophic levels. Moreover, its transparency makes the visualization of the biodistribution of fluorescent NPs inside convenient.

1.5.4 Fish larvae *Danio rerio*

Zebrafish (*Danio rerio*) is regarded as a model freshwater species for studying genetic effects in vertebrate development (David P. Clark, Nanette J. Pazdernik, 2019). It has been widely used in toxicity studies to evaluated the effect of pollutants. The advantages of *D. rerio* include their ease of culturing and in the laboratory, the large amount of embryos that females produce, and the optically transparent embryos which develop externally (Internal Control Genes, 2017; Xu et al., 2016). We used zebrafish larvae up to 5 days post fertilization.

1.6 Objectives and research questions

Taken together, the toxicity, bioaccumulation, and trophic transfer of selected ENPs are still poorly studied, especially when considering the realistic conditions such as the exposure of ENP mixtures and the influence of NOM. Therefore, this thesis aimed to (scheme as shown in Figure 1.3):

1) investigate the fate, toxicity and bioaccumulation of both individual and mixture ENPs to aquatic organisms, and the impact of NOM on these processes;

2) evaluate the trophic transfer of ENPs through simulated aquatic food chains, and the following biodistribution and toxic effect of ENPs on the predators;

3) assess the key factors affecting the extent of trophic transfer among particle sizes and food chain types.

According to the objectives, the research questions were addressed:

1) How does NOM affect the stability and toxicity of **individual ENP** to aquatic organisms? (Chapter 2)

2) How does NOM affect the fate, accumulation and toxicity of **ENP mixtures** (Chapter 3)?

3) To what extent do ENPs **transfer** in particulate, and ionic forms and how does the particle size and number change in different organisms? (Chapter 4)

4) How do **particle sizes** and **food chain types** affect the trophic transfer of ENPs and their subsequently biodistribution and toxicity to the predators? (Chapter 4 and 5)

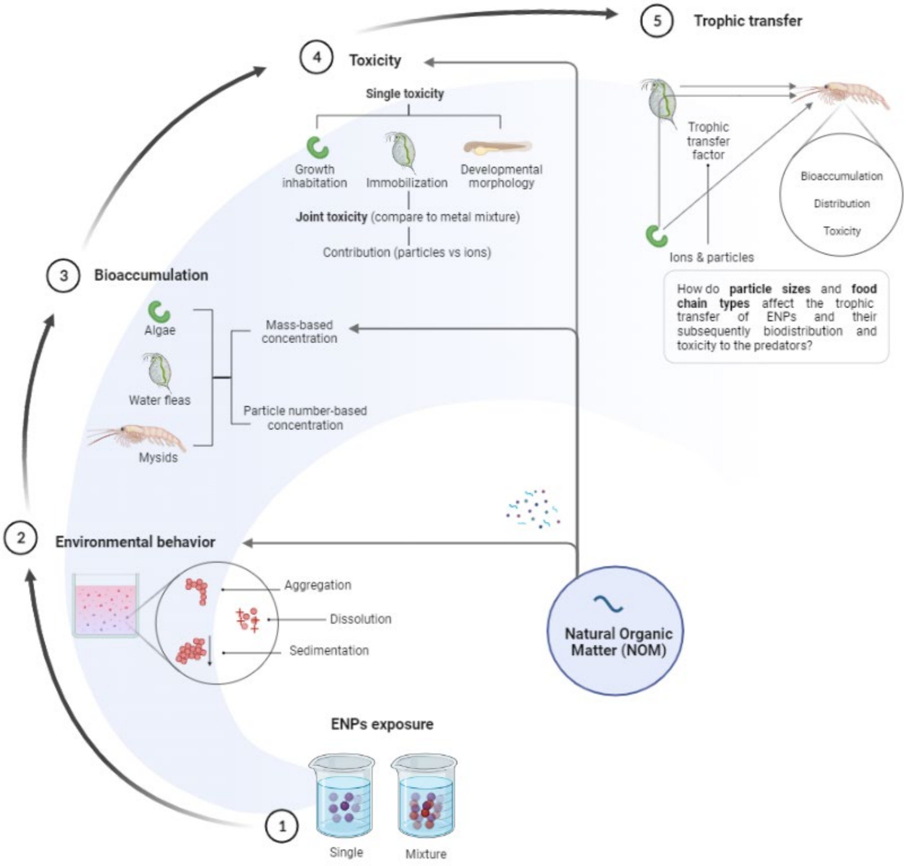

Figure 1.3 Scheme of investigating the toxicity, bioaccumulation and trophic transfer of engineered nanoparticles (ENPs) in the aquatic environment in this thesis.

1.7 Thesis outline

Chapter 1 General introduction on the application and release of ENPs and their fate, toxicity, accumulation and trophic transfer in the aquatic environment, as well as the test organisms used for nanotoxicity testing. The objectives and research questions of this thesis were proposed.

Chapter 2 The impacts of humic substances (HS) on the aquatic stability and toxicity of cerium dioxide nanoparticles (CeO_2NPs) to three aquatic organisms with different exposure characteristics were investigated.

Chapter 3 The assessment of the joint toxicity and accumulation of copper nanoparticles (CuNPs) and zinc oxide nanoparticles (ZnONPs) in *D. magna* in the absence and presence of Suwannee River natural organic matter (SR-NOM), compared to the joint toxicity and accumulation of corresponding metal salts.

Chapter 4 This work investigated the uptake and transfer of different sized polystyrene particles (PSPs) in *Daphnia magna* to mysid *Limnomysis benedeni*, explicitly PSPs' fate in the aquatic system as a function of particle size (26, 500 and 4800 nm) was accounted. Moreover, the accumulation kinetics of particles in mysid fed by exposed daphnia were calculated.

Chapter 5 The trophic transfer of copper nanoparticles (CuNPs) was studied in a food chain consisting of the microalgae *Pseudokirchneriella subcapitata* as a representative of primary producers, the consumer waterflea *Daphnia magna,* and the omnivorous mysid *Limnomysis benedeni*. The impact of food chain types on the transfer extent of CuNPs, and the change of the profile of particulate Cu through food chains were investigated.

Chapter 6 Discussion on the research questions and main findings of the thesis. Single and mixture toxicity of ENPs towards aquatic organisms, and how the persistence of NOM affects the toxicity were understood. The extent of accumulation and trophic transfer of ENPs, the main driver of the transfer among particle sizes and food chain types were integrated. Future perspectives in terms of nanotoxicity, food chain transfer and risk assessment of ENPs were proposed.

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