Microplastics and associated contaminants in the aquatic environment: A review on their ecotoxicological effects, trophic transfer, and potential impacts to human health

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Abstract

The microplastic pollution and related ecological impacts in the aquatic environments have attracted global attention over the past decade. Microplastics can be ingested by aquatic organisms from different trophic levels either directly or indirectly, and transferred along aquatic food chains, causing different impacts on life activities of aquatic organisms. In addition, microplastics can adsorb various environmental chemical contaminants and release toxic plastic additives, thereby serving as a sink and source of these associated chemical contaminants and potentially changing their toxicity, bioavailability, and fate. However, knowledge regarding the potential risks of microplastics and associated chemical contaminants (e.g., hydrophobic organic contaminants, heavy metals, plastic additives) on diverse organisms, especially top predators, remains to be explored. Herein, this review describes the effects of microplastics on typical aquatic organisms from different trophic levels, and systematically summarizes the combined effects of microplastics and associated contaminants on aquatic biota. Furthermore, we highlight the research progress on trophic transfer of microplastics and associated contaminants along aquatic food chain. Finally, potential human health concerns about microplastics via the food chain and dietary exposure are discussed. This work is expected to provide a meaningful perspective for better understanding the potential impacts of microplastics and associated contaminants on aquatic ecology and human health.

Keywords: Microplastics; Associated contaminants; Aquatic organisms; Combined effects; Trophic transfer; Human health

Content

Abbreviations:

Mt, million tonnes.

PRISMA, Preferred Reporting Items for Systematic reviews and Meta-Analyses.

PE, polyethylene; LDPE, low-density polyethylene; MDPE, medium-density polyethylene; HDPE, high-density polyethylene; PS, polystyrene; PS-COOH, carboxylated polystyrene; PVC, polyvinyl chloride; PP, polypropylene; PET, polyethylene terephthalate; PC, polycarbonate; PA, polyamide; POM, polyoxymethylene; PU(F), polyurethane (foam); PMMA, polymethyl metacrylate; PTFE, polytetrafluoroethylene; ABS, acrylonitrile-butadiene-styrene; PHB, polyhydroxybutyrate.

DDTs, sum of dichloro-diphenyltrichloroethane; PCBs, polychlorinated biphenyls; PAHs, polycyclic aromatic hydrocarbons; PBDEs, polybrominated diphenyl ethers; BPA, bisphenol A; PFOS, perfluorooctane sulfonic acid; HBCDs, hexabromocyclododecanes; Ag, silver; Cd, cadmium; Cr, chromium; Cu, copper; Pb, lead; Ni, nickel; Hg, mercury; Zn, zinc.

1. Introduction

Currently, various plastic products have been widely applied to human daily life and global plastics annual production reached almost 359 million tonnes (Mt) in 2018 from 348 Mt in 2017 (PlasticsEurope, 2019). Along with the conveniences brought about by plastic products, the negative sides of “Plastic Era” are gradually emerging (Geyer et al., 2017, Law and Thompson, 2014). Due to overuse, mismanagement and environmental durability of plastic products, about 6300 Mt plastic wastes had been continuously produced from 1950 to 2015, 79% of which was discharged into landfills or natural environments (Geyer et al., 2017). Aquatic environments are the base of material circulation and energy flow on earth and have become an important sink of plastic wastes. An estimated 4.8-12.7 Mt plastic wastes from land were discharged into the marine environments in 2010 (Jambeck et al., 2015). Between 1.15-2.41 Mt plastic wastes were projected to transport into the ocean from the global rivers every year (Lebreton et al., 2017).

The plastics released into the environments may be gradually broken up into microplastics through synergistically environmental and biological stresses. Microplastics and nanoplastics existed in nature are either primary or secondary from their origin. Primary microplastics are derived from microbeads widely added to consumer products including cosmetics, exfoliants, facial scrubs, detergents, sunscreens, and drug vectors (McDevitt et al., 2017, Hernandez et al., 2017, Rochman et al., 2015a). Another source of primary microplastics include industrial abrasives and accidental pellet spills with a size less than 5mm, which are intentional or unintentional released from industrial manufacture (McDevitt et al., 2017, Lechner et al., 2014). Secondary microplastics originate from the extremely slow fragmentation/degradation from large plastics through complicated weathering processes, such as mechanical abrasion by sand or water scour, hydrolysis, UV photodegradation, biodegradation, and temperature (Alimi et al., 2018, Chubarenko et al., 2019, Hernandez et al., 2019). Evidence also showed that Antarctic krill by the internal digestive function can break down the ingested PE microplastics (31.5 μm) into the smaller debris (<1 μm) (Dawson et al., 2018). Moreover, the structure and reactivity changes of the plastic polymer occur in the aging and fragmentation processes of plastics, including the peeling off of plastic surface coatings, the formation of pore and changes in the mechanical strength, oxygen content and molecular weight of microplastics (Song et al., 2017, Liu et al., 2019a, Liu et al., 2020a). Plastic properties and nature weathering processes also impact how microplastics absorb/desorb hydrophobic organic chemicals and heavy metals in environments, and the extent to which they leach toxic chemicals into the aquatic environment (Liu et al., 2020a, Liu et al., 2019b, Lee et al., 2018). Notably, microplastics can enter aquatic environments through the diverse and complex pathways (**Fig. 1**). Recent evidence also showed that the floating atmospheric microplastics derived from terrestrial areas can be considered as a nonnegligible source of ocean microplastic pollution (Liu et al., 2019c). Microplastics were generally defined as plastic fragments <5 mm in size (Arthur et al., 2009, Thompson et al., 2004). There is a higher possibility of further degradation and fragmentation of microplastics to nanoplastics by environmental weathering and biodegradation (Hernandez et al., 2019, Mattsson et al., 2018, Hartmann et al., 2019). Nanoplastics were usually termed as plastic particles <100 nm or 1 μm in size (Hartmann et al., 2019, Koelmans et al., 2015), but still lack of the internationally specified microscopic size boundaries. Herein, 100 nm was suggested as the upper size limit for nanoplastics, because this threshold has been widely adopted in nanotechnology field and used in many microplastic toxicology studies for over a decade. Also, tire wear particles can be considered as another common source of microplastic pollution with a high emission rate of millions of tons annually, and mainly transported to aquatic ecosystems through the road runoff and complex transport pathways (Kole et al., 2017, Wagner et al., 2018). Microplastics, as a diversified and complex contaminant, have raised the wide concern about their potential toxic effects on diverse organisms and ecosystems due to its persistence, ubiquity, and diversity of plastic polymer, type, size, morphology, color, leaching additives and adsorbed environmental chemicals (Rochman et al., 2019).

Once input into the aquatic environments, microplastics can distribute in different water layers (e.g., surface water, water column and bottom sediment) because of the polymer properties (e.g., density, plastic shapes, polarity), surface biofilm, and water flow conditions (Kane et al., 2020, Kooi et al., 2017, Van Melkebeke et al., 2020), influencing their availability and toxicity to aquatic biota (Wang et al., 2019a). In recent years, studies about the impacts of microplastics on aquatic organisms from different trophic levels have been widely performed (Wang et al., 2019a, Shen et al., 2019, Carbery et al., 2018, Wright et al., 2013). Microplastics were detected in zooplanktons (Botterell et al., 2019, Canniff and Hoang, 2018), mussels (Li et al., 2016a, Li et al., 2018a), oysters (Graham et al., 2019, Teng et al., 2019), fish (Jabeen et al., 2017, Azevedo-Santos et al., 2019), waterbirds (Fossi et al., 2018), penguins (Le Guen et al., 2020, Bessa et al., 2019), and cetaceans (Zhu et al., 2019a, Burkhardt-Holm and N'Guyen, 2019). Microplastics can be ingested by aquatic organisms from different trophic levels, and their impact on the aquatic ecosystem might be worse than those caused by large plastics (Wright et al., 2013), even causing a threat to the aquatic food chain (Carbery et al., 2018, Gross, 2015). Aquatic organisms have different sensitivity to microplastics due to the diverse habitats and regulatory ability, which results in the difference of microplastic distribution in aquatic organisms. Microplastics in aquatic organisms of low trophic level can be transferred to the higher trophic levels along aquatic food chain from prey to predator (Wang et al., 2019a, Santana et al., 2017). For example, microplastics have been found in top predators, such as waterbirds (Fossi et al., 2018, Brookson et al., 2019), seals (Hernandez-Milian et al., 2019), humpbacked dolphins (Zhu et al., 2019a), beluga whales (Moore et al., 2020), sharks (Maes et al., 2020), and even humans (Schwabl et al., 2019). Furthermore, microplastics could absorb various environmentally relevant contaminants (e.g., heavy metals, hydrophobic organic contaminants) and release plastics additives (Alimi et al., 2018, Koelmans et al., 2016, Wang et al., 2018a, Brennecke et al., 2016), and transfer these associated chemical contaminants to aquatic organisms (Boyle et al., 2020, Bakir et al., 2016, Rochman et al., 2013). At present, the combined effects of microplastics and associated chemical contaminants on typical aquatic organisms have become a research hotspot. Although the effects and trophic transfer of microplastics have been verified, several topics remain to be further investigated, such as whether the interaction between microplastics and associated chemical contaminants cause the biomagnification effects, and whether the amounts of microplastics entering top predators and even humans lead to enough health impacts.

Additionally, microplastic exposure by the food chains and human dietary is an important pathway to human beings, and poses a potential threat to food safety and human health (Carbery et al., 2018, Zhang et al., 2020a, Cox et al., 2019). Based on the available knowledges, microplastics have been widely detected in commercial aquatic products (Li et al., 2018a, Li et al., 2020a, Garrido Gamarro et al., 2020, Feng et al., 2020a, Barboza et al., 2020a, Baechler et al., 2020, Cho et al., 2019, Abidli et al., 2019), table salts (Kim et al., 2018, Peixoto et al., 2019, Karami et al., 2017), drinking water (Oßmann et al., 2018, Tong et al., 2020, Zuccarello et al., 2019, Mintenig et al., 2019, Koelmans et al., 2019), and other human dietary exposure (Kosuth et al., 2018, Mühlschlegel et al., 2017, Oliveri Conti et al., 2020, Karami et al., 2018, Prata et al., 2020). Also, human intakes of microplastics via air inhalation have gradually attracted attention (Zhang et al., 2020a, Cox et al., 2019, Prata, 2018). Notably, Schwabl et al. (2019) found the presence of various microplastics in human faeces with 2 particles/g. Nevertheless, studies on the nano- and micro-plastic toxicology and pathology of humans are in infancy and need to further developed in the future. Moreover, the combined effects of microplastics and associated contaminants to human food safety and health deserve more attention.

According to the PRISMA Statement (Moher et al., 2009), we conducted a literature review using databases (ISI Web of Science and Science Direct) and published volumes in some environment field journals (e.g., Environmental Science & Technology, Water Research, Journal of Hazardous materials), for studies published up to May 2020. Search terms used in this study were included: microplastics, aquatic organisms, combined effects, trophic transfer, and human health. We also tracked back to some literature with the relevant topics from these selected references. After the selection and removal process, we identified 202 studies consisted of “microplastics-combined effects” (n=97), “microplastics-trophic transfer” (n=27), and “microplastics-human health” (n=78). This review aims to summarize the combined effects of microplastics and associated chemical contaminants on typical aquatic organisms, and emphasizes their trophic transfer from different trophic levels along aquatic food chains. Next, the potential risks to human health caused by microplastics via the dietary exposure and food chains are discussed. Finally, the current knowledge gaps and future research priorities about microplastics and associated contaminants in the aquatic environment are prospected.

2. Effects of microplastics on typical aquatic organisms

Microplastic ingestion, or interaction by the multiple ways, has been reported in a variety of aquatic organisms such as planktons, aquatic plants, invertebrates, fish, waterbirds and other top predators. Microplastic properties, such as environmental concentration (Gutow et al., 2016), size (Desforges et al., 2015, Yuan et al., 2019), shape and color (Ory et al., 2017), and released chemicals or odours (Savoca et al., 2016, Savoca et al., 2017, Allen et al., 2017), can affect microplastic ingestion by different aquatic organisms. Another important factors influencing microplastic ingestion include plastic surface biofilm (Allen et al., 2017, Kach and Ward, 2008, Vroom et al., 2017, Goss et al., 2018), aquatic habitat conditions (Peters and Bratton, 2016, Horton et al., 2018, McGoran et al., 2018, Ferreira et al., 2019, Collard et al., 2019), species difference (Botterell et al., 2019, Azevedo-Santos et al., 2019, Setälä et al., 2014, Cartraud et al., 2019), life stages (Horton et al., 2018, Cartraud et al., 2019, McNeish et al., 2018), and feeding strategy (Collard et al., 2019, Reynolds and Ryan, 2018, Cuthbert et al., 2019, Kim et al., 2019, Van Colen et al., 2020, Germanov et al., 2018). Also, trophic transfer can serve as an indirect approach of microplastic uptake by different trophic level predators (Chagnon et al., 2018, Nelms et al., 2018). After ingested or interacted, the impacts of microplastics vary from different aquatic organisms. Microplastics in the aquatic organisms and surrounding environment might affect the trophic transfer of microplastics from different trophic levels along the food chain/web.

2.1 Effects of microplastics on plankton

Phytoplankton, as an important primary producer in the aquatic ecosystems, takes CO_2 from atmosphere through photosynthesis and provides food sources and oxygen supply for aquatic primary predator. The ubiquitous microplastics in the aquatic environments can disturb phytoplankton feeding, physical ingestion and photosynthesis, and cause negative impacts on growth, development and reproduction, potentially affecting phytoplankton communities and even aquatic ecosystem sustainability (Wang et al., 2019a, Bhattacharya et al., 2010, Wu et al., 2019a, Liu et al., 2020b, Besseling et al., 2014). Laboratory experiments have revealed that microplastic exposure have toxic effects on various microalgae, with the smaller the particles and the greater the toxicity (Anbumani and Kakkar, 2018, Sjollema et al., 2016, Zhang et al., 2017). Also, the toxicity of nanoplastics are affected by plastic properties (e.g., type, concentration, surface modification), solution chemistry (e.g., ionic strength and dissolved organic matter), and particle-algae cell wall interactions (e.g., adsorption, complexation, agglomeration) (Liu et al., 2020b, Nolte et al., 2017). Larger microplastics can lead to adverse effects by blocking the light and influencing the photosynthesis, while smaller nanoplastics result in the destruction of algae cell wall by attaching to the phytoplankton surface (Liu et al., 2020b). Smaller microplastics interact with phytoplankton by adherence to their surface (Casabianca et al., 2020). PS nanoplastics can be attached on the surface of freshwater microalgae *Chlorella* and *Scenedesmus* (Bhattacharya et al., 2010), as well as *Pseudokirchneriella subcapitata* (Nolte et al., 2017, Bellingeri et al., 2019) due to interaction of the electrostatic interaction, plastic surface properties, solution chemistry and algal exudates, which hinder photosynthesis and result in increase of the reactive oxygen species in algae cells. Additionally, Marine phytoplankton aggregates, such as the diatom *Chaetoceros neogracile* and cryptophyte, could secrete extracellular polysaccharides and some viscous substances to form algae clusters, and polymerize and concentrate 2 μm PS microbeads in their surrounding environment, potentially influencing microplastic vertical distribution and bioavailability in aquatic systems (Long et al., 2017, Long et al., 2015). Recently, Feng et al. (2020b) revealed that the exposure of PS-NH_2 nanoplastics (50 nm) at the concentrations of 3.40 and 6.80 μg/mL can inhibit photosystem-II efficiency and enhance the microcystin synthesis and release from cyanobacterial species. Thus, it increases the threats of eutrophication and cyanobacterial blooms, and potentially leads to negative consequences to freshwater ecosystems and human health.

Microplastics have been found in the various zooplanktons such as copepod, rotifer and cladocera, which interact with microplastics by the surface adherence and feeding behavior (Botterell et al., 2019, Desforges et al., 2015, Setälä et al., 2014, Cole et al., 2013, Jeong et al., 2016). The uptake and bioavailability of microplastics by zooplankton depend on either species, taxa and life-stage of zooplankton, or the size, concentration, type and shape of microplastics (Botterell et al., 2019, Cole et al., 2013). When exposed to 20 μm PS microbeads and cultured algae, copepod *Calanus helgolandicus* could ingest 11% less algae, cause reductions of ingested carbon biomass and significantly decrease the fecundity (Cole et al., 2015). Rehse et al. (2016) reported that ingestion of 1 μm PE microplastics led to immobilization of the limnic *Daphnia magna* with the concentration and exposure time increasing, but the 100 μm that not be ingested by *Daphnia magna* did not cause the physical effects. A recent study also reported that exposure of PE microbeads at size of 63-75 μm have no significant impacts on survival and reproduction of *Daphnia magna* although their guts were blocked, and promote the algal *Raphidocelis subcapitata* growth for 21 day experiment (Canniff and Hoang, 2018). Notably, exposure of microplastics in different sizes could result in significant size-dependent effects on zooplankton, such as feeding capacity, reduced growth rate and fecundity, increased mortality, long reproduction time and even affect the next generation (Besseling et al., 2014, Jeong et al., 2016, Lee et al., 2013). The smaller plastic particles including nanoplastics are generally more toxic and harmful to zooplankton (Lee et al., 2013, Rist et al., 2017). Moreover, the excretion ability of microplastics may be significantly correlated with its particle size. Jeong et al. (2016) found that 0.05/0.5 μm and 6 μm nonfunctionalized PS microbeads were excreted by Monogonont Rotifer *Brachionus koreanus* within 48 hours and 24 hours, respectively. In short, microplastic ingestion by zooplankton indicated that primary predators can interact with microplastics in surrounding environments.

2.2 Effects of microplastics on aquatic plants

Microplastics had been widely spread in various aquatic environments, so they can interact with aquatic plants such as duckweed (Dovidat et al., 2020), seagrass (Goss et al., 2018), and mangrove (Li et al., 2018b). Aquatic plants could absorb and accumulate microplastics to plant surface by phytostabilization, and “trap” microplastics from the surrounding water environments by different potential mechanisms such as plastic properties, electrostatic interactions, plant surface morphology and biofilm (Yuan et al., 2019, Goss et al., 2018, Bhattacharya et al., 2010, Nolte et al., 2017). Notably, microplastics absorbed on the plant surface are easily ingested by various herbivorous species, thus it represent an underappreciated pathway for transferring to the higher trophic levels via the food chain (Gutow et al., 2016, Goss et al., 2018, Dovidat et al., 2020, Kalčíková, 2020).

Up to now, far less research focused on the impact of microplastics on the aquatic higher plants. According to several limited researches, microplastics have slight impacts on higher plants. For example, the growth rate and chlorophyll content of duckweed *Lemna minor* were not affected by PE microplastics with a size range of 4-45μm (Kalčíková et al., 2017, Mateos-Cárdenas et al., 2019), but their root growth and cell viability were significantly reduced (Kalčíková et al., 2017). Dovidat et al. (2020) also reported that 50 nm PS nanoplastics and 500 nm microplastics were adsorbed externally to the roots of duckweed species *Spirodela polyrhiza*, while had no significant impacts on the growth of fresh weight, leaves and roots, and chlorophyll concentrations. Another study showed that PS nanoplastics (50-190 nm, 3% sediment dry weight) and PS microplastics (20-500 μm, 10% dry weight) have slight effects of root and shoot on the growth of two macrophytes *Myriophyllum spicatum* and *Elodea sp*. (van Weert et al., 2019). Notably, only nanoplastics (<20 nm) can efficiently penetrate plant cell wall (Dietz and Herth, 2011) and some large nanoparticles (<100 nm) may also enter by inducing the form of larger pores in cell wall surface (Rastogi et al., 2017). Thus, the potential risk of nanoplastics on the aquatic higher plants is nonnegligible. Bandmann et al. (2012) demonstrated that PS nanobeads (20 nm) rapidly enter the BY-2 cells by endocytosis and accumulate in different endosomes, while the nano-beads (100 nm) are excluded. Recently, Yuan et al. (2019) reported that PS nanoplastics (100 nm, 0-100 μg/mL) were massively accumulated in the spore surface of aquatic plant fern *Ceratopteris pteridoides* and penetrated into the roots of gametophytes. Moreover, PS nanoplastics exposure posed seriously negative effects on the growth and reproduction of fern in different life stages, and threatened the survival of this endangered ferns. Although microplastic and nanoplastic toxicology of phytoplankton especially various microalgae have been widely studied over a decade, the potential effect of plastic particles on higher aquatic plants remain further explored (Kalčíková, 2020).

2.3 Effects of microplastics on aquatic invertebrates

Aquatic invertebrates generally feed on primary producers and are served as an important food source for aquatic carnivores, which play a vital ecology role. Due to their feeding characteristics and trophic level of primary predator, aquatic invertebrates are more likely to be impacted by microplastic pollution. Various molluscs (Teng et al., 2019; Cho et al., 2019), arthropods (Desforges et al., 2015) and worms (Van Cauwenberghe et al., 2015), as the typical species in aquatic invertebrates, have been widely investigated. For example, Van Cauwenberghe and Janssen (2014) reported that mussels *Mytilus edulis* and oysters *Crassostrea gigas* cultured for human consumption contain microplastics with the average 0.47 and 0.35 particles/g, respectively. Another similar research showed that the total microplastic abundance in 9 commercial bivalves from China was 2.1-10.5 particles/g wet weight and 4.3-57.2 particles per individual (Li et al., 2015). According to an investigation of

17 coastal cities in China, the average concentration of microplastics in four cultured oyster species was 0.62 particles/g of tissue and 84% individuals ingested microplastics (Teng et al., 2019). Also, Li et al. (2016a) reported that the abundance of microplastics in mussels *Mytilus edulis* ranged from 0.9 to 4.6 particles/g from 22 sites along the China coast. Catarino et al. (2018) showed that the average abundance of microplastics in wild mussels *Mytilus spp.* and subtidal *Modiolus modiolus* from eight sampling stations of Scottish coast was 3.0 ± 0.9 and 0.086 ± 0.031 particles/g. Moreover, Li et al. (2018a) reported that wild mussels *Mytilus edulis* sampled from the United Kingdom coast all contain microplastics with the concentration of 0.7-2.9 particles/g of tissue. As the ubiquity and ecotoxicity of microplastics in bivalves such as mussels and clams, the species have been proposed as a meaningful biological indicator for aquatic microplastic pollution (Li et al., 2016a, Li et al., 2019, Su et al., 2018). On the other hand, Desforges et al. (2015) reported that 816 ± 108 μm microplastics were found in the krill *Euphausia pacifia* in the Northeast Pacific. Microplastics were also detected in wild lugworm *Arenicola marina* with a concentration of 1.2 ± 2.8 particles/g (Van Cauwenberghe et al., 2015). In an field investigation by Abidli et al. (2019), diverse microplastics was found in six commercial mollusk species including three bivalves *Mytilus galloprovincialis*, *Ruditapes decussatus* and *Crassostrea gigas*, two gastropods *Hexaplex trunculus* and *Bolinus brandaris*, and one cephalopod *Sepia officinalis* in Bizerte lagoons, whose microplastic abundances ranged from 703.95 ± 109.8 to 1482.82 ± 19.2 particles/kg wet weight. Noticeably, Windsor et al. (2019) reported that microplastics were

detected in 50% of freshwater macroinvertebrates (included Baetidae, Heptageniidae and Hydropsychidae) in the urban river systems of South Wales, with an average abundance of 0.14 particles/mg tissue. Additionally, different aquatic invertebrate species have different living characteristics, so it affects the biological uptake models of microplastics and its distribution in invertebrates. For instance, the respiratory exposure can serve as a pathway of microplastic uptake into the common nonfilter-feeder marine shore crab (Watts et al., 2014). Additionally, Kolandhasamy et al. (2018) found that microplastic adherence to soft tissue of mussels cause accumulation of miroplastics exceeding the ingestion.

Toxicological effects of microplastic ingestion vary from different aquatic invertebrates (Trestrail et al., 2020). The majority of ecotoxicological studies showed that microplastics have negative consequences (e.g., feeding, growth, development, reproduction, and survival) to the aquatic invertebrates (Trestrail et al., 2020, de Sá et al., 2018, Foley et al., 2018, Sussarellu et al., 2016), while limited effects were also reported. For example, Weber et al. (2018) reported that the exposure of PET microplastics (10-150 μm, 0.8-4000 particles/mL) for 24h have no significant impact on feeding, growth and development of the freshwater amphipod *Gammarus pulex*. Santana et al. (2018) also found that the exposure to PVC microplastics (0.1-1.0 μm, 0.125 g/L) for 90 days did not result in significant physiological damages to mussel *Perna perna*. Evidence showed that Pacific oyster *Magallana gigas* can expel from the majority of ingested PS microplastics in size range 100-500 μm, suggesting that the harm to the next trophic level is slight (Graham et al., 2019). Furthermore, Catarino et al. (2018) found that the potential impacts to human resulting from microplastics ingestion by mussel consumption are lower than the household fibres exposure. Accordingly, the potential risks of the trophic transfer of microplastics from aquatic invertebrates remain further studied.

2.4 Effects of microplastics on fish

Fish can uptake microplastics either from aquatic environment or via the secondary plastic ingestion from their prey (Kim et al., 2019, Chagnon et al., 2018). According to the field investigations, microplastics have been found in a variety of wild fish living in freshwater, estuarine, and marine systems (Jabeen et al., 2017, Azevedo-Santos et al., 2019, Collard et al., 2019, Lusher et al., 2013, Foekema et al., 2013). The ingestion of microplastics by fish is mainly influenced by the fish characteristics (e.g., species, life stages, feeding strategy and living habitat), exposure conditions, plastic properties (e.g., type, size, shape, color), and biofilm aging of microplastics (Ory et al., 2017, Goss et al., 2018, Collard et al., 2019, Adeogun et al., 2020, Neves et al., 2015). In 2013, Lusher et al. (2013) examined 504 fish with ten pelagic and demersal species collected from the English Channel, and found plastic debris (0.13-14.3 mm) in 36.5% of fish intestinal tracts, 92.4% of which was composed of microplastics. Then, Foekema et al. (2013) reported that microplastics (0.04-4.8 mm) were present in 2.6% of the 1203 fish and the five of seven species that caught from the North Sea. Recently, a global assessment showed that microplastics can be ingested by 427 fish species in different aquatic environments such as freshwater, estuarine, and marine, and exposed to different trophic levels of fish such as carnivore, omnivore, herbivore, algivore and detritivore (Azevedo-Santos et al., 2019). In the Clyde and Thames estuaries at UK watersheds, McGoran et al. (2018) found that microplastics can be ingested by 36% of 876 individual fish and the fourteen of twenty fish species. The average microplastics in digestive tracts of flatfish, other benthic fish and pelagic fish in Clyde was 3.92, 2.00 and 5.83 particles per fish, and at Thames Estuary, an average of 2.93, 1.50 and 3.20 particles per fish were observed, respectively. Moreover, Renzi et al. (2019) reported an average microplastics of 4.63 and 1.25 particles per fish in stomach contents of two pelagic fish species sardine *Sardinia pilchardus* and anchovy *Engraulis encrasicolus* caught from the Adriatic Sea, respectively. By contrast, the microplastic abundance in three benthic fish species (snailfish *Liparis tanakae*, point-head flounder *Cleisthenes herzensteini*, and anglerfish *Lophius litulon*) collected from 14 sites in the South Yellow Sea was 27.5, 19.2 and 5.9 particles/g wet weight in the soft tissues, respectively, suggesting that the surface sediments and benthic organisms were severely polluted by microplastic pollution (Wang et al., 2019b). Compared to the marine studies, the interactions between microplastics and freshwater fish still exist in knowledge gaps (Azevedo-Santos et al., 2019).

Fig. 2 shows the entry, migration and excretion of microplastics in fish. Microplastics can interact with fish through the direct feeding, indirect trophic transfer, respiratory exposure and skin absorption, but its distribution in fish is complex. These plastic particles can be mainly accumulated in the gills and gastrointestinal tracts (Barboza et al., 2020a, Peters and Bratton, 2016, Horton et al., 2018, Romeo et al., 2015, Zhang et al., 2019a, Bessa et al., 2018), and especially nanoplastics, via the complex mechanisms, transported to different tissues and organs such as liver, blood, muscle, and even brain (Barboza et al., 2020a, Kashiwada, 2006, Mattsson et al., 2017, Lu et al., 2016). Ecotoxicological effects of microplastics and nanoplastics on fish were verified in experimental studies, mainly affecting tissue and organ health, behavioral and neurological functions, intestinal permeability, metabolism, intestinal microbiome diversity, and even brain (Jacob et al., 2020). Somewhat differently, Ašmonaitė et al. (2018) found that ingestion of the relatively-large PS microplastics (100-400 μm) pre-polluted by environmental contaminants might resulted in a limited impact on the hepatic stress and lipid peroxidation of rainbow trout fish, and even did not influence fillet quality. Generally, the smaller plastic particles show the great hazard than the larger one, and the higher plastic concentration also plays an important role (Yang et al., 2020a, Gu et al., 2020). Notably, in micro-size levels of plastic particle, the toxic effect might not be simply negatively correlated with its size and size-dependent effects need to be further studied (Ding et al., 2020). As a common model species for evaluating toxicity, the negative influences on zebrafish, such as plastic particle accumulation, intestinal inflammation, tissues damage, developmental and reproductive impact, disorders of intestinal microbiome, metabolomics changes, and immune dysfunction, have been observed (Gu et al., 2020, Qiao et al., 2019a, Pitt et al., 2018, Lei et al., 2018). Interestingly, Ding et al. (2020) found that the exposure of 5 μm PS microplastics in red tilapia lead to the more severe metabolism effects and oxidative stress than the

70-90 μm and 0.3 μm microplastics. Yang et al. (2020a) reported that PS microplastics (50 μm) accumulated in the digestive tracts of goldfish Larvae *Carassius auratus* can cause oxidative stress, organs (e.g., gills, guts, liver) damage and inhibit the growth and movement, and nanoplastics (70 nm) can penetrate the epidermis of larvae into muscle tissues, resulting in the greater adverse effects. In addition, the nanoplastics may pass through the blood-to-brain barrier of crucian carp fish, causing brain damage and its behavior disorder (Kashiwada, 2006, Mattsson et al., 2017). The negative combined effects of microplastics and other multi-stressors (e.g., nanoparticles, temperature) on fish were also observed (Ferreira et al., 2016). However, some field investigation demonstrated that microplastics retained in fish are so few that it can be not accumulated inside the intestinal tracts for very long periods and have limited effects on wild fish, especially the top predatory fish (Chagnon et al., 2018, Foekema et al., 2013). Thus, exploring the profound impacts of nanoplastics at environmentally relevant concentrations on various fish is particularly needed. Furthermore, microplastic pollution in aquatic organisms remains challenging to monitor and to identify its quantities and distribution, and meanwhile, microplastics would be environmentally co-polluted with various chemical contaminants.

2.5 Effects of microplastics on waterbirds and other top predators

Waterbirds, including freshwater bird and seabird, would like to collect food from the aquatic environments, thus they can be inevitably affected by the ubiquitous microplastics (Fossi et al., 2018, Reynolds and Ryan, 2018, Basto et al., 2019). It is worth noting that the migratory behavior of waterbirds may cause the movement of microplastics due to the presence of microplastics in avian feathers and faeces (Reynolds and Ryan, 2018, Provencher et al., 2018a). Evidence showed that the species, life stages and foraging behavior of birds, and availability of plastics in its habitats affect microplastic ingestion by birds (Cartraud et al., 2019, Reynolds and Ryan, 2018). These ingested microplastics be mainly retained in the gastrointestinal tracts of birds (Brookson et al., 2019, Cartraud et al., 2019, Basto et al., 2019, Kühn and van Franeker, 2012, Nicastro et al., 2018). Then, a portion of microplastics can be excreted via their faeces (Provencher et al., 2018a), but the movement dynamics of plastics in bird gastrointestinal tracts are largely unknown (Terepocki et al., 2017). Notably, some bird species such as Eurasian dippers, great skua and gulls ingest the preys contaminated by plastic pollution and then regurgitate the undigested residues containing microplastics, suggesting that regurgitation behavior of birds represents an alternative route to excrete microplastics (Furtado et al., 2016, Hammer et al., 2016, D'Souza et al., 2020). Many studies have shown that seabirds in different regions can ingest the different levels of microplastics (Cartraud et al., 2019, Basto et al., 2019, Nicastro et al., 2018, Masiá et al., 2019). As the majority of northern fulmars *Fulmarus glacialis* in its stomachs contain plastic debris (Kühn and van Franeker, 2012, Terepocki et al., 2017), the species had been used as a bio-indicator for monitoring and evaluating the microplastic pollution levels in oceans (van Franeker et al., 2011, Herzke et al., 2016). Cartraud et al. (2019) reported that nine seabird species in the western Indian Ocean ingested plastic debris, and the most contaminated species were the tropical shearwaters (79% with plastics in guts) and Barau's petrels

(63%), with an average of 3.84 ± 0.59 and 6.10 ± 1.29 particles per bird, respectively. Recently, two studies showed that Gentoo penguin and King penguin in the Antarctic regions can uptake microplastics (mostly fibers), with a total of 20% and 77% of penguin scats containing microplastics, respectively (Le Guen et al., 2020, Bessa et al., 2019). However, it is unclear whether microplastics in penguins are derived from the direct ingestion from surroundings or the trophic transfer through the polluted preys.

Compared with the seabirds, little studies focused on the microplastic abundance in freshwater birds. For example, Holland et al. (2016) found the presence of microplastics (50 μm-5 mm) in eight of eighteen freshwater bird species (e.g., ducks, geese, and loons) in Canada and 15 of 350 individuals. In an investigation by Brookson et al. (2019), the double-crested cormorant chicks *Phalacrocorax auritus* collected from the Laurentian Great Lakes were investigated, 86.7% of which contained an average of 5.8 particles per bird in its gastrointestinal tracts, indicating the trophic transfer of microplastics from the contaminated preys to cormorant parents and then feeding on chicks. Moreover, Reynolds and Ryan (2018) reported seven African duck species from the contaminated freshwater wetlands in South Africa, and found that a total of 5% of faeces and 10% of feathers include microfibers. Liu et al. (2019d) also reported that the average microplastic abundance in migratory bird faeces in Poyang Lake wetlands is 4.93 particles/g, and microplastics in the active range of birds significantly increase. Although the presence of microplastics in various waterbirds including freshwater bird and seabird was confirmed, the toxicological effects of microplastics on waterbirds are largely unknown. The first feeding experiment demonstrated that ingestion of PP microplastics (3-4.5 mm) by Japanese quail *Coturnix japonica* at two environmental dose have no significant impacts on the lasting toxicological effects, survival or population outcomes over parental and two filial generations, but lead to the delays of growth and sexual maturity (Roman et al., 2019). More seriously, Lavers et al. (2019) revealed that the ingested plastic debris in Flesh-footed Shearwaters fledglings negatively affected its morphometrics and blood calcium levels, and were positively correlated with the concentration of uric acid, cholesterol, and amylase the concentration of uric acid, cholesterol, and amylase, suggesting that plastic pollution may be related with the blood chemistry parameters of birds and potentially cause negative health consequences. Furthermore, the combined effects of microplastics and associated contaminants (e.g., absorbed chemicals and plastic additives) on birds are exploring (Herzke et al., 2016, Guo et al., 2020a, Coffin et al., 2019). In short, waterbird as a typical predator easily influenced by aquatic environments, can be used as a meaningful bio-indicator for monitoring the microplastic pollution.

In addition to waterbirds, seals are also affected by microplastics. Bravo Rebolledo et al. (2013) first reported that ingestion of plastic debris by 11.2% of 107 harbour seals *Phoca vitulina* in the Netherlands was observed and young seals contain more microplastics in its stomach. Few studies had directly detected microplastics in the intestines of seals, while these retained microplastics may affect parasite aggregations (Hernandez-Milian et al., 2019). By investigating the samples of seal scats, microplastics exist in the South American fur seals *Arctocephalus australis*

(Perez-Venegas et al., 2018), harbor seals *Phoca vitulina vitulina* and grey seals *Halichoerus grypus atlantica* (Hudak and Sette, 2019), and northern fur seals *Callorhinus ursinus* (Donohue et al., 2019). Furthermore, the trophic transfer of microplastics from Atlantic mackerel to grey seals *Halichoerus grypus* was proved through a feeding study (Nelms et al., 2018), which provides a valuable insight into understanding the trophic transfer mechanisms of microplastics from low trophic levels to top predators.

The megafauna species is one of most affected by microplastics due to their unintentional ingestion, filter-feeding, and trophic transfer across the food chains (Zhu et al., 2019a, Maes et al., 2020, Germanov et al., 2018, Xiong et al., 2018). Studies on microplastic ingestion by cetaceans have been conducted primarily by dissecting the death individuals from stranding or fishery bycatch (Nelms et al., 2019a). To date, the presence of microplastics in the stomach or intestinal tracts of several dolphin species, such as short-beaked common dolphin *Delphinus delphis* (Hernandez-Gonzalez et al., 2018), East Asian finless porpoises *Neophocaena asiaeorientalis sunameri* (Xiong et al., 2018), harbour porpoises *Phocoena phocoena* (van Franeker et al., 2018), and *Sousa chinensis* (Zhu et al., 2019a), has been reported. Nelms et al. (2019a) also found 261 microplastic particles in the gastrointestinal tracts of 50 stranding marine mammal individuals around the coast of Britain that derived from 10 species including 7 dolphin species, 2 seals, and 1 whale. Moreover, Sala et al. (2019) found the high concentration levels (24.7 μg/g lipid weight) of total organophosphorus flame retardant additives in tissues of common dolphins *Delphinus delphis* from the Alboran

Sea. Additionally, microplastics may be an un-ignorable problem for the filter-feeding megafauna such as filter-feeding sharks and baleen whale, because they would like to filter plenty of water daily to gain adequate food and nutrition (Germanov et al., 2018). Since 2012, Prof. Maria Cristina Fossi and her co-workers have continuously reported the impacts of plastic pollution on Mediterranean fin whales *Balaenoptera physalus*, and found the presence of microplastics and their associated contaminants (e.g., additive phthalates, persistent organic pollutants) in whales, suggesting the direct microplastic ingestion and filter-feeding of contaminated prey (Fossi et al., 2014, Fossi et al., 2012, Fossi et al., 2016). Furthermore, they proposed the possible overlap between the microplastic hot spot areas and whale feeding habitat (Fossi et al., 2017a). Also, by a two-step literature review approaches successively to identify the main prey species of two baleen whales and microplastic ingestion by whale prey species, results showed that prey preferences and feeding strategies can affect microplastic ingestion by minke whale *Balaenoptera acutorostrata* and sei whale *Balaenoptera borealis* (Burkhardt-Holm and N'Guyen, 2019). Notably, Lusher et al. (2015) developed an effective method for detecting microplastics ingestion by marine megafauna, and found microplastics and macroplasticss in the stomach and digestive tracts of True's beaked whales. Recently, microplastics with an average of 97 ± 42 particles per individual were also reported in the gastrointestinal tracts of omnivorous beluga whales *Delphinapterus leucas* (Moore et al., 2020). In addition, the microplastic ingestion has been demonstrated in several shark species, including basking shark *Cetorhinus maximus* (Fossi et al., 2014), whale shark *Rhincodon typus*

(Germanov et al., 2019), blackmouth catshark *Galeus melastomus* (Alomar and Deudero, 2017), and Porbeagle shark *Lamna nasus* (Maes et al., 2020). Fossi et al. (2017b) conducted a toxicological investigation on 12 whale sharks from the California Gulf by the indirect skin biopsies, and found the high levels of organochlorine compounds (PCBs, DDTs), plastic additives (PBDEs) and CYP1A-like protein in the subcutaneous tissues, suggesting the underlying impacts of microplastic pollution to the endangered filter-feeding shark. Generally, top predator species, such as seal, dolphins, sharks and whales, play an important ecological role in biological indicators and monitoring the ecosystem health. However, the research fields of microplastic ingestion by these megafauna are still fraught with challenges, because of the difficulty in gaining accurate results from the large animals (e.g., gastrointestinal tracts). In addition, knowledge on the toxicological and clinical pathology effects of potential exposure to microplastics and plastic-associated contaminants is still scarce, thus it requires to be explored in the further works.

3. Combined effects of microplastics and associated chemical contaminants on aquatic organisms

In addition to toxicity and impacts of microplastics itself, its vector effects can affect the bioavailability (e.g., distribution in *vivo*, bioaccumulation, toxicity, transgenerational effects) of associated chemical contaminants to the aquatic organisms. Over the past decades, scientists have started to explore the role of plastic debris in transporting and releasing diverse chemical contaminants to the environment and wildlife (Teuten et al., 2009). Due to the microscopic size, hydrophobic surface, large specific surface area, and strong mobility, microplastics have a high affinity for hydrophobic chemical contaminants and absorb them from environment (Wang et al., 2018a, Teuten et al., 2007, Mato et al., 2001, Velzeboer et al., 2014, Wang et al., 2018b). In addition, microplastics can serve as a vector for transporting heavy metals in aquatic environments (Brennecke et al., 2016, Godoy et al., 2019). Meanwhile, studies suggested the desorption of these chemical contaminants from different microplastics under natural aquatic environments and simulated physiological conditions (Liu et al., 2019b, Lee et al., 2018, Bakir et al., 2016, Bakir et al., 2014). On the other hand, diverse additives and byproducts (e.g., PBDEs, phthalathes, nonylphenol, BPA, antioxidants) are added to plastic products during the manufacturing process to improve material performance. In recent years, evidence showed that these additives can leach from plastic debris or microplastics (including micro-rubber) into the environment (Liu et al., 2019b, Chen et al., 2019a, Khaled et al., 2018, Paluselli et al., 2019, Turner et al., 2020), causing non-negligible health risks (e.g., toxicity, endocrine disrupting, gene mutation) to aquatic organisms (Boyle et al., 2020, Kolomijeca et al., 2020, Capolupo et al., 2020, Oliviero et al., 2019, Pikuda et al., 2019). As a result, microplastics can be served as both sources and sinks for associated chemical contaminants in different media environments, and enhance them migration (Alimi et al., 2018, Wang et al., 2018a).

Three primary combined types of microplastics and associated chemical contaminants are included: the interaction of microplastics and organic contaminants, microplastics and heavy metals, as well as the leaching of plastic additives. Generally, there are two combined pathways to affect aquatic organisms: microplastics spiked with associated contaminants and co-exposure to a combination of both microplastics and associated contaminants. When exposed or ingested by animals, microplastics can provide a feasible pathway to transfer absorbed chemical contaminants and released additives into their tissues, posing a potential health risk (Bakir et al., 2016, Teuten et al., 2009, Browne et al., 2013, Campanale et al., 2020). However, these combined toxicities of microplastics and associated chemical contaminants may be chemical-specific and species-specific. Consequently, the extent to which diverse types of microplastics and nanoplastics enhances or mitigates the environmental and health impacts of these associated pollutants remains unclear because of the complexity of test organisms, microplastic properties, pollutants, environmental conditions, and exposure methods. With regard to the impacts of microplastics and associated chemical contaminants on aquatic organisms, the relevant studies are increasingly performing to better understand the potential risks of microplastics in the realistic aquatic environments. In this section, these combined effects of different microplastics and associated chemical pollutants on typical tested organisms were summarized and discussed.

3.1 Combined effects of microplastics and hydrophobic organic contaminants

Under laboratory conditions, microplastics (e.g., PE, PVC, PP, and PS) have been shown to adsorb chemical pollutants from the surrounding environment, with a high sorption capacity for hydrophobic organic pollutants such as PAHs, PCBs, DDT, hexachlorocyclohexanes, chlorinated benzenes, pharmaceuticals, personal care products (Wang et al., 2018a, Teuten et al., 2007, Velzeboer et al., 2014, Koelmans et al., 2013, Zhu et al., 2019b). In field investigations, microplastics can efficiently concentrate hydrophobic organic pollutants (e.g., PCBs, dichlorodiphenyl dichloroethylene, nonylphenol) from surrounding aquatic environments, due to the hydrophobicity of these compounds and to the high specific surface area of microplastic particles (Mato et al., 2001). Thus, microplastics can serve as carriers for accumulation and transfer of hydrophobic organic contaminants to organisms in the aquatic environments and affect wildlife populations and humans via the food chain and daily exposure (Teuten et al., 2007, Ziccardi et al., 2016, Rochman, 2019, Gassel and Rochman, 2019, Avio et al., 2015). As shown in **Table 1**, the knowledges regarding the combined effects of microplastics and organic contaminants on aquatic organisms are systematically summarized.

So far, there are studies on co-exposure of microplastics and hydrophobic organic contaminants, and their biological interaction mechanism is extremely complex. More available exploration about these combined effects is needed. In the sediments polluted by PCBs, the low concentration (0.074% and 0.74% dry weight) of PS microplastics (400-1300 μm) significantly increased the PCBs bioaccumulation in marine benthic lugworm *Arenicola marina*, while PCBs bioaccumulation reduced at the 7.4% of PS microplastics (Besseling et al., 2013). Then, Browne et al. (2013) added 230 μm PVC microplastics (5% of sands) pre-absorbed with environmentally-relevant hydrophobic organic pollutants (nonylphenol and phenanthrene) and additives (Triclosan and PBDEs-47) into sands, and found that these chemical contaminants can be transferred from ingested PVC to the gut tissues of lugworm *Arenicola marina*. Results showed the ecophysiological function damage of lugworms. In water environments, microplastics can affect the bioaccumulation of hydrophobic organic contaminants and their combined toxicity (Ziccardi et al., 2016, Yi et al., 2019a, Qu et al., 2020, Pittura et al., 2018). For example, Oliveira et al. (2013) reported that PE microplastics (1-5 μm) slowed PAHs pyrene-induced the mortality of common goby *Pomatoschistus microps* and modulated the pyrene biotransformation in bile. Meanwhile, PE microplastics in combination with pyrene significantly inhibited the acetylcholinesterase activity and reduced the isocitrate dehydrogenase activity. Somewhat differently, Paul-Pont et al. (2016) reported that PS microplastics (mixture of 2 and 6 μm) in combination with fluoranthene did not modify the bioaccumulation of fluoranthene in the tissues of marine mussels *Mytilus spp.*, but resulted in the toxicity (e.g., high histopathological damages, levels of anti-oxidant markers). Ma et al. (2016) found that 50 nm PS nanoplastics remarkably increased the bioaccumulation of phenanthrene in *Daphnia magna* and both of exhibit joint toxicity, while 10 μm PS microplastics did not show significant effects. In another chronic toxicity test, the increased concentrations of PE microbeads from personal care products significantly increased toxic effects of paraquat to carp fish and changed their biochemical parameters of blood (Nematdoost Haghi and Banaee, 2017). Guven et al. (2018) reported that the exposure to polystyrene divinilbenzene microspheres (97 μm, 100 particles/L) can influence the foraging/swimming behavior of barramundi juvenile *Lates calcarifer* and not significantly affect the acute effect of pyrene on predatory performance. Interestingly, Qu et al. (2018) found that the higher level of PVC microplastics (1-10 μm) enhance accumulation of antidepressant venlafaxine and its metabolites in loaches and sediments in four lab-scale freshwater ecosystems (including sediments, duckweed *Lemna minor*, loaches *Misgurnus anguillicaudatus*). Then, their following study reported that in the food chain from green algae *Chlorella pyrenoidosa* to freshwater snails *Cipangopaludian cathayensis* that co-exposed to the chiral methamphetamine and PS microplastics (700 nm), PS increased the bioaccumulation, biomagnification and acute toxicity of methamphetamine to snails (Qu et al., 2020). Following this, Brandts et al. (2018) assessed the effects of PS nanoplastics (110±6.9 nm, 0.05 mg/L) in combination with carbamazepine (6.3 μg/L) on Mediterranean mussel, and revealed that co-exposure induce physiological alterations and cause genotoxicity and oxidative damage. Zhang et al. (2019b) demonstrated that PS nanoplastics (100 nm) increased the bioaccumulation of roxithromycin in red tilapia *Oreochromis niloticus* and affected their metabolisms, but alleviated the neurotoxicity and oxidative damage caused by roxithromycin. Also, the co-exposure of PS microplastics (1 and 10 μm) and roxithromycin led to the acute toxicity, oxidative stress and strong biological responses in *Daphnia magna* (Zhang et al., 2019c). Another investigation by Felten et al. (2020) into the combined effects of pesticide deltamethrin and PE microplastics (1-4 μm) on Daphnia magna for 21 days found the synergistic adverse impacts on the survival, brood number, and fertility. Additionally, Tang et al. (2020) investigated the immunotoxicity of PS microplastics (30 μm and 500 nm) and two persistent organic pollutants (PAHs benzo[a]pyrene and 17β-estradiol) to the blood clams *Tegillarca granosa*, alone or in combination. In their study, results revealed the synergistic immunotoxicity, and size dependent effect of microplastics on toxicity of benzo[a]pyrene and 17β-estradiol. Under environmentally realistic conditions, microplastics usually coexist with the complex matrices, such as NOM and salinity. By the modeling calculation of the bioaccumulation effects in the complex matrices, Lin et al. (2020a) first reported that the bioaccumulation of PAHs mixtures mainly attribute to the dermal uptake of *Daphnia magna*, while the NOM or NOM-PS nanoplastics (100 nm) mixtures enhanced the mass transfer of PAHs to lipids in the gut.

Additionally, exposure to microplastics spiked with hydrophobic organic contaminants indicated the biomarker responses at cellular and sub-cellular level, such as alterations in oxidative stress, immune and neurological responses, and gene expression profiles. To begin with, Prof. Chelsea M. Rochman and her co-workers deployed PE pellets in San Diego Bay for three months, and then conducted a chronic microplastic dietary exposure to Japanese medaka *Oryzias latipes* for two month (Rochman et al., 2013, Rochman et al., 2014). According to their reported results, ingestion of PE microplastics contaminated by the environmentally-relevant PCBs, PAHs and PBDEs can result in the bioaccumulation of chemical pollutants and liver toxicity and pathology (e.g., increased glycogen depletion, fatty vacuolation, and cell necrosis) to medaka. Particularly, the endocrine-disrupting effects in fish and change of gene expression were also observed. Similarly, in another microplastic feeding experiments, the chemical-polluted LDPE microplastics (125-250 μm, 2% of feeding composition) enhanced the bioaccumulation and bioavailability of typical hydrophobic organic contaminants in zebrafish and European seabass, and exacerbate their toxic effects to tissues (Rainieri et al., 2018, Granby et al., 2018). Moreover, Avio et al. (2015) reported that PE and PS microplastics pre-absorbed with PAHs pyrene can be transfer pyrene to the tissues (e.g., digestive tissues, haemolymph, gills) of mussel *Mytilus galloprovincialis*. Results demonstrated the adverse molecular and cellular effects (e.g., immunological responses, peroxisomal proliferation, reduced antioxidant defenses, neurotoxicity, genotoxicity), and gene expression alterations. In another studies, the accumulation and trophic transfer of microplastics (1-5μm proprietary polymer and 10-20 μm PE) adsorbed with PAHs benzo[a]pyrene from *Artemia* sp. nauplii to zebrafish *Danio rerio* was observed (Batel et al., 2016, Batel et al., 2018). Karami et al. (2016) found that HDPE microplastics can cause toxicity to African catfish *Clarias gariepinus* and modulate the adverse impacts of PAHs phenanthrene on biomarker responses. Also, HDPE microplastics adsorbed with PAHs benzo[a]pyrene enhanced the Benzo[a]pyrene bioaccumulation in whole tissues and resulted in the chronic ecotoxicological effects to the two bivalve species *Mytilus galloprovincialis* and *Scrobicularia plana* (Pittura et al., 2018, O'Donovan et al., 2018). Another study done by Pannetier et al. (2019) assessed the combined toxicity of pollutants adsorbed on virgin mixture microplastics (40% of LDPE, 25% of HDPE, 25% of PP and 10% of PS) and environmental microplastics collected on beaches.

Their results revealed the adverse effects (e.g., high embryo mortality, low hatching rate, biometry and swimming behavior changes, increase of EROD activity, gene damage) on Japanese medaka embryos and prolarvae. Recently, the combined effects of PE microplastics in combination with triclosan on two bivalve species including oyster *Crassostrea brasiliana* and green-lipped mussel *Perna canaliculus* were investigated (Nobre et al., 2020, Webb et al., 2020). According to these results, microplastics promoted the uptake of triclosan by bivalves, and both of interaction increased different biochemical biomarker responses and affected bivalve health.

However, some studies have demonstrated that the combined effects of microplastics and hydrophobic organic contaminants on aquatic organisms may be antagonistic or slight. Based on the present results, the combined influences of microplastics (PE, PA, PS) and nonylphenol on the growth of microalgae *Chlorella pyrenoidosa* was antagonistic (Yang et al., 2020b). Yang et al. (2020c) observed that 5 μm PS microplastics reduced the bioaccumulation and bioavailability of chlorinated polyfluorinated ether sulfonate in zebrafish larvae but induced oxidative stress and inflammatory response. Another studies were reported by (Yi et al., 2019a, 2019b), their results suggested that the combined effect of PS microplastics (0.55 μm) and triphenyltin chloride on the green algae *Chlorella pyrenoidosa* was synergistic and increased their bioavailability and toxicity, but the combined effect of PS microplastics (0.1 and 5 μm) and triphenyltin on the marine diatom *Skeletonema costatum* was antagonistic and significantly reduced the toxicity with the smaller size. Also, Li et al. (2020b) observed that 10 μm PS microplastics at the 20 and 200 μg/L did not change the toxicity of PAHs phenanthrene, but 2 μg/L of PS microplastics alleviated the development toxicity of phenanthrene (e.g., increased 25.8% of hatchability, decreased malformation and mortality rates, restored abnormal expressions of cardiac development-related genes). Similarly, several studies also reported that the interaction between microplastics (e.g., PE, PVC, PS) and hydrophobic organic contaminants (e.g., PAHs phenanthrene, triclosan) were antagonistic and reduced the joint toxicity (Zhu et al., 2019b, Guo et al., 2020b). Additionally, Garrido et al. (2019) reported that PE microplastics (2-22 μm) decreased the acute toxicity of pesticide chlorpyrifos to the microalgae *Isochrysis galbana* due to the adsorption of chlorpyrifos onto microplastics. However, Bellas and Gil (2020) found that PE microplastics (1.4-42 μm) significantly increased acute toxicity (e.g., reduced feeding and egg production, decreased survival) of chlorpyrifos to marine copepod *Acartia tonsa*. Noteworthy, highest toxicity of production of feeding and egg was observed with the co-exposure PE microplastics and chlorpyrifos, while microplastics spiked with chlorpyrifos remarkably decreased survival rates of copepods. In a study done by Trevisan et al. (2019), it proved that PS nanoplastics (44 nm) reduced the bioavailability, bioaccumulation and toxicity of the environmentally complex sediment-PAHs mixtures to zebrafish embryos and larvae, but nanoplastics in combination with PAHs disturbed mitochondrial metabolism and efficiency, and impaired energy production. After spiking microplastics with 4-n-nonylphenol and 4-methylbenzyliden, Beiras et al. (2019) found that PE microplastics (4-6 μm) did not increase the bioavailability and acute toxicity of two hydrophobic chemicals to copepod *Acartia clause* and sea urchin larva *Paracentrotus lividus*. Based on studies by (Magara et al., 2018, 2019), the co-exposure and pre-spiked exposure of 10-90 μm microplastics (PE and PHB) and PAHs fluoranthene did not result in the synergistic toxic effects to the blue mussel *Mytilus edulis*, and only have a slight impact on the fluoranthene bioaccumulation and antioxidant responses. Collectively, these studies provide evidences that the interactions between diverse microplastics and hydrophobic organic contaminants to the aquatic organisms are extremely complex, and thus further efforts to deeply understand joint toxicity of microplastics with different chemical contaminants are needed. Besides, several modelling studies suggested that the pollutants transfer from aquatic environments to plastic debris is naturally driven and the "carrier-role" of microplastic transfer the adsorbed hydrophobic organic chemicals to living organisms would be minimal (Bakir et al., 2016, Koelmans et al., 2013). In the field investigations, the negligible impacts of ingested microplastics on bioaccumulation and tissue concentrations of persistent organic pollutants (e.g., PCBs, DDTs, PBDEs) in the northern fulmars *Fulmarus glacialis* were reported (Herzke et al., 2016, Provencher et al., 2018b). However, whether the bioconcentration, biomagnify and trophic transfer of microplastics and hydrophobic organic contaminants along aquatic food chains in the complex conditions is required to further explored and verified (Diepens and Koelmans, 2018).

On the other hand, studies regarding the combined effects of hydrophilic chemicals and microplastics to aquatic organisms still remain scarce. For example, Fonte et al. (2016) found that PE microplastics (1-5 μm) affected the toxicity (e.g., predatory performance, acetylcholinesterase activity, lipid peroxidation levels) of antibiotic cefalexin to the common goby juveniles *Pomatoschistus microps*. Noteworthy, temperature rising from 20 to 25 ℃ increased combined toxicity of PE and cephalexin, especially the higher predatory performance inhibition. Moreover, Guilhermino et al. (2018) investigated the short-term toxicological interactions between the polymer microspheres (1-5 μm) and antimicrobial florfenicol, alone and in combination, to the freshwater bivalve *Corbicula fluminea*. Their results demonstrated that the mixtures containing microplastics and florfenicol were more toxic and cause adverse effects (e.g., feeding inhibition, alterations of histopathology and other biomarkers). Prata et al. (2018) reported that the mixtures of 1-5 μm polymer microspheres and two pharmaceuticals procainamide and doxycycline led to the higher toxicity (e.g., inhibition of growth rate, reduced chlorophyll) to the marine microalgae *Tetraselmis chuii* than the pharmaceuticals alone. More recently, a study by Zhou et al. (2020) assessed the effects of PS microplastics (500 nm) on the bioaccumulation of two veterinary antibiotics oxytetracycline and florfenicol in the edible blood clam *Tegillarca granosa*, and subsequent health risks to seafood lovers. They found that microplastics aggravated the bioaccumulation of these two antibiotics, and observably suppressed the clam glutathione-S-transferase activity and detoxification processes. Although the direct toxicity caused by ingested contaminated clams is lower, the potential antibiotic resistance risks are non-negligible due to the dietary antibiotics exposure of human gut microbiota. Conversely, Zhang et al. (2018) showed that PS-NH_2 microplastics (200 nm) alleviated the growth inhibition of herbicide glyphosate to blue-green algae *microcystis aeruginosa* due to the glyphosate adsorption onto microplastics.

Thus, the above results revealed that the combined toxicities of microplastics and organic pollutants on the aquatic organisms are chemical-specific and species-specific. According to the present toxicity studies, whether the combined effects of microplastics and organic pollutants are antagonism or synergism remains under debate. It might depend on the complex factors, such as microplastic properties (e.g., type, size, surface functional groups), chemical pollutants, tested species and exposure conditions. Furthermore, operable assessment methods about the mixture toxicities caused by microplastics and multiple component chemicals should raise more attentions. Additionally, desorption and transfer kinetics of surface-absorbed hydrophobic organic contaminants from the ingested microplastics to organism tissues are need to explored in the future studies (Bakir et al., 2014, Mohamed Nor and Koelmans, 2019).

3.2 Combined effects of microplastics and heavy metals

Microplastics as vectors for heavy metal ions have been verified (Brennecke et al., 2016, Godoy et al., 2019). These heavy metals might be transferred from microplastics to aquatic organisms. The studies regarding the combined effects of microplastics and heavy metals (e.g., Hg, Cd, Cu, Pb, Cr, Ag, Au) are summarized in **Table 2**.

In recent years, the toxicity of co-exposure of microplastics and heavy metals to aquatic organisms has been investigated. For instance, Luís et al. (2015) investigated the impacts of PE microplastics (1-5 μm) on the short-term Cr(VI) toxicity to the common goby juveniles *Pomatoschistus microps* collected from two wild estuarine, and found that microplastics can affect the Cr(VI) acute toxicity to goby juveniles. Notably, the difference of natural living habitat significantly influence the sensitivity and responses (e.g., predatory performance, oxidative damage) of fish inhabiting two estuaries to the mixture of Cr(VI) and PE microplastics, suggesting the complexity of toxicological effects of microplastics and associated contanminants to aquatic organisms in long-term exposure to natural environmental conditions. In 2018, Dr. Luís Gabriel Antão Barboza and his co-workers systematically reported the combined effects of 1-5 μm polymer microspheres (0.26 and 0.69 mg/L) and Hg (0.010 and 0.016 mg/L) on the European seabass juveniles *Dicentrarchus labrax* for 96h exposure (Barboza et al., 2018a, Barboza et al., 2018b, Barboza et al., 2018c). In their experiments, results indicated that microplastics can slightly decrease the Hg bioaccumulation in fish tissues (e.g., brain, muscle) due to microplastic adsorption, but the both mixtures led to neurotoxicity, lipid oxidative stress and damage, and altered activities of energy-related enzymes. Then, the co-exposure of microplastics and Hg adversely affected swimming performance of European seabass, causing the erratic behavioural responses and decay of the swimming velocity and resistance time. The Hg bioconcentration in gills and bioaccumulation in liver of European seabass caused by microplastics was also observed. In addition, Lu et al. (2018) found that PS microplastics (5 μm) promoted the Cd bioaccumulation in zebrafish tissues (e.g., gills, guts, livers) and increase the Cd toxicity. Meanwhile, the co-exposure of PS and Cd for three weeks led to oxidative damage and inflammation in zebrafish. Then, Lee et al. (2019) investigated the bioaccumulation and in-vivo toxicity of PS nano- and micro-plastics (50, 200 and 500 nm) in combination with Au ion. Based on the microscopic observation and embryonic toxicity analysis, the smaller PS nanoplstics can penetrate into the zebrafish embryo, accumulate in the whole body, and cause limited marginal effects (e.g., survival, hatching rate, developmental abnormalities, cell death). More seriously, the interaction of PS and Au synergistically exacerbated these marginal effects to zebrafish embryos and induced additional toxicity (e.g., production of reactive oxygen species, pro-inflammatory responses and mitochondrial damage). Moreover, the combination of Cd and PE microbead from scrub products synergistically exacerbated the sub-lethal toxic effects to the common carps *Cyprinus carpio* and altered their biochemical and immunological parameters (Banaee et al., 2019). In another study, Roda et al. (2020) showed that the exposure of PE microspheres (10-90 μm) and Cu both in alone and combination can lead to DNA damage, oxidative stress, neurotoxicity, and physiological effects to the neotropical teleost *Prochilodus lineatus*. Considering the interaction in plasma Ca^{2+}, combined effects of PE and Cu might cause a greater impact than that of alone. Interestingly, Yan et al. (2020) evaluated the combined toxicity of three heavy metal mixtures (10 μg/L Cd, 50 μg/L Pb, and 100 μg/L Zn) and PS microplastics (2.5 μm, 100 μg/L) to the gut microbiota and gonadal development of marine medaka *Oryzias melastigma*. Their results demonstrated that PS microplastics enhanced the bioaccumulation of Cd, Pb, and Zn in the guts, brains, livers and gonads of marine medaka, and mainly caused reproductive disturbance by affecting gonad development. Also, the combination of heavy metal mixtures and PS microplastics increased combined-pollution load in the gut, and significantly perturbed the specific bacterial species and gut function in the male medaka. Additionally, the polyacrylonitrile microplastics (0.05-0.8 μm) combined with Cu inhibited the growth of microalgae *Chlorella pyrenoidosa* populations, negatively influenced the levels and function of the photosynthetic pigments (e.g., chlorophyll a, b, total chlorophyll), and increased antioxidant stress (e.g., H_2O_2 content, catalase activity, and malondialdehyde content) (Lin et al., 2020b). Recently, Tunali et al. (2020) showed that the exposure of PS microplastics (0.5 μm, 100 mg/L) and metals (Cu, Mn, Zn, 0.25 mg/L) for 18 days caused the greater inhibiting effect on the growth and chlorophyll a concentration of microalgae *Chlorella vulgaris* than the single contaminants.

However, some studies demonstrated that combined effects of microplastics and heavy metals to aquatic organisms might be slight and even antagonistic. Davarpanah and Guilhermino (2015) reported the effects of PE microplastics (1-5 μm) in mixture with Cu on the growth rates of marine microalgae *Tetraselmis chuii*. Their results showed that Cu alone significantly decreased the microalgal population growth with the increasing concentrations (0.02-0.64 mg/L), but the enhanced Cu-induced toxicity was not observed in the co-exposure to PE microplastics for 96 h. Khan et al. (2015) contrasted the uptake and localization of Ag in zebrafish between PE microplastics (10-106 μm) spiked with Ag and the co-exposure of microplastics and Ag. In the co-exposure experiment, the presence of PE did not affect Ag uptake and localization in tissues (e.g., body, intestine, gills). Yet, the Ag-spiked PE microplastics significantly decrease Ag uptake and observably increased its localization in intestine. Moreover, Kim et al. (2017) found that immobilization of *Daphnia magna* exposed to Ni and PS-COOH microplastics (182.7 nm) was higher than that of exposed to Ni and PS microplastics (194 nm). PS microplastics led to mildly antagonistic effects on Ni-induced toxicity to Daphnia, while PS-COOH in combination with Ni was slightly synergistic. Their experiment showed combined toxic effects probably attributing to the specific properties of microplastic surface functional groups and associated contaminants. Also, Bellingeri et al. (2019) reported no additional effect of PS-COOH nanoplastics on the growth inhibition of freshwater microalgae *Raphidocelis subcapitata* exposed to Cu in 72 h or 7days. In another study for 14 days, the co-exposure of polymer microspheres (1-5 μm) and Hg to freshwater bivalve *Corbicula fluminea* reduced the filtration rates and Hg bioconcentration, and led to oxidative stress and neurotoxicity (Oliveira et al., 2018). Nevertheless, these effects (e.g., filtration rate, activity of cholinesterase enzymes, activity of glutathione peroxidase and glutathione S-transferases, lipid peroxidation) caused by microplastics combined with Hg were lower than the sum of single effects, suggesting the slight antagonism in combination of microplastics and Hg. Similarly, Sıkdokur et al. (2020) reported that co-exposure of PE microbeads (10-45 μm) and Hg to Manila clam *Ruditapes philippinarum* can decrease uptake of both Hg and PE and the filtration rates, and cause alterations of histopathology (e.g., gills, digestive gland tissues), indicating a negligible carrier role of microplastics in Hg uptake. Additionally, the mixture of PS microplastics (32-40 μm) and Cd promoted severe oxidative response and enhanced the innate immune of the discus fish juveniles, but the co-exposure did not affect their growth and survival and decreased the Cd bioaccumulation (Wen et al., 2018). Interestingly, Zhang et al. (2020b) reported that the toxic effects of PS (10 μm, 0.05, 0.1, 1, 5 and 10 mg/L) and Cd (0.01 mg/L) to embryo development (e.g., body length, heart rate) are synergistic, while lethal toxicity (mortality rate) show antagonistic effects. Also, these combined effects are positively related with microplastic concentration.

On the other hand, microplastics absorbed with heavy metals can affect aquatic organisms. As shown by Khan et al. (2015), Ag-spiked PE microplastics significantly decrease Ag uptake and facilitated its localization in intestine. Additionally, Jinhui et al. (2019) prepared the *Mysis* bait containing 15-80 μm HDPE microplastics pre-spiked with heavy metals (including Cu, Cd, Pb), and analyzed the impacts of polluted bait on the yellow seahorse *Hippocampus kuda*. The unhealthy feeding model enhanced the bioaccumulation of HDPE and heavy metals, adversely influenced the seahorse growth and suivival, and caused oxidative damage. By comparison of three exposure pathway (e.g., HDPE microplastics spiked with Hg, microalgae spiked with Hg, water-dissolved Hg) to mussels *Mytilus galloprovincialis*, Rivera-Hernández et al. (2019) found similar Hg bioaccumulation amounts in tissues and Hg distribution among tissues varied. It is worth noting that more than 70% of Hg uptake through HDPE microplastics can be rapidly eliminated due to the body surface adhesion, faeces pathway and high adsorption of Hg by microplastics. Similarly, Fernández et al. (2020) contrasted and investigated the role of HDPE microplastics (10-15 μm in mean size), microalgae *Isochrysis galbana* and water media as carrier for the bioaccumulation of Hg, respectively. They also proved that HDPE microplastics significantly enhanced the bioaccumulation and elimination of Hg, indicating the limited toxicological risks of Hg adsorbed onto HDPE.

In the real aquatic environments, diverse microplastics would suffer from the complex nature weathering or aging behaviours, such as UV-irradiation, mechanical forces and microbial degradation. Aged-microplastics may change the adsorption behavior, bioavailability and toxicity of different heavy metals due to the modification of physicochemical properties in the plastic surface. Fu et al. (2019) observed the single and combined effects of UV-aged PVC microplastics (<183 μm) and Cu on microalgae *Chlorella vulgaris*, and found that UV-aged PVC significantly inhibited algal growth than the virgin one. However, their results showed that the combined interaction of UV-aged PVC microplastics (10 mg/L) and Cu (0.5 mg/L) alleviated the negative single effects (e.g., cell damage, growth inhibition, oxidative stress) and enhanced growth of microalgae. Noteworthy, the reason of decreased toxicity may be due to the pollutant adsorption ability of aged-microplastics with large surface and oxygen-containing functional groups, and microplastic precipitation behavior. In addition, Kalcikova et al. (2020) reported biofilm-aged behavior promoted Ag adsorption onto PE microbeads from cosmetic products and affected its subsequent leaching. Then, the biofilm-aged microbeads spiked with absorbed Ag significantly increased combined toxicity to aquatic organisms, reducing the growth rates and root length of duckweeds *Lemna minor* and causing 100% mobility inhibition of daphnids *Daphnia magna*. Moreover, Wang et al. (2020a) observed the chronic combined effects of biofilm-aged PE microbeads with absorbed Cd on cladoceran *Moina monogolica* for 21 day exposure. In their experiment, evidence suggested the greater adverse dose-dependent toxicity to cladoceran on the growth, development, and reproduction at the population level. Parental mortality, and poor nutritional and energy reserves in offspring also appeared. These studies revealed that the different aging behaviors of microplastics can significantly influence the microplastic properties, interaction with associated chemicals, and its combined toxicity. Additionally, microplastic issues are environmentally-relevant complex and usually related to environmental parameters (e.g., NOM, co-existing mixtures). Qiao et al. (2019b) explored the interactions between nano/microplastics (100 nm and 20 μm) and NOM to the bioaccumulation and toxicity of Cu in zebrafish *Danio rerio*. Based on their results, Cu adsorption and bioaccumulation in the livers and guts of zebrafish were increased, and its toxicity (e.g., increased contents of malonaldehyde and metallothionein, decreased superoxide dismutase) were also aggravated.

3.3 Effects of plastic additives

As plastic items break down into the smaller debris during weathering/aging processes, diverse additives of organic and metal compounds (e.g., plasticizers, flame retardants, antimicrobials, antioxidants, lubricants, colour pigments) may be released into the environment. In addition to the combined effects of microplastics and absorbed chemical contaminants, these leaching additives cause potential ecotoxicological risks to various aquatic organisms (Hermabessiere et al., 2017). Estimated 35-917 tons of additives can be released into oceans annually (Suhrhoff and Scholz-Böttcher, 2016), and PBDEs, phthalathes, nonylphenol, BPA and antioxidants are the common plastic additives (Hermabessiere et al., 2017).

Different environmental conditions such as water movement, salinity, UV irradiance and other stressors can affect leaching behavior of additives from plastic items, and its related toxicity to organisms (Kolomijeca et al., 2020, Suhrhoff and Scholz-Böttcher, 2016, Luo et al., 2019). For example, Khaled et al. (2018) found that the solar simulator and outdoor irradiations enhance the fragmentation of PS film (100 μm) and accelerate leaching of various brominated flame retardants and its photoproducts. Similarly, four organotin compounds (e.g., dimethyltin, monomethyltin, dibutyltin, monobutyltin) were released from PVC microplastics (10-300 μm) under UV/visible light irradiation during 0.5-56 h, and meanwhile photodegradation of partial organotin occurred (Chen et al., 2019a). They further demonstrated that the high salinity exposure inhibited the release and photodegradation of organotin compounds, while the presence of humic acid enhance organotin release and indirectly increase their degradation. Moreover, Paluselli et al. (2019) reported that two commercial plastic debris including PVC-cable and PE-bag significantly released different plasticizer phthalates into their surrounding seawater samples during 0-12 weeks. According to their measurement, light condition and bacterial exposure can affect the quantities and dominant types of phthalates leached from two plastics, respectively. Also, Chen et al. (2019b) showed that marine-collected PE microplastics (0.5-5 mm) and mesoplastics (5-15 mm) released into endocrine disrupting chemicals, which mainly include estrogens (e.g., bisphenol A, bisphenol S, octylphenol, nonylphenol). Smaller microplastic sizes and natural solar irradiation can enhance the leaching concentrations of endocrine disrupting chemicals, while microwaving and autoclaving are the opposite. More recently, Kolomijeca et al. (2020) demonstrated the impacts of environmental stressors (e.g., temperature, UV irradiation, water turbulence, CO_2) on the leachate properties of tire particles. In their experiment, changes to temperature and water turbulence may increase the leaching amounts of additive chemicals from tire particles and further influence the toxic effects of leachates to fathead minnow fish. Notably, evidences have shown that presence of Pb additives in marine plastics results in a greater adverse impacts (e.g., Pb concentrations, bioaccessibility) than Pb adsorption from surrounding environment (Turner et al., 2020). In field investigations, Jang et al. (2016) found that mussel *Mytilus galloprovincialis* inhabiting marine PS styrofoam debris can accumulate PS microparticles and 5160 ng/g of brominated flame retardant HBCDs, suggesting the transfer of additives from styrofoam debris to mussels. Barboza et al. (2020b) reported that levels of seven bisphenols in tissues (e.g., muscle, liver) of wild fish in North East Atlantic Ocean were correlated with the higher microplastic intake. These results revealed diversified and toxic organic and metal compounds in the plastic leachates, thus the release mechanisms of plastic additives under complex environmental stressors and their potential toxicity to aquatic organisms required to be further studied.

Some studies have verified toxic effects of plastic additives (including organic and metal compounds) to aquatic organisms by the leaching experiments, as shown in **Table 3**. According to wide investigations to diverse commercial plastic products, plastic debris can leach additives into its surrounding water environments for a short-term exposure and partial leachates lead to acute toxicity (e.g., embryo development, immobility, physical activity, mortality) to typical tested species (e.g., *Daphnia magna*, copepod, shellfish, fish) (Lithner et al., 2009, Lithner et al., 2012, Bejgarn et al., 2015, Li et al., 2016b, Gandara e Silva et al., 2016). Moreover, Oliviero et al. (2019) reported that three commercial PVC microplastics (<250 μm,100 g/L) with different colors can leach out metal compound mixtures for 24 h. These leachates contained heavy metal coloring agents, and thus inhibit larval development of sea urchin and cause larval morphological alterations with the increasing exposure concentrations, while pristine PVC leachate has no toxicity. Notably, by the comparison of acute toxicities of non-dialyzed PS nanoplastics (20 and 200nm), dialyzed PS nanoplastics, and an antimicrobial preservative sodium azide, experimental results indicated that commercial additives from PS at the high doses be mainly responsible for mortality of *Daphnia magna* (Pikuda et al., 2019). This study highlights the importance of assessment to ecotoxicological effects of additives in commercial plastic products. In addition, Schrank et al. (2019) observed that flexible PVC microplastics with its leachable plasticizer diisononylphthalate led to slight alterations in body length and reduce offspring numbers of crustacean *Daphnia magna*. Luo et al. (2019) reported that the additive leaching concentrations of light-aged PUF microplastics varied from the simulated and natural water media, and leachates inhibited growth and cell photosynthesis of microalgae *Chlorella vulgaris* with the increasing concentrations. In order to distinguish the role of additives in leachate toxicity of PVC, HDPE, and PET microplastics, Boyle et al. (2020) investigated the changes in biomarker expression of zebrafish larvae. In their experiment, the leaching Pb from PVC elicited the response of metallothionein 2 gene expressions in zebrafish, but HDPE and PET itself do not affected the expression. Currently, Chae et al. (2020) evaluated the impacts of leachate from nine fragmented and spherical expanded PS microplastics/macroplastics on the photosynthetic performance of four marine microalgal species (*Dunaliella salina*, *Scenedesmus rubescens*, *Chlorella saccharophila*, and *Stichococcus bacillaris*). However, leachate exposure generally promoted the photosynthetic activity of all microalgal species with a slight different trend. Additionally, the toxicity of leachates from wild-collected microplastics has rarely been studied. Leachates from beach-collected micro-pellets had a slightly abnormal effect on the embryos development of sea urchin, which was lower compared with that of virgin PE pellets (Nobre et al., 2015). Conversely, Gandara e Silva et al. (2016) reported that toxicity (e.g., abnormal embryo) of the leachate from beach-collected micro-pellets to brown mussels was higher than that of commercially virgin PP pellets. These different outcomes may be due to the microplastic surface-adsorbed contaminants from surrounding environments.

Furthermore, additives interacted with microplastics could result in different impacts to aquatic organisms. In the previous study, Chua et al. (2014) investigated whether PBDEs absorbed in microbeads (11-700 μm) from facial cleaning soap were assimilated by marine amphipod *Allorchestes compressa* by microplastic ingestion. Results showed that the presence of PE microbeads decreased the uptake of total PBDEs into amphipod, but led to the greater proportion uptake of their higher-brominated congeners into amphipod. Differently, Wardrop et al. (2016) found that PE microbeads (10-700 μm) from face scrub soap enhanced the bioaccumulation of PBDEs in the rainbow fish *Melanotaenia fluviatilis*, and lower brominated congeners had the highest assimilation but higher brominated congeners can be not transferred. Similarly, PS nanoplastics (50 nm) significantly promoted BPA uptake and bioaccumulation in zebrafish tissues, and their co-exposure treatment enhanced BPA bioavailability and neurotoxicity (Chen et al., 2017). Also, Xia et al. (2020) reported that vector role of PS microplastics (2 μm) for bioaccumulation of decabromodiphenyl ether (BDE-209) in the marine scallop *Chlamys farreri* was greater than the scavenger role, thus PS microplastics increased the adverse impacts of BDE-209 on phagocytosis rate and DNA damage of hemocyte, and ultrastructural changes in scallop tissues. Furthermore, co-exposure of tetrabromobisphenol A and PE microbeads (100-400 μm) from two facial cleanser products to zebrafish *Danio rerio* altered the integrated biomarker response index (e.g., glutathione S-transferase, glutathione reductase, activities of Lactate dehydrogenase, acid phosphatase) and induced significantly antioxidative stress response (Yu et al., 2020). Additionally, PS microplastics (65 nm and 20 μm) in combination with butylated hydroxyanisole (BHA) increased the bioaccumulation of BHA in zebrafish larvae and developmental toxicity (e.g., reduced hatching rates, increased malformation rates, decreased calcified vertebrae), and affected the development-related metabolism (Zhao et al., 2020). However, Li et al. (2020c) observed that the combined effects of PS microplastics (0.1, 0.55 and 5 μm) and dibutyl phthalate (DBP) to the microalgae *Chlorella pyrenoidosa* were variable at different concentration ranges. When the PS concentration was less than 10 mg/L, the interaction between PS microplastics and DBP was antagonistic at low concentrations of DBP and was synergistic at relatively high concentrations of DBP, but it was antagonistic at more than 10 mg/L PS microplastics. Noteworthy, PE microplastics (10-45 μm) can both serve as a vector and effective scavenger for the bioaccumulation of PBDEs in *Talitrus saltator*, suggesting a limited impacts (Scopetani et al., 2018). As suggested by Rehse et al. (2018), the mixtures of BPA and PA microplastics (5-50 μm) caused the reduced immobilization of *Daphnia magna* than that of BPA alone. Another study by Horton et al. (2020) into the combined effects of PA microplastics (<50 μm, 1% of sand sediments) and PBDEs on the pond snail *Lymnaea stagnalis* for 96 h showed the alleviated weight change and no significant influence on the total PBDE uptake, and the diversity and composition of the snail microbiome.

On the other hand, tire wear particles have become a common microplastic pollution and a worthy concern due to the combination of physical interactions between particles and organisms, toxic chemical compounds released from the tire particles, and high emission quantities with millions of tons annually (Kole et al., 2017, Wagner et al., 2018). Some studies regarding the impacts of tire particle and its leachates on aquatic organisms have been performed. For example, Villena et al. (2017) prepared leachate from tire particle (<0.59 mm) for a week, and assessed its adverse effects on the development and survival of the invasive mosquito *Aedes albopictus* larvae and native mosquito *Aedes triseriatus* larvae. Their results revealed that the high concentrations of tire leachate including Zn negatively affect population growth of two mosquito species, but this invasive mosquito show a significantly stronger tolerance than the native species. Furthermore, compared with the leaching of PP, PET, PS and PVC microplastics, Capolupo et al. (2020) evaluated the adverse impacts leachate from car tire particles (1-2 mm) on the two microalgae (freshwater *Raphidocelis subcapitata* and marine *Skeletonema costatum*) and Mediterranean mussel *Mytilus galloprovincialis*. By combining the non-target and target chemical analytical methods, their results indicated the complex polymer-specific mixtures of metals and organic compounds in these leachates, and the high concentrations of benzothiazole and *n*-cyclohexylformamide in car tire particles, phthalide in PVC, acetophenone in PP, cobalt in tire particles and PET, Zn in tire particles and PVC, Pb in PP and antimony in PET, respectively. Also, tire particle and PVC leachate showed significantly higher growth inhibition to two microalgae species and toxicity to mussel embryo development, survival and mobility than that of other microplastics. Recently, Kolomijeca et al. (2020) explored the effects of typical environmental stressors (e.g., turbulence, temperature, CO_2, UV irradiation) on the impacts of tire particle leachate on fathead minnow embryos *Pimephales promelas*. According to their analysis, these leachates mainly contained Zn and diverse PAHs congeners, and its ecotoxicological effects (e.g., hatching success, deformities) were significantly affected by tire types and environmental conditions (especially water turbulence and temperature). By contrast, Panko et al. (2013) reported that tire particles up to 10g/kg sediments or its leachate from mixed sediments had a limited toxicity to four freshwater aquatic biota (*Ceriodaphnia dubia*, *Pimephales promelas*, *Chironomus dilutus*, and *Hyalella azteca*). As shown in Redondo-Hasselerharm et al. (2018), in-situ adverse effects (e.g., feeding rates, growth, survival, populations) of tire particles and associated leachate to aquatic organisms when exposed in sediments might be lower than the previous studies after forced additive leaching from car tire particles. These widely varied outcomes might attribute to the discrepancies of tire properties, leaching approaches, tested species, and exposed media environments. Further efforts should be require to standardizing the methods of leachate preparation and toxicity assessments, and exploring the long-term effects of plastic additives exposure in different environment media on aquatic organisms.

Apart from the exposure to diverse environmental plastic additives, few studies on desorption of additives in the gastrointestinal tracts of aquatic organisms (e.g., fish, bird) have been gradually raised attention. Koelmans et al. (2014) first proposed a bio-dynamic model for estimating the leaching of nonylphenol and BPA from ingested microplastics by lugworm *Arenicola marina* and North Sea cod. Their results showed that microplastic ingestion by lugworm do not form an exposure pathway to leaching chemicals in the intestinal tracts, while for sea cod, it serve as a potential exposure pathway. Using both fish and seabird in-vitro laboratory gut mimic mode, evidence showed that gut conditions can enhance leaching of estrogenic chemicals (e.g., BPA, phthalates) from sixteen macro/micro-sized commercial plastic items (including LDPE + nylon, POM, PP, PS, PP, PA, LDPE, HDPE, PP, nylon + polyester, PE, LDPE, PP, latex, isoprene and PS), and lead to significantly biological estrogenicity (Coffin et al., 2019). Also, the leaching of additive-derived brominated flame retardants from ABS microplastics (100 μm-2 mm) was reported in simulated gastric and gastrointestinal fluid (Guo et al., 2020a, Guo et al., 2019). In their following experiment, results revealed that the co-ingested sediments and bird diets (e.g., fish, clam, and rice) can affect the leaching proportions of additive chemicals through the migration and adsorption behaviors. Moreover, Smith and Turner (2020) observed the release of Br, Cd, Cr, Hg, Pb and Sb from nine microplastic samples (including PE, PP, PVC, PC+ABS, and PU) exposed in digestive conditions of seabirds over 168 h, and found that its mobilization kinetics fit simple diffusion models. Thus, future researches need to identify the full suite of possible toxic chemicals leaching from ingested microplastics in real gastrointestinal environment, and adequately understand their potential impacts to aquatic organisms.

Up to now, although combined effects of microplastics and their associated contaminants (e.g., hydrophobic organic contaminants, heavy metals, plastic additives) to aquatic organism have been widely studied, several perspectives need to concern. (1) Which lead to the dominant toxicity of microplastics to aquatic organisms, due to the microplastics itself, their associated contaminants, or both of combined effect？

According to the previous section, microplastics itself, especially nanoplastics can interact with different trophic level organisms by the multiple ways and affect their physiological activity. Neverthless, relevant studies distinguishing between the effects of the synthetic polymer itself and incorporated additives or environmentally-absorbed chemicals in same polymer are still scarce. As shown by Pikuda et al. (2019), the acute toxicity of commercial PS nanoplastics (20 and 200 nm) can be mainly attributed to the additive preservatives (e.g., sodium azide) rather than the PS itself, suggesting that toxicity assessments may be disturbed by the additives in commercial plastic formulations. Similarly, PVC microplastics with different colors showed the different toxicity mainly due to the heavy metals in coloring agents (Oliviero et al., 2019). Additionally, the pre-added Pb in plastic pellets collected from sandy beaches may lead to a greater environmental impact than surface-adsorbed Pb (Turner et al., 2020). Consequently, future studies should consider the full suite of chemicals in microplastic leachate and use effect-directed analysis to determine which microplastics itself or associated chemicals are causing adverse effects.

(2) Should we pay more attention to the ecotoxicological impacts of weathering/aging microplastics and associated chemical contaminants? Until now, few studies have focused on the complex interaction between aged microplastics and associated chemical contaminants, and its ecotoxicological effects to aquatic organisms (Fu et al., 2019, Kalcikova et al., 2020, Wang et al., 2020a). Also, the impacts of environmentally relevant factors (e.g., temperature, NOM, exposure condition and pattern) on these combined effects should concern (Lin et al., 2020a, Fonte et al.,

2016, Qiao et al., 2019b).

(3) According to the present toxicity studies, whether the combined effects of microplastics and associated chemical contaminants are antagonism or synergism remains under debate. Why are the toxicity assessment contradictory? These discrepancies may be due to differences in microplastic properties, associated chemicals, tested organisms, or exposure conditions, which are inconsistent across studies. In addition, combined toxicities of microplastics and associated chemical contaminants are chemical-specific and species-specific. The reduction of combined effects can be not only mainly attributed to the adsorption of chemicals by microplastics (Garrido et al., 2019, Fu et al., 2019), surface functional groups (Kim et al., 2017), and particle agglomeration (Trevisan et al., 2019, Li et al., 2020c), and the underlying mechanism needs to be further explained.

(4) Does the interaction of microplastics and associated chemical contaminants result in their bioaccumulation, bioconcentration and biomagnify? Combined effects of microplastics and associated contaminants from the lower trophic level organisms to the higher levels along aquatic food chains are urgently required to explore.

4. Trophic transfer of microplastics and associated contaminants along aquatic food chain

Based on existing studies, microplastics can be transferred along the food chains from prey to predator. It is thought that predators from aquatic environments, especially top predators, are easier at risks than the lower trophic level organisms due to the high demands of food and energy, as well as possibility of microplastic trophic transfer (Germanov et al., 2018, Chagnon et al., 2018, Nelms et al., 2018, D'Souza et al., 2020). In addition, the microplastic bioaccumulation in prey and purification capacity and rates of predators affect the trophic transfer process of microplastics in different level predators (Santana et al., 2017, Au et al., 2017). To date, several studies on trophic transfer of microplastics and associated chemical contaminants have been performed on organisms at lower trophic levels, but the top predators are still poorly investigated. As shown in **Table 4**, the information regarding the trophic transfer of microplastics alone or with associated contaminants in different trophic level organisms along aquatic food chains was systematically summarized.

4.1 Trophic transfer of microplastics

In the aquatic environment, microplastics would be not only directly ingested by different organisms intentionally or unintentionally, but also indirectly transferred from low to high trophic levels via aquatic food chains (Wang et al., 2019a, Carbery et al., 2018, Au et al., 2017). Recent studies have indicated that microplastics trophic transfer represent an indirect, yet non-negligible pathway of microplastic ingestion for the higher trophic level organisms and even humans (Nelms et al., 2018, Catarino et al., 2018, Nelms et al., 2019b) (**Fig. 3**). Consequently, it is particularly crucial to research the transfer effect of microplastics along aquatic food chains. At present, we summarize the imformation regarding the trophic transfer of microplastics along aquatic food chains.

The fluorescently labeled technique of microbeads has been widely applied to laboratory studies on distribution and trophic transfer of microplastics in the typical organisms. Farrell and Nelson (2013) firstly reported that PS microplastics (0.5 μm) were transferred to the tissues and haemolymph of crab *Carcinus maenas* from mussel *Mytilus edulis* that filter-feed microplastics, but there were only a slight amount of microplastics in haemolymph of crab after 21 days exposure. Then, Watts et al. (2014) contrasted two uptake pathways of PS microplastics (10 μm) in crab *Carcinus maenas*, via both the ventilation exposure by gills and feeding on mussel containing microplastics. Results showed that during 2-3 weeks, the retention time and organs (gill and gut) of microplastics in crabs vary from different exposure pathways, and no microsplastics exist in the hemolymph of crabs. Moreover, Setälä et al. (2014) found that various zooplankton taxa can ingest PS microplastics (10 μm), and the microplastics ingested by *Marenzelleria spp.* and copepods can be individually transferred to mysid shrimps *Mysis relicta* via predation. Seaweed *Fucus vesiculosu* adhered PS microplastics (10 μm) can be ingested by the periwinkle *Littorina littorea*, suggesting that this marine snail not recognized non-food microplastics as a hazard (Gutow et al., 2016). Goss et al. (2018) also reported that parrotfish can ingest the wild collected seagrass *Thalassia testudinum* attached marine microplastics and prefer to eat the seagrass with high densities of epibionts and biofilms. Another study showed that the PE microplastics (10-45 μm) can be transferred from the polluted duckweed *Lemna minor* to freshwater amphipod *Gammarus duebeni* and only 28.57% of amphipod retained 1-2 microplastics in the gut after the chronic exposure, but the ingested microplastics did not affect the growth and mobility of amphipod

(Mateos-Cárdenas et al., 2019). Therefore, herbivory is a considerable pathway for transferring microplastics from the primary producer to aquatic food webs. Additionally, Santana et al. (2017) demonstrated that trophic transfer of PVC microplastics (0.1-1.0 μm) occurred from the Brown mussel *Perna perna* to blue crab *Callinectes ornatus* and puffer fish *Spheoeroides greeleyi*, but there is no microplastics in tissues and gut cavity of two predators after 10 days due to their depuration ability. Also, trophic transfer of PS microplastics (2 μm) happen in larval stages from mosquitoes *Culex pipiens* to midge *Chaoborus flavicans* via predation, but the functional responses (attack rates and handling times) of larval midge and reproduction of adult mosquitoes were not significantly affected by the presence of microplastics (Cuthbert et al., 2019). In the previous model analysis, Griffin et al. (2018) demonstrated that trophic transfer plays a vital role in microplastic uptake by the filter feeders, such as mussels and large filter feeders. Recent finding was reported by Van Colen et al. (2020) for trophic transfer of PS microbeads (4.8 μm) from the zooplankton Baltic tellin embryos to filter-feeding common cockles, and first explored whether microplastic ingestion alters the predator-prey interactions. In their experiments, the effect of ingested microplastics on zooplankton swimming behavior lowered the 30% of predation rates by cockles and thus disturbed the predator-prey interactions.

For nanoplastics, the threats of trophic transfer along food chain might be greater with the smaller size. Cedervall et al. (2012) firstly revealed that uptake and transfer of commercially PS nanoplastics (24 nm) through a tertiary food chain (Green algae

Scenedesmus sp.-Zooplankton *Daphnia magna*-Crucian carp *Carassius carassius*). Alarmingly, ingestion of zooplankton containing nanoplastics can change the feeding time and result in lipid metabolism decrease and weight loss of the Crucian carp fish. Similarly, Dr. Karin Mattsson and her co-workers reported that sulfonated PS nanoplastics (24 and 27 nm) can be transferred via a three trophic level food chain from algae-zooplankton-fish, affecting the feeding and social behaviors of the crucian carp fish, as well as its metabolism of liver, muscles and brain (Mattsson et al., 2015). Furthermore, they found that the amino-modified PS nanoplastics (53 and 180 nm) through food chain transfer can penetrate the blood-to-brain barrier of fish and lead to its behaviour disorder, thus potentially threatening the top predators health and natural ecosystem function (Mattsson et al., 2017). Then, Chae et al. (2018) observed that the PS nanoplastics (51 nm) can be transferred through a four trophic level food chain comprised by the freshwater algae *Chlamydomonas reinhardtii*, zooplankton *Daphnia magna*, fish *Oryzias sinensis*, and fish *Zacco temminckii*. The direct exposure of nanoplastics partly reflects the adverse effect of nanoplastic transfer on the locomotive activity both of two fish, liver histopathological changes of fish Zacco temminckii, and embryo of fish *Oryzias sinensis* (Chae et al., 2018). Thus, these studies implied that nanoplastics can be easier transferred via food chain and enter the organs of top predators by the complex mechanisms, potentially posing the greater risks to the different trophic levels of aquatic organisms and even ecosystem level.

In addition to the laboratory studies, several field-sampling researches have been performed to explore the trophic transfer of microplastics in nature. Remy et al. (2015)

reported that the artificial fibers (0.1-6 mm) with industrial coloring agents were found in the digestive tracts of the nine dominant macroinvertebrate species in different trophic levels, which live in the detritus accumulation areas of the Mediterranean zone, implying that the marine invertebrate communities have been polluted by microplastics through environmental exposure and trophic transfer. Notably, two studies in 2016 investigated the presence of plastic debris in the regurgitated pellets of top-predatory seabird yellow-legged gulls and great skua (Furtado et al., 2016, Hammer et al., 2016). Results showed that the majority of regurgitated pellets containing plastic debris (including microplastics) from the digestive tract of animal remains (e.g., prey birds, fish) that are captured by these predatory seabirds, suggesting microplastic transfer from preys to predators. By the comparative microplastic analysis between the in-situ collected sea cucumbers and sediments of its habitat, Renzi et al. (2018a) revealed that microplastics (100-2000 μm) in the benthic environment can be selectively ingested by sea cucumber and transferred from abiotic to biotic component of the aquatic food chain. Another field investigation in Easter Island waters within the South Pacific found that microplastics can be transferred from the flying fish *Cheilopogon rapanouiensis* to yellowfin tuna *Thunnus albacares* but not accumulate in the digestive tract of the tuna, suggesting that microplastic transfer may not pose a direct risk on the top predatory fish (Chagnon et al., 2018). Also, Zhang et al. (2019a) investigated the microplastic pollution in wild fish and crustacean species collected from Zhoushan fishing ground, China, and indirectly found that microplastics can be transferred to the marine fish species at higher trophic level via the food chain. Interestingly, Nelms et al. (2018) analyzed the scat of captive grey seals *Halichoerus grypus* and the digestive tracts of wild collected Atlantic mackerel *Scomber scombrus*, and verified microplastic trophic transfer existing in marine top predators. Furthermore, they put forward to a novel methodology pipeline combining the scat-based DNA extraction techniques with microplastic analytical methods, which can be applied to the most food webs to analyze the relationships between the ingested microplastic abundance and its prey composition in the high trophic levels (Nelms et al., 2019b). According to a recent field study at 15 sites from South Wales in UK, D'Souza et al. (2020) found plastic particles in the 46.9% of 166 faecal and regurgitated pellet samples from free-living Eurasian dippers *Cinclus cinclus*, 74.2% (n=112) of which are categorized as microplastics (0.5-5 mm). Interestingly, they proposed a steady-state model equation to predict the flux of plastic particles through the food chain of individual Eurasian dippers, with an average ingestion of 216.3 ± 226.4 plastic particles per day, indicating the trophic transfer of microplastics along the river food chains.

Evidence for the trophic transfer of microplastics from preys to predators has been verified. Generally, microplastics may not accumulate gradually inside the digestive tracts of aquatic organisms but are mostly expelled with its feces after some time (Graham et al., 2019, McGoran et al., 2018, Watts et al., 2014). Because aquatic organisms especially higher animals can excrete the majority of ingested microplastics by its metabolism approach (Santana et al., 2017, Chagnon et al., 2018, Batel et al., 2016), the evidence for bioaccumulation and biomagnification effect of microplastics via aquatic food chains remains uncertain. Different factors, such as the concentration of microplastics in prey and depuration ability and rate of predator, can affect the toxic effect and trophic transfer process of microplastics (Santana et al., 2017). After digestion, microplastics would be excreted from the organisms and re-enter the aquatic environment. Whether the physicochemical properties of the surface of microplastics will be changed and their effects on the filter-feeding and omnivorous organisms need to be further studied. Furthermore, although the microplastic trophic transfer in the low-trophic levels and simple aquatic food chains in laboratory experiment and field investigation has been studied, enough evidences about the higher trophic levels and multilevel aquatic food chains are lacking (Nelms et al., 2018). The acute and chronic toxicity mechanisms of trophic transfer of nanoplastics along the food chain also require further explored (Chae et al., 2018).

4.2 Trophic transfer of microplastics and associated chemical contaminants

As microplastics can absorb various environmental chemical contaminants and release the toxic plastic additives, its combined effects on different trophic level aquatic organisms along food chain should be further assessed (**Fig. 3**). So far, the knowledges regarding trophic transfer of microplastics and associated chemical contaminants are still poorly understood (**Table 4**).

Firstly, Batel et al. (2016) reported the trophic transfer of microplastics (1-20 μm) and PAHs benzo[a]pyrene along an artificial food chain from *Artemia sp. nauplii* and zebrafish *Danio rerio*. They found that the benzo[a]pyrene can be desorb in the intestinal tracts of zebrafish and subsequently transferred to the intestinal epithelium and liver. Subsequently, the short-term trophic transfer of PE microspheres (38-45 μm) and PAHs with an environmentally concentrations from the beach hopper to ray-finned fish was investigated, but the exposure of a microplastic-PAHs contaminated diet has no significant impacts on the boldness and exploration personality of ray-finned fish (Tosetto et al., 2017). Furthermore, Diepens and Koelmans (2018) put forward to a theoretical model that simulated trophic transfer of microplastics and hydrophobic organic chemicals (PCBs and PAHs) along the food chains including nine species from different trophic levels, indicating that PCBs have no obvious biomagnification effects along the food chain but PAHs show obvious biomagnification. In addition, Qu et al. (2018) observed the removal efficiencies of chiral venlafaxine varied from 58-96% in four aquatic ecosystems including sediments, duckweed and loaches, and found that PVC microplastics (1-10 μm) at the high concentration promoted accumulation of venlafaxine and its metabolites in loaches and sediments. Following this, they investigated how PS microplastics (700 nm) affect chiral chemical methamphetamine through the aquatic food chain from the microalgae *Chlorella pyrenoidosa* to freshwater snail *Cipangopaludian cathayensis* (Qu et al., 2020). In their experiment for 45 days, results revealed that the toxicity, bioaccumulation, biomagnification and distribution of methamphetamine were significantly increased in the freshwater snail. Nevertheless, the biomagnification effects of chemical contaminants caused by microplastics still remain unpredictable because the effects of associated chemicals on organisms and ecology attribute to the chemical species, relative concentrations and their complex mutual effects (Diepens and Koelmans, 2018). Moreover, the ability of the ingested microplastics to desorb chemical contaminants and release plastic-additives through the intestinal digestion of the high trophic level organisms is not negligible (Coffin et al., 2019, Batel et al., 2016).

Consequently, there is an urgent need to clarify the role of microplastics in bioaccumulation and biomagnification of the microplastic-associated contaminants with environmentally relevant concentrations in the complex aquatic food chains. For better understanding the complex desorption mechanisms and health risks among microplastics and associated chemical contaminants in body of organisms, more experimental studies and related models should be performed. The mechanism of chemical partitioning, role of contaminants associated with plastics, and mode of action of both nano/microplastics and associated chemicals in a range of organisms and associated compartments/tissues also requires further research (Ribeiro et al., 2019). Furthermore, it is vital to assess the potential factors influencing the trophic transfer of microplastics and associated contaminants, such as the different abiotic and biotic conditions that related to their ingestion, bioaccumulation, biomagnification, and egestion (Au et al., 2017).

5. Potential risks of microplastics to human health

More recently, research on the impacts of microplastics to human health has become a hotspot. A recent study firstly demonstrated that the mean abundance of microplastics in human faeces is 2 particles/g, with a total of the nine different types of microplastics (50-500 μm) and the abundant PP and PET, suggesting the inevitable ingestion of microplastics by humans from different sources (Schwabl et al., 2019). The ubiquitous microplastics can be intake via the two exposure pathways (e.g., ingestion, inhalation) and potentially posed a threat to human health (Zhang et al., 2020a, Cox et al., 2019, Wright and Kelly, 2017). Among them, the exposure of microplastics by the food sources and dietary exposure is a vital pathway to humans (Walkinshaw et al., 2020, Bouwmeester et al., 2015, Mercogliano et al., 2020, Toussaint et al., 2019). Potential risks of microplastics to human health via the food chains and dietary exposure were demonstrated in **Fig. 4**. To our knowledge, many studies have focused on microplastics in a wide variety of commercial aquatic products for food consumption (Baechler et al., 2020, Dehaut et al., 2016, Santillo et al., 2017, Akhbarizadeh et al., 2019, Hantoro et al., 2019, Rochman et al., 2015b), such as commercial fish (Barboza et al., 2020a, Collard et al., 2019, Adeogun et al., 2020, Neves et al., 2015, Bessa et al., 2018), bivalves species (Li et al., 2018a, Teng et al., 2019, Cho et al., 2019, Abidli et al., 2019, Van Cauwenberghe and Janssen, 2014, Li et al., 2015, Beyer et al., 2017), sea cucumbers (Renzi et al., 2018a), and sea urchins (Feng et al., 2020a). On the other hand, the daily dietary has been contaminated by the ubiquitous microplastics, because the presence of microplastics are in various food sources (Cox et al., 2019), including table salts (Kim et al., 2018, Peixoto et al., 2019, Karami et al., 2017, Yang et al., 2015, Gündoğdu, 2018, Iñiguez et al., 2017), seaweed nori (Li et al., 2020a), canned fish (Karami et al., 2018), beer (Kosuth et al., 2018, Liebezeit and Liebezeit, 2014), wine (Prata et al., 2020), sugar or honey (Mühlschlegel et al., 2017, Gerd and Elisabeth, 2015, Liebezeit and Liebezeit, 2013), tap water (Tong et al., 2020, Mintenig et al., 2019, Kosuth et al., 2018, Pivokonsky et al., 2018, Wang et al., 2020b, Uhl et al., 2018, Paredes et al., 2020), and even in bottled water (Oßmann et al., 2018, Zuccarello et al., 2019, Schymanski et al., 2018, Mason et al., 2018). Recently, Oliveri Conti et al. (2020) showed the presence of nanoplastics and microplastics in edible fruits and vegetables purchased from markets in Catania and firstly evaluate the estimated daily ingestion by adults and children.

The ubiquitous microplastics may threaten human food security and health (Bouwmeester et al., 2015, Barboza et al., 2018a). When evaluating the risk of microplastics to humans, the plastic particle numbers in contaminated foods and the quantity transferred along the food chain should be understood. Firstly, aquatic products have been originally recognized as an important source of microplastics to human diet. According to the two different European recommendations for dietary consumption by human individuals at different life stages, the estimated microplastic intake through fish consumption based on three wild edible fish species (European seabass, Atlantic horse mackerel, Atlantic chub mackerel) ranged from 112-842 particles/year and 518-3078 particles/year/capita, respectively (Barboza et al., 2020a). Also, the degree of microplastic pollution and bivalves consumption vary greatly from countries, resulting in different levels of per capita microplastic intake in different countries annually (Li et al., 2018a, Cho et al., 2019, Van Cauwenberghe and Janssen, 2014, Li et al., 2015). For example, the microplastic ingestion by European and

Korean bivalves consumers was estimated to be 1800-11000 and 283 particles/year/capita, respectively (Cho et al., 2019, Van Cauwenberghe and Janssen, 2014). Additionally, Catarino et al. (2018) predicted that the mean amount of microplastic ingestion by UK humans via mussel consumption was 123 particles/year/capita, while it reached 4620 particles/year/capita in some countries (e.g., Spain, France, Belgium) that prefer to ingest mussels. Therefore, mussels can be considered as a global bio-indicator of microplastic pollution in aquatic products for human consumption (Li et al., 2019, Beyer et al., 2017). Secondly, microplastics have been found in commercial salts (mostly sea salt) from more than 120 brands around the world (Zhang et al., 2020a, Kim et al., 2018, Peixoto et al., 2019). According to an investigation about 28 sea salt brands from 16 countries on six continents, Kim et al. (2018) reported that microplastics in sea salts ranged from 0-1674 particles/kg significantly beyond rock salts and lake salts, and Asian region had the relatively high microplastic contents, suggesting that sea salts also can be served as an indicator of microplastic pollution in human daily dietary. However, the abundances of microplastics in salts varied greatly from different countries such as Croatia, Indonesia, Italy, USA, China, UK, Korea, India, Australia and France, with a wide range from 0 to tens of thousands particles/kg (Zhang et al., 2020a). These differences of microplastic abundance may be caused by regional microplastic pollution, salt processing technologies and microplastic analytical methods. Thirdly, the presence of microplastics in human drinking water, such as raw water, tap water and bottled water, is an emerging issue in nearly two years (Koelmans et al., 2019, Xu et al., 2019a, Shen et al., 2020). Similar to aquatic products and salts, the microplastic abundances in tap water and bottled varied from different countries and spanned several orders of magnitude, with a wide range of 0-930 particles/L (Tong et al., 2020, Mintenig et al., 2019, Kosuth et al., 2018, Pivokonsky et al., 2018, Wang et al., 2020b, Uhl et al., 2018, Paredes et al., 2020) and 0-5.42×10^7 particles/L (Oßmann et al., 2018, Zuccarello et al., 2019, Schymanski et al., 2018, Mason et al., 2018), respectively. Based on the dietary guidelines for Americans, the average microplastic intake by humans (e.g., children, adults) via only bottled water and only tap water was estimated to be 90000 and 4000 particles/year/capita, respectively (Cox et al., 2019). Consequently, it is necessary to develop an advanced treatment processes and schemes for microplastics removal in drinking water treatment plants (Wang et al., 2020b, Shen et al., 2020). Noteworthy, nano/microplastics and plastic additives may be released from drinking water distribution plumbing systems due to the aging behavior of synthetic plastic pipes (mostly PVC and PE) caused by disinfectants, water erosion, temperature, and biofilms (Xu et al., 2019a), thus possible exposure pathways of these plastic particles should be identified and treated before the adverse effects are found. Drinks package with the plastic materials can be served as an important source of microplastics, potentially releasing microplastics and nanoplastics due to the complex erosion effect (Prata et al., 2020). Overall, to better explore the underlying implications to human health, more effective, accurate and standard analytical methods (e.g., sampling, extraction, identification, data analysis) about microplastics in the diverse foods and dietary exposure are required. Also, considering the current presence of microplastics in a variety of food sources and the potential of exposure increase in the future, it is recommended that human food safety management guidelines should include the detection and quantification of microplastics and nanoplastics.

So far, it is still difficult to evaluate and confirm the actual risks of microplastics on human health, based on the available data contained in aquatic products and other food sources. If microplastics are very rare in foods, its harm may be negligible. For example, Karami et al. (2017) reported that the lower human intake of <149 μm microplastics (maximum 37 particles/year/capita) from 17 salt brands from 8 different countries has a negligible health impacts. Another similar research performed on honey samples from Switzerland showed lacking of evidence for significantly contaminated by microplastics (Mühlschlegel et al., 2017). Recently, Zhou et al. (2020) showed that the ingested PS microplastics (500 nm) promoted the bioaccumulation of two veterinary antibiotics oxytetracycline and florfenicol in edible blood clams, but direct health impacts of consuming these polluted clams on humans by are negligible due to the estimated hazard quotients far below threshold. Moreover, the direct risks to humans through consumption of aquatic products (e.g., fish, bivalves, sea cucumbers) may be low because these edible animals are often eviscerated before ingestion (Garrido Gamarro et al., 2020, Renzi et al., 2018a). Also, Renzi et al. (2018b) found that cooking process decrease the microplastics abundance (-14%) of the cooked mussel meat compared with the raw, due to natural variability and thermal degradation of microplastics. Nevertheless, the trophic transfer of microplastics in edible parts along food chains and other food source in daily dietary remains unknown. It is urgent to develop a standardized and practical analytical method for accurately identifying and quantifying the number of nanoplastics and microplastics in the food chains and dietary exposure. For example, the evaluation method on sugar and honey was challenged due to the potential misidentification of microplastics and contamination of background (Liebezeit and Liebezeit, 2013). On the other hand, some evidences showed that microplastics may be not biomagnified via edible parts from commercial aquatic products to humans, while the lower trophic level organisms are at the highest risks (Walkinshaw et al., 2020, Akhbarizadeh et al., 2019). Considering these influencing factors that require further studied, there is currently insufficient evidence to estimate whether microplastics via the food chains and dietary exposure will lead to enough adverse impacts on human health (Walkinshaw et al., 2020, Rist et al., 2018).

In addition to the food chains and dietary exposure, evidence for the ubiquity of microplastics (including micro-rubbers) have been reported in the atmospheric environments from indoor to outdoor, from urban to remote regions, with a suspension/fallout concentrations spanning 1-3 orders of magnitude at different sampling sites (Liu et al., 2019c, Zhang et al., 2020c, Abbasi et al., 2019, Zhang et al., 2020d, Allen et al., 2019). The majority of floating microplastics are fibers. Human intakes of microplastics via air inhalation exposure pathway have raised wide attention (Zhang et al., 2020a, Cox et al., 2019, Prata, 2018, Wright and Kelly, 2017). Once entering the respiratory tracts, most microplastics might be deposited on the airway or trapped by the lung lining fluid. Nevertheless, the partial plastic particles, especially nanoplastics, may avert the clearance mechanisms of the respiratory tracts and lung, and then participate in human life activities. By the complex mechanisms of dust overload, endocytosis, persorption, oxidative stress, and gene mutation, the inhalation of atmospheric microplastics by humans may cause the airway diseases, interstitial lung inflammatory and immune responses, and even cancer (Prata, 2018, Wright and Kelly, 2017). Therefore, it is meaningful to contrast the differences and characteristics of two microplastic intake pathways between ingestion and inhalation. A study reported that the human intake of microfibers (13731-68415 particles/year/capita) via household dust fallout during evening meal period was significantly higher than the microplastic ingestion (4620 particles/year/capita) via the higher mussel consumption in some countries (Catarino et al., 2018). According to the recommended dietary for Americans, Cox et al. (2019) extrapolated that microplastic intakes ranged from (3.9-5.2)$\times10^4$ particles/year/capita depending on age and sex, and increased to (7.4-12.1)$\times10^4$ particles/year/capita when inhalation is considered. By comparison, Zhang et al. (2020a) estimated that human intakes of microplastics via table salts, drinking water, and air inhalation were (0-7.3)$\times10^4$, (0-4.7)$\times10^3$, and (0-3.0)$\times10^7$ particles/year/capita, respectively. Thus, these results suggested that microplastic intake via air inhalation may be the major pathway entering human body, and lead to more adverse impacts than via ingestion pathways including food sources and dietary exposure.

Furthermore, researches on the microplastics toxicology and pathology of humans are so far in its infancy and require further developed (Amereh et al., 2020, Rubio et al., 2020). If inhaled or ingested by humans, microplastics may accumulate and exert localized particle toxicity by inducing or enhancing an immune response and chronic effect. The potential molecular mechanisms regarding cell effects induced by nanoplastics and microplastics are showed in **Fig. 5**. The exposure to PS microplastics has been used in human *in-vitro* and rodent *in-vivo* studies (Rubio et al., 2020, Stock et al., 2019). Microplastics can be considered as an inert hazardous “micromaterials” because it could result in inflammation, cytotoxicity (e.g., oxidative stress, cells injury, cell viability, membrane function) (Schirinzi et al., 2017, Wu et al., 2019b), genotoxicity (Wu et al., 2020), and immune response (Lehner et al., 2020) at the cell and tissue levels. By the *In-vitro* experiment with multispectroscopic techniques, Ju et al. (2020) found that PVC microplastics (5 μm) can interact with human serum albumin (HSA) due to the electrostatic forces, induce the HSA alteration of the microenvironment and secondary structure at molecular level, and then transferred to different tissues following with the blood, potentially causing the adverse impacts in *vivo*. These adverse impacts of microplastics may be mainly affected by the exposure duration, particle properties (e.g., size, type, concentration, surface charge and functionalization) and biological response of cells and tissues, as well as the chemicals transfer caused by the adsorbed chemicals and released additives (Amereh et al., 2020, Wu et al., 2020, Wang et al., 2020c, Xu et al., 2019b). Moreover, the smaller particle size may cause the greater uptake and cytotoxicity of PS microplastics, and meanwhile, the synergistic toxicity between nano-scale particles and BPA on human Caco-2 cells also increased (Wang et al., 2020c). Nanoplastics can interact with different human cell lines and potentially penetrate the outer cell membrane. The smaller size, the easier internalization into cell cytoplasm (Xu et al., 2019b). *In-vitro* studies have reported the adverse effects (e.g., endocytosis internalization, cytotoxicity, intracellular oxygen species (ROS), oxidative stress, genotoxicity and even DNA damage) caused by PS nanoplastics in human cell monocultures or even more complex human cell models (Xu et al., 2019b, Poma et al., 2019). Then, Amereh et al. (2020) found the in *vivo* adverse impacts of virgin PS nanoplastics (25 and 50 nm) on endocrine perturbation and reproductive toxicity of male Wistar rats. Using the fluorescence imaging technologies, the results indicated nanoplastics bioaccumulation, histological damage and semen biomarkers alterations of rats, and further revealed the potential risks of nanoplastics exposure to mammals and human. Somewhat differently, Cortés et al. (2020) reported that although a relevant portion of PS nanoplastics (<100 nm), with a positively related dose-dependent effects at the range of 1-100 μg/mL, can be uptake and internalized by human colorectal adenocarcinoma Caco-2 cells, their associated biological impacts were not statistically significant, suggesting the slight toxicity of nanoplastics exposure at cellular and gene level. Until now, the cellular uptake routes, intracellular fate, and tissue impacts of microplastics and nanoplastics have been still little studied. In addition, knowledge gaps remain to be filled to gain accurate and comparable data and results regarding the adverse health effects. There are currently no operable and standardization analytical technologies and hazard assessment of microplastics. The comprehensive human bio-monitoring investigations regarding risk assessment of microplastics and nanoplastics should be performed, rather than focusing on only few plastic types and specific shape (e.g., spherical PS microspheres), as well as specific tissues and organs (e.g., lung, gastrointestinal tracts). Also, in *vivo* studies regarding long-term health adverse effects exposed to microplastics need to be sufficiently explored. Overall, in spite of no observed clinical manifestations, there is an urgent need to further comprehend the potential impacts of microplastics and nanoplastics on human health, as well as its harm at the cellular and tissue level.

In addition, several non-negligible questions about microplastics and nanoplastics to humans remain further studied. Firstly, microplastics and associated contaminants (e.g., released additives, adsorbed chemical contaminants) may threaten the food safety, transferring chemicals to human bodies and causing negative health effects (Baechler et al., 2020, Campanale et al., 2020, Wright and Kelly, 2017, Bouwmeester et al., 2015, Naik et al., 2019). For instance, the pigmented particles (<5 μm) and plastic additive Tris(2,4-di-tert-butylphenyl)phosphite with high quantities were detected in 32 samples of bottled mineral water from 21 different brands (Oßmann et al., 2018). Barboza et al. (2020b) reported that the levels of leaching BPA and several analagous compounds in the liver and muscles of wild commercial fish were correlated with the higher microplastic ingestion, suggesting the potential exposure risks of microplastics and associated contaminants to humans by daily dietary. Moreover, although evidences about desorption of chemical contaminants and release plastic-additives from the ingested microplastics through the gastrointestinal digestion of animals (e.g., fish, birds) have been proved (Coffin et al., 2019, Batel et al., 2016), there are lacking of adequate simulation experiments to explore desorption mechanisms of these chemicals on human health. More seriously, microplastics may interact with human biological systems and transfer associated chemicals into different tissues and circulation systems. As suggested by Zhou et al. (2020), the consumption of edible bivalve blood clams contaminated both by microplastics and veterinary antibiotics change the dietary exposure to antibiotics and potentially increase the antibiotic resistance risk in human gut microbial communities. Secondly, microplastics can serve as a carrier for spreading human pathogenic bacteria and parasite (Naik et al., 2019, Imran et al., 2019). Hence, microplastics combined with drug-resistant bacterial pathogens that co-selected by environmental metals and antibiotics are an emerging hotspot, and pose serious threats to humans by food chains and dietary exposure. Furthermore, when microplastics with biofilms are intake by humans and partially accumulated in bodies, the complicated interaction between microplastics and gut microbiota as well as human health is largely unknown (Lu et al., 2019). Also, microplastics can serve as carriers for different antibiotics and bacterial assemblages, and thus result in the enrichment of antibiotic resistant genes (Ma et al., 2020, Wang et al., 2020d), potentially increasing the dietary exposure risks to human gut microbiota through the food chain (Zhou et al., 2020). Thirdly, the cellular uptake pathways, intracellular fate and potential impacts of nanoplastics (<100 nm) on human health have so far been little studied (Lehner et al., 2019). Generally, nanoplastics easily penetrated into tissues and may accumulate in the brain, liver and other tissues of various organisms. On the other hand, the exposure to nanoplastics at the concentration of μg/mL can enhance the microcystin synthesis and release from cyanobacteria species and potentially increase the threats of harmful cyanobacterial blooms, causing negative consequences to freshwater ecosystems, food and water safety, and human health (Feng et al., 2020b).

6. Conclusions and outlook

In conclusion, evidence for the combined effects and trophic transfer of microplastics and associated chemical contaminants has been proved. These research topics gradually raised attention to understand their potential impacts on human health. Research on trophic transfer of microplastics mainly include the monitor of microplastics in field sampling organisms and its predators, and laboratory feeding experiments to simulating trophic transfer model in controlled food chains. However, the potential impacts of combined effects and trophic transfer of microplastics and associated contaminants on the aquatic organisms, especially top predators, are still not fully understood. In addition, the risk assessment to trophic transfer of microplastics and associated contaminants along food chains and their implication for human health exists in knowledge gaps in due to lacking of data on complicated prey-predator relationships for microplastics and standardized quality criteria for the assessment of microplastics in biota. Further researches should be considered, and recommended suggestions to address this issue of microplastics in aquatic environment are prospected.

(1) Standardize the identification and assessment of microplastics and nanoplastics in biological organisms. Quality standardization of microplastic characterization and analytical methods can promote the effective and accurate evaluation of the occurrence of microplastics in aquatic organisms and its surrounding environment (Hermsen et al., 2018). Experimental researches on distribution and trophic transfer of microplastics in typical organisms generally use fluorescence labeling technique. This detection and analysis method has some limitations, such as complex operation and high cost, difficulty in detecting the microplastics particle numbers in the actual water sample accurately. More advanced and practical analytical methods were expected to be developed in the future.

(2) Establish comprehensive research on the multilevel trophic levels and comprehend the chronic effects of microplastic exposure on the higher animal health. Knowledges regarding trophic transfer of microplastics and associated contaminants in the multilevel aquatic food chains are still scarce. Researches on effects of microplastics on trophic transfer along the food chain mainly focused on the secondary food chain and laboratory feeding experiments in the controlled food chains, which is not sufficient for fully reflecting the real and complex biological system. Generally, higher trophic level predators have stronger ability to clear contaminants than the lower prey. Therefore, it is necessary to establish full-scale experimental conditions to explore the biological effects of microplastics on the top predators and eventually human. In addition, *in-situ* investigation of microplastics on trophic transfer along the food chain should be paid more attention.

(3) Explore the factors influencing the combined effects of microplastics and associated contaminants on aquatic organisms. Based on the previous studies, the combined effects (e.g., bioaccumulation, toxicity, biological responses) of microplastics and associated contaminants are antagonism or synergism remains uncertain due to the chemical-specific and species-specific interaction. It may be affected by the complex factors, such as microplastic properties (e.g., type, size, surface functional groups), chemical pollutants, tested species and exposure conditions. The underlying mechanism needs to be further explained.

(4) Evaluate the risk of “secondary” microplastics. Laboratory studies showed that aquatic organisms can excrete a portion of microplastics, and their surface physicochemical properties (e.g., size, surface functional groups, suspension stability) may be changed after digestion. The change of physicochemical properties may affect fate, bioavailability and toxicity of microplastics. These excreted microplastics in the aquatic environments may be re-ingested by filter feeder and other aquatic organisms intentionally or unintentionally, and potentially result in additional ecological risks.

(5) Investigate the bioconcentration and biomagnification effect of microplastics and associated contaminants from different trophic levels. Different factors such as the microplastic abundance in surrounding environments, concentration of microplastics in preys, and depuration ability and rate of predator can influence the ecotoxicological effects and trophic transfer process of microplastics. Whether trophic transfer of microplastics and associated contaminants affects their bioaccumulation, biomagnification along aquatic food chains/web also needs to be further discussed.

(6) Assess the potential risks of the chemical additives and degradation byproducts released from microplastics. Most of previous studies have focused on microplastics as vectors for chemical pollutants and microorganisms, but these plastic additives and degradation byproducts presented a toxicological hazard on the aquatic organisms and even human health are not well understood. Actually, weathering and fragmentation behaviors of microplastics in the natural environment lead to the leaching of various toxic additives and degradation products, such as organotin compounds, bisphenol A, diethylhexyl phthalate and other endocrine disrupting chemicals (EDCs) (Liu et al., 2019b, Chen et al., 2019a). Additionally, so little is known regarding the desorption of plastic additives from the ingested microplastics through the intestinal digestion of higher animals (Coffin et al., 2019).

(7) Understand the potential impacts of nanoplastics. In addition to the greater ecotoxicological effects cause by their nanoscale size and special physicochemical properties, recent studies showed that nanoplastics potentially interact with cyanobacterial blooms (Feng et al., 2020b) and climate change (Yang et al., 2020d), affecting aquatic organisms and ecology. Developing operable methods to identify and quantify nanoplastics in the environments and fully understanding their ecological and human health impacts are urgently required.

(8) Explore the impacts of nano/microplastics and associated contaminants with an environmentally relevant concentration on human health. So far, studies about the human toxicology and pathology of microplastics and nanoplastics are in its infancy and require further developed. Identification and quantification of microplastics and

associated contaminants in human daily dietary is also necessary.

(9) Several emerging issues need to concern: a. Impacts of weathering/aging behavior of microplastics on their combined toxicity assessment (Fu et al., 2019, Kalcikova et al., 2020); b. microplastics as carriers for pathogen microbials and related ecological risks (Hernandez-Milian et al., 2019, Naik et al., 2019, Imran et al., 2019); c. Microplastics enrich antibiotic resistant genes due to its “vector-effect” for different antibiotics and bacterial assemblages (Ma et al., 2020, Wang et al., 2020d), potentially affect aquatic organisms and even human health (Zhou et al., 2020).

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