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Research Paper

Insight into chemical features of migrated additives from plastics and associated risks to estuarine ecosystem

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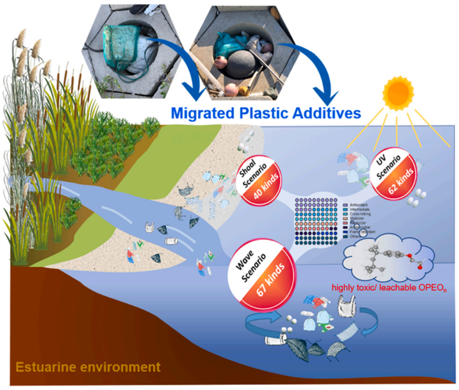
HIGHLIGHTS

- Yangtze Estuary is proved to be a plastic debris pollution hotspot.
- Plastics weathered under wave forces leach greater abundance of additives.
- More additives migrate from plastic bags than from fishing nets and floating foams.
- $OPEO_n$ deserve our special attention because of its high response and toxicity.

GRAPHICAL ABSTRACT



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ABSTRACT

Distinct hydrodynamic conditions created a hotspot of plastic and associated additive pollution within estuaries, which is of considerable scientific interest. However, the effects of specific estuarine weathering (severe mechanical wear, constant turbulence, and strong ultraviolet radiation) on migration of additives remain unclear. Therefore, we investigated the release of migrated plastic additives (MPAs) from three representative plastics, namely floating foam, fishing nets, and packaging bags, under simulated estuarine conditions. Sixty-seven MPAs leached out under the wave scenario, greater than those under the ultraviolet radiation (62) and shoal (40) scenarios. We detected forty MPAs in the plastic bag leachates, whereas fewer MPAs were released from the foam and nets. Several MPAs were peculiar to specific plastics, e.g., antistatic and curing agents in the bag and foam leachates, respectively. Particularly, a suite of nonionic surfactants, octylphenol polyethoxylates ($OPEO_n$), exhibited outstanding responses in the packaging bag leachates and had elevated toxic potential. $OPEO_n$ significantly inhibited the hatching of zebrafish and caused cardiovascular system disorder and morphological distortions even at environmentally relevant concentrations as in estuaries. Collectively, the leaching of MPAs

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was significantly enhanced by wave actions, and the plastic leachates, particularly those of plastic bags, can cause detrimental risks to the estuarine ecosystem.

1. Introduction

Plastics are everywhere in our lives because of their lightness, flexibility, cheapness, and long service life, from packaging to building construction and from agricultural to electronic application. The production of plastic is 367 million metric tons worldwide in 2020 [1], among which more than 10 million tons of plastic will finally reach oceans through a variety of routes, including illegal dumping, fishery activities, and discharges from landlocked runoff [2,3]. Plastics can also be rushed back to estuarine regions from oceans due to physical forces such as the wind, tidal regime, waves, and maritime currents [4]. Therefore, the specific hydrodynamic conditions have led to one order of magnitude higher concentrations of plastics in the estuarine area compared to the open ocean [5,6], and thus, the estuary is deemed a plastic pollution hotspot.

Once plastics enter the estuarine environment, they will endure different weathering scenarios, including photooxidative degradation in the intertidal zone, mechanical abrasion around the shoal area, and seawater soaking when submerged by wave forces [7–9]. After undergoing these conditions, the surface of the plastics wears out, and then plastics can be gradually broken down into smaller debris, which is termed microplastics, when their size is smaller than 5 mm [10]. Meanwhile, chemicals blended with plastics will be released and might subsequently pose severe hazards to aquatic organisms [11,12]. Although quantities of studies have investigated the adverse impacts of microplastics on biota [13,14], limited attention has been paid to the release, fate, and toxic potential of chemical additives migrated from plastics [15,16].

To maintain plastic stability and improve its performance, various additives are incorporated into plastics, such as plasticizers, antioxidants, surfactants, stabilizers, flame retardants, and antistatic agents [15,17]. Migrated plastic additives (MPAs) exhibited negative effects on organisms, e.g., declined feeding rate, reduced body weight, decreased fertility, and impaired immune and nervous systems [18–21]. These industrial additives can be released into the surroundings via processes such as biota inhabiting and chemical desorption [9,22], and the leaching of plastic additives could be accelerated following the size breakdown of plastic matrices [23].

The chemical release from plastics would be very intricate in the estuarine area because of complex environmental conditions (i.e., strong ultraviolet (UV) radiation, severe mechanical wear, fluctuation of tides, and constant turbulence) [24,25]. Though scientists have detected high concentrations of halogens and massive dissolved organic carbon contents in plastic leachates [26], more elaborate characteristics of MPAs and influences of plastic sources/types on their migration behavior remain largely unknown and thus warrant further investigation.

We hypothesize that the high plastic abundance in the estuary will trigger strong leaching of plastic additives, and the MPA concentrations will vary largely under different estuarine weathering conditions. Additionally, the released MPAs may pose risks to aquatic organisms. Therefore, in the present study, we determined the typical plastic debris categories and quantify their abundances in the Yangtze Estuary, which has been reported to deposit a high plastic load [27]. Then, during the laboratory simulation experiments, we weathered three representative plastic debris, namely floating foam, fishing net, and plastic bag, under typical estuarine conditions (i.e., shoal condition, wave motion, and UV radiation). The profile of MPAs was probed in terms of suspected screening on high-resolution mass spectrometry, and their toxic capacities were predicted using a toxicity estimation software tool. Finally, *in vivo* assays were carried out to evaluate biological effects of octylphenol polyethoxylates ($OPEO_n$, the compounds of highest priority due to their considerable response and elevated toxicity) on zebrafish *Danio rerio*.

2. Materials and methods

2.1. Field investigation of estuarine plastic pollution

The studied estuary is located at the intersection of the Yangtze River and the East China Sea. Sampling sites were evenly distributed along the coastline (Fig. S1A–B, Table S1). The plastic debris was gathered at low tidal lines using pre-cleaned stainless-steel tweezers within a randomly selected 5 m^2 area at each location during August 2020, and brought back to the laboratory immediately for characterization and classification.

2.2. Plastics and chemicals

For the simulation experiments, the floating foam (polystyrene, PS) and fishing nets (polyethylene, PE) were purchased from Xiaolou Fishing Corp. (Shanghai, China); the packaging bags (PE) were obtained from Lianhua Supermarket (Shanghai, China). The plastic types were selected according to those found most abundantly in the Yangtze Estuarine field investigation, and the detailed information of these commercial plastics was provided (Table S2). The polymers were determined by a Fourier Transform Infrared Spectroscopy (Nicolet iS 5, Thermo Fisher Scientific, Waltham, USA), and only when the matching index ≥ 70 % to the commercial spectra libraries, the plastic compositions were considered to be identified (Fig. S2). Chemicals of analytical reagent grade or higher, including methanol, dimethyl sulfoxide (DMSO), and 3,4-dichloroaniline (DCA), were bought from Titan Scientific Corp. (Shanghai, China). The authentic standard of $OPEO_n$ (a technical mixture, purity > 98 %) was purchased from Macklin Biochemical Corp. (Shanghai, China).

2.3. Plastic weathering under simulated estuarine conditions

Three typical weathering scenarios that are commonly occurred in estuarine regions were simulated in this study, including physical abrasion due to tides and unique topography around the shoal regions (shoal scenario) [28], gentle water-wave flow (wave scenario) [29], and UV radiation (UV scenario) [8]. The primeval plastic products were carefully cut into 5 mm × 5 mm pieces with thickness below 5 mm by pre-cleaned stainless-steel scissors and soaked in artificial freshwater (AFW) for weathering. Here we did not take salinity alteration in the estuarine environment into consideration, because the salinity change only causes slight and non-significant effects on the additives leaching [30]. The concentration of the plastic fragments was 10 g/L (within the range of our field investigations) for all three scenarios. To cover the plastic concentration ranges in the real estuarine environment, the leachates were further diluted 2–16 times for the subsequent *in vivo* exposure experiments. Detailed procedures of simulation experiments are provided in the Supplementary materials (Text S1).

2.4. Scanning electron microscope observation

After the weathering simulation experiments, plastic fragments were removed from the AFW and air-dried at ambient temperature. Surficial features of the weathered and the original/untreated plastics were delineated by a scanning electron microscope (SEM, S-4800, Hitachi, Japan). The operating parameters of the SEM were as follows: accelerating voltage, 3 kV; emission current, 14 mA; and the working distance, 10.9–11.7 mm.

2.5. Solid phase extraction of MPAs

The solid-phase extraction (SPE) for MPAs and the chemical quantification followed the procedures described in previous studies [16,19] with minor modifications. The aqueous leachates (without the plastics) containing MPAs were loaded onto SPE cartridges (Oasis HLB 6cc 500 mg, Waters Corp., Milford, USA), which had been initially conditioned using 10 mL of methanol followed by 10 mL of Milli-Q water. Then, chemicals trapped on the SPE sorbents were eluted with 10 mL of methanol and collected in glass vials. The eluants were blown to dryness under gentle nitrogen, and reconstructed in 1 mL methanol. A half aliquot (500 μL) was used for chemical analysis, while the other half was solvent-exchanged to 500 μL of DMSO for biological analysis. The HLB cartridges were adopted here due to their satisfactory affinity with chemicals of a wide range of polarities and the strong capacity to generate both hydrophobic and hydrophilic intermolecular forces [31, 32]. To evaluate possible background contamination from laboratory operations, procedural blanks were analyzed along with the real samples following the same protocols, except for the loading of plastic leachates which was substituted by Milli-Q water. The responses of MPAs reported in this study were blank-corrected.

2.6. Zebrafish culture and exposure

Adult wild-type AB strain zebrafish (*Danio rerio*) were cultured at a 14 h light:10 h dark cycle in a recirculating aquatic system at 26 ± 1 °C (Haisheng Biotech., Shanghai, China) in our lab continuously. Detailed descriptions of the fish culture and the collection of well-fertilized embryos are provided in the Supplementary materials (Text S2). For the exposure experiments, zebrafish embryos were exposed to plastic leachates at a series of concentrations of 0.625, 1.25, 2.5, 5, and 10 g plastic/L (abbreviated as 1 ×, 2 ×, 4 ×, 8 ×, 16 ×). These concentrations included three magnitudes, which well covered the environmental plastic concentration magnitudes measured in the estuary. In the field, the average plastic concentrations were 7.12, 2.96, and 0.31 g plastic/L for floating foam, fishing nets, and plastic bags, respectively (Fig. 1). Thirty healthy fertilized embryos were selected and exposed in each replicate of exposure groups ($n = 3$). According to the German Standard DIN protocol [33], pure AFW was used as a negative control (40 embryos per replicate), and the highest concentration of DMSO (0.5 %) was selected as a solvent control (30 embryos per replicate). The requirement for the negative control was strict and only when the lethality of the negative control was below 10 %, the whole experiment was valid [33]. The positive control consisted of 3.7 mg/L of 3,4-dichloroaniline (3,4-DCA) [34] in AFW (30 embryos per replicate). The embryos or larvae were observed at 24-hour post-fertilization (hpf) for survival rate, 48 hpf for heartbeat rate, 72 hpf for hatching rate, as well as 96 hpf for body length and morphological monitoring. The experimental solutions were exchanged daily throughout the 5-d exposure following the standard protocol. Five-day duration has been widely used in toxicity evaluation to check the early development embryo-larval stages of zebrafish which can provide a sensitive window for investigating the developmental toxicities of contaminants [35,36]. At the end of the exposure, zebrafish larvae were anesthetized with 200 mg/L of benzocaine then quickly frozen with liquid nitrogen and stored at − 80 °C. The experiments were conducted follow the regulations of the Animal Experimental Ethics Committee of East China Normal University.

2.7. mRNA expression analysis

We used the Trizol lysis method to extract RNA from the frozen samples and reverse transcribed RNA into cDNA, and employed the quantitative reverse transcriptase-polymerase chain reaction (qRT-PCR) technique to measure the mRNA expression of the target genes. Thirty zebrafish larvae were pooled as one replicate ($n = 3$). Samples were homogenized in the Trizol reagent (Invitrogen, Waltham, USA) by tissue grinders (Tissuelyser-48, Jingxin Technology Corp., Shanghai, China), and then shaken and mixed for 10 min prior to centrifugation at 12,000 *g* for 10 min. The resultant supernatant was analyzed on a NanoDrop 2000 Spectrophotometer (Thermo Fisher Scientific, Waltham, USA) for its total RNA concentration. The cDNA was acquired using the cDNA Reverse Transcription Kit (Reference code: RRR037b, Takara Biotechnology Inc., Kusatsu, Japan). The qRT-PCR assay was performed on a quantitative PCR instrument (Bio-Rad Laboratories, Hercules, USA) after treatment with SYBR Green Master Mix (Takara Biotechnology Inc., Kusatsu, Japan). Primer sequences for the *vtg* and reference *gapdh* genes are listed in Table S3.

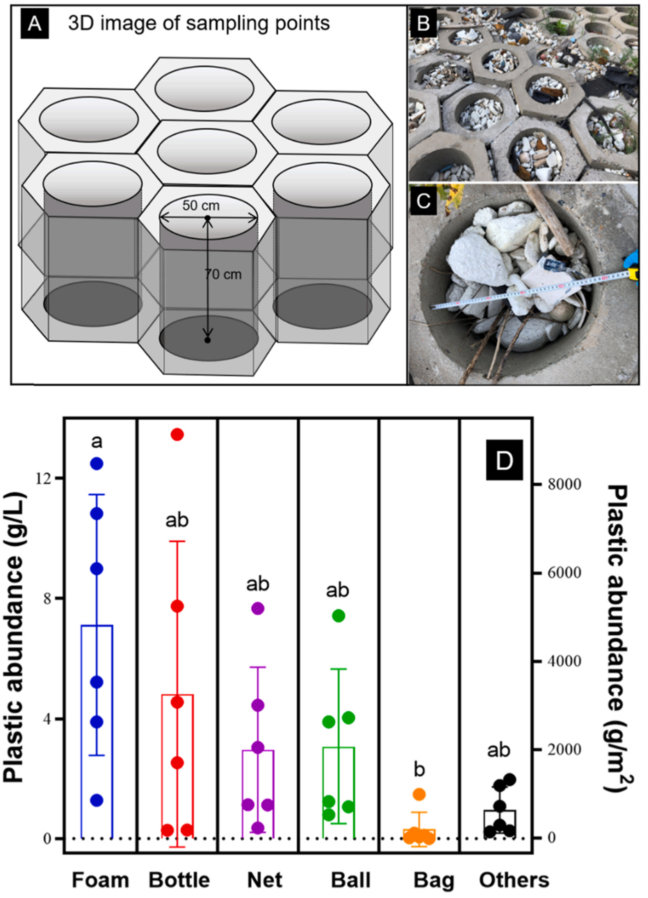

Fig. 1. (A) 3D image of sampling locations, and (B–C) photos of plastic debris along the Yangtze estuarine coastline; (D) abundances of different types of plastic debris at sampling sites along the Yangtze River Estuary ($n = 6$). Foam: floating foam; Bottle: beverage bottles; Net: fishing nets; Ball: floating balls; Bag: plastic bags; Other: other collected plastic debris. Letters a and b represent the significant differences among groups based on the Kruskal-Wallis test.

2.8. Suspected screening of MPAs in plastic leachates

Concentrated plastic leachates (eluents from the SPE cartridges; dissolved in methanol) were screened for MPAs on an ultra-performance liquid chromatograph interfaced with a quadrupole time-of-flight tandem mass spectrometer (ACQUITY UPLC/Xevo G2 Q-TOF-MS, Waters, Milford, USA) operated in both positive and negative electrospray ionization modes (ESI$^+$ and ESI$^-$). The compound separation was achieved on an Acquity column (HSS T3, 2.1 × 100 mm × 1.8 μm, Waters, Milford, USA) at 65 °C. The capillary voltage was set at 3 kV, and the voltage applied to the sample cone was 40 V. The temperature setting for the electrospray desolvation heater and the nitrogen gas flow for solvent evaporation was 150 °C and 600 L/h, respectively. The UPLC mobile phases were 10 mM ammonium acetate in MeOH (A) and 10 mM ammonium acetate in water (B). To limit ionization suppression and source contamination, samples were injected under aqueous conditions, and the column was washed and equilibrated for 5 min after each sample run (see Table S4 for the LC elution gradient). The obtained data were subjected to a suspected screening workflow, including peak recognition, adduct and isotope detection using MassLynx software (Waters, Milford, USA), and matching with our in-house MS database of approximately 500 plastic additives established based on the information provided by SpecialChem website (https://polymer-additives.specialchem.com) (Table S5). Over ten categories of additives were covered by the database, including antimicrobials, adhesion promoters/compatibilizers, blowing/foaming agents, anti-rodent/insect repellents, antioxidants, anti-foaming agents/defoamers, antistatic agents, flame retardants, plasticizers, surfactants, and other additives for thermoplastics. Furthermore, the predicted toxicity to fathead minnow (described in terms of median lethal concentration, LC_{50}) and octanol-water partition coefficients (XLogP3) of MPAs tentatively identified in the plastic leachates were retrieved from Toxicity Estimation Software Tool (TEST, United States Environmental Protection Agency) and PubChem (National Center for Biotechnology Information, USA), respectively (Table S6).

2.9. *Data analysis*

The results were presented as arithmetic mean ± standard error of the mean (s.e.m.). SPSS software (version 23.0, International Business Machine Corp., Armonk, USA) was used for statistical analysis. The data normality and homogeneity of variance across groups were confirmed by the Shapiro-Wilk test and the Levene test, respectively. If the data was not normally distributed, the Kruskal-Wallis test with the Dunn-Bonferroni post-hoc mean comparison was utilized to compare group differences. If normally distributed, one-way ANOVA with the least significant difference (LSD) was utilized. The Spearman correlation analysis, multi-factor variance analysis, and linear regression were also performed to evaluate the relationship between $OPEO_n$ and the bioassay endpoints. Throughout the manuscript, the level of significance was set at $\alpha < 0.05$.

3. Results and discussion

3.1. *Plastic debris in the estuarine environment*

Large quantities of plastic debris are generated in our daily life, and estuarine areas are becoming their potential sinks [37]. In the Yangtze River Estuary, various kinds of plastics, including floating foam, fishing nets, beverage bottles, plastic packaging, floating balls, and hard foam buoys, were spotted along the coastline (East China; Fig. 1).

Among the plastic debris we collected, foam was the most commonly found plastic type, with an average concentration of 4984.0 ± 3040.5 g/m^2 (7.1 ± 4.3 g/L). Beverage bottle was the second most abundant type which was 3368.1 ± 3567.5 g/m^2 (4.8 ± 5.1 g/L), followed by fishing nets of 2074.5 ± 1927.8 g/m^2 (3.0 ± 2.5 g/L). It was noteworthy that most plastic debris derived from packaging bags was widely scattered within the estuary in rather small-size pieces (8.4 ± 6.5 g/m^2), and some of them were seriously aged, indicating their vulnerability to weathering in the estuarine environment (Fig. S3). Similarly, previous research also suggested that despite the gigantic production and consumption of plastic packaging materials worldwide, they have been rarely seen in the wild [38], likely because packaging bags are easily degraded in the environment and destroyed or shredded by amphipods, generating numerous little plastic fragments [39]. Therefore, the migration of chemical additives from the plastic packaging warrants further investigations as the larger specific surface area of smaller particles may facilitate the desorption of MPAs.

Thus, three representative categories of plastics were selected for the simulation experiments to elucidate migration behavior of plastic additives; they are floating foam (the most prevalent plastic items in our studied estuary), fishing nets (the broadly identified ghost fishing material around the world) [40], and packaging bags (the easily fragmentable plastics in the estuarine environment according to both our field investigation and previous reports) [41,42]. These three types of plastics together can represent more than 54 % of the plastic debris distributed alongside the Yangtze River Estuary. The prevalence of these three types of plastics in estuaries is consistent with their high production and consumption levels [1]. Discarded fishing nets and polystyrene foam are not yet regulated and lack of mandatory control, and the recycling rate for plastic bags is also quite low [43,44]. Therefore, these plastic residues are commonly found marine litter, and their potential environmental risks warrant our attention.

3.2. *Weathering caused wear of plastic surface and release of MPAs*

The surface of plastics largely altered after our weathering treatment (see Fig. S4). Under the shoal scenario, abrasion and grinding marks were spotted on all three types of plastics, such as condensation and wrinkles on foam, lifted and burst dots on nets, and peeling and drag deformation on bags. Under the wave scenario, the weathered bags showed obvious holes and cracks on the surface, and even some microplastics were formed, but only slight wrinkles and holes were observed on the other two plastic types (foam and nets). Under the UV scenario, apparent holes and wrinkles on bags were more prominent if compared with the foam and nets.

Weathering can promote the migration of chemical additives from plastics. A total of 70 MPAs were tentatively identified in leachates of the weathered plastics via our suspected screening on UPLC/MS. The chromatographic features varied greatly among different plastic types and weathering scenarios. More groups of MPAs with responses $> 10^4$ were detected in the bag leachates, e.g., surfactants, antioxidants, cross-linking agents, and antistatic agents (Fig. 2). Additionally, most MPA responses for bag leachates under the wave and UV scenarios significantly exceeded those under the shoal scenario (Fig. 2D, G, J).

The numbers of identified MPAs under the wave and UV scenarios were higher than that under the shoal scenario (Fig. 3A). This is mainly attributable to the following possible factors. First, it has been found that plastic is possibly buried beneath the water column and sediment [45]. This is because the hydrodynamics in the shoal environment can roll and wrap plastics, and bury part of them into the bottom boundary layer (i.e., sand). Plastic fragments confined underneath would receive modest interaction with the aqueous phase, and hence the release of MPAs may be hindered. Second, the wave scenario generated the most diverse MPAs (Fig. 3D–L), which may be attributed to the continuous and effective hydraulic interaction between plastics and water. Clearly, wave-generated shear stresses can easily fracture objects, such as biofilms [46], and we also found microplastics were formed under the wave scenario (Fig. S3). The surface damage described above can both accelerate the MPA leaching process [47].

3.3. *Influence of plastic types on the release of MPAs*

The number of MPAs detected in leachates was dependent on the type of plastics as well. The plastic bags leached out 40 MPAs, greater than those from the foam (35) and nets (26) (Fig. 3B), consistent with the fact that the chemicals blended with plastic packaging materials cover almost all kinds of additives [17]. Whereas in foam and net plastics, relatively fewer kinds of additives such as flame retardants, antioxidants, plasticizers, pigments, and stabilizers are often reported [22,48–50].

The main MPAs we identified were generally dominated by two categories, namely antioxidants and plasticizers (Fig. 3D–L). Several phenolic, amino and organophosphite antioxidants were frequently detected in our plastic leachates (Table S6). Organic antioxidants have been broadly applied as plastic additives to scavenge free radicals and

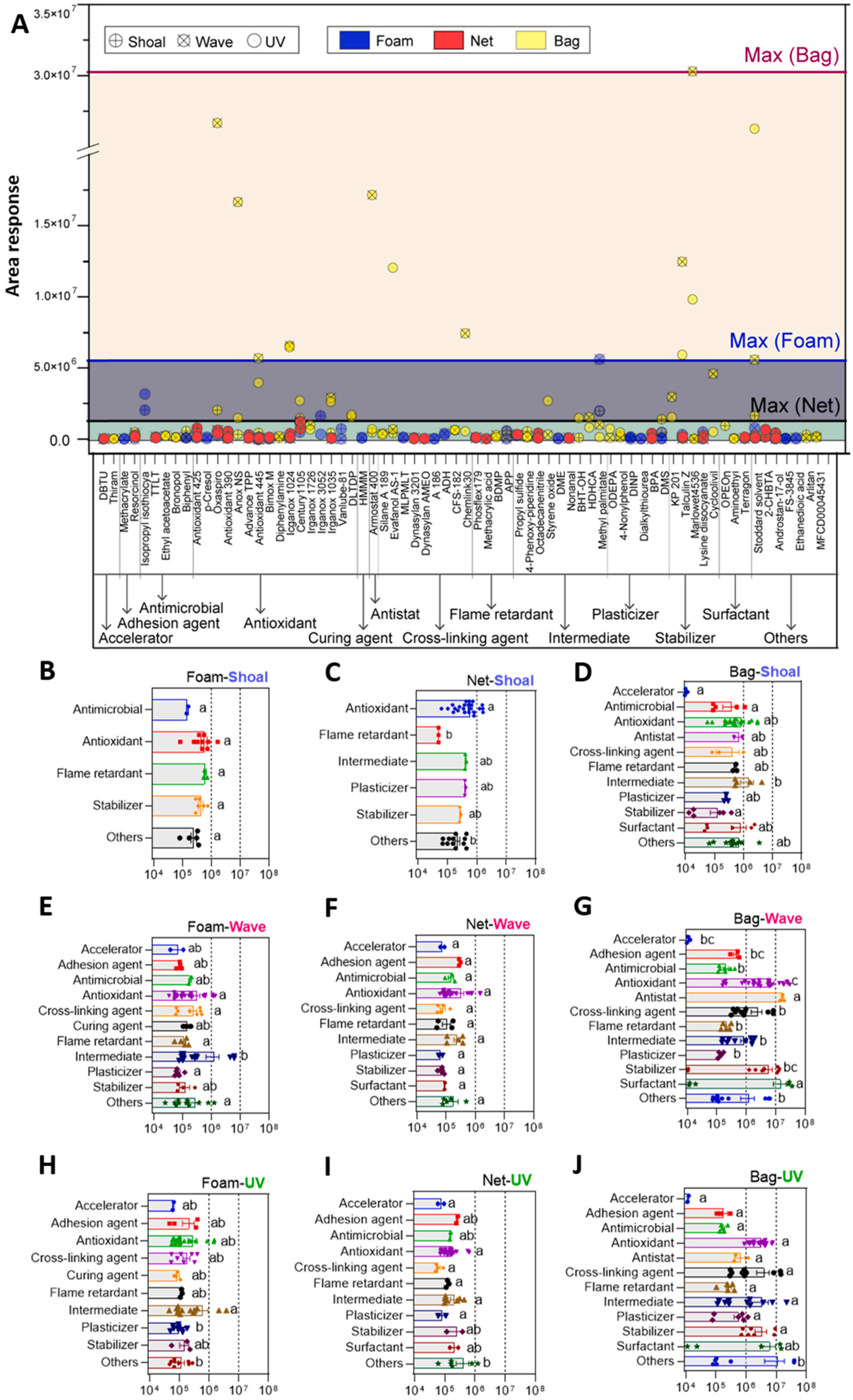

Fig. 2. Responses of migrated plastic additives (MPAs) in the plastic leachates under different weathering scenarios. (A) Overall responses of MPAs released from 3 types of plastics; (B–D) responses of MPAs released under the shoal scenario; (E–G) responses of MPAs released under the wave scenario; (H–J) responses of MPAs released under the UV scenario. Foam: floating foam; Net: fishing nets; Bag: plastic bags. Different letters of a, b, and c represent significant differences among groups based on the one-way ANOVA test. Error bars indicate the s.e.m.

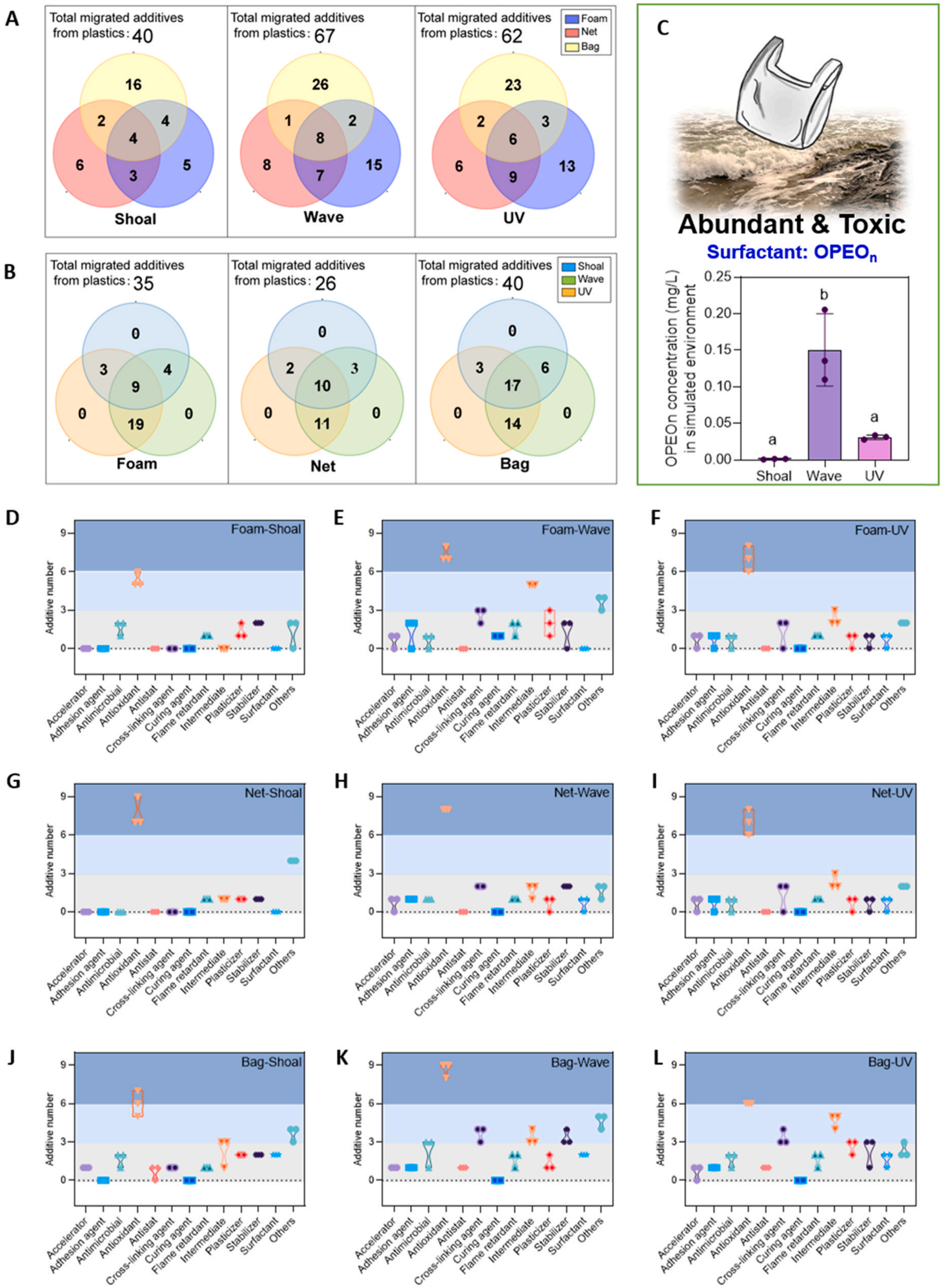

Fig. 3. Categories and numbers of migrated plastic additives (MPAs) in the leachates. (A) numbers of MPAs released under different weathering scenarios; (B) numbers of MPAs released from different plastic types; (C) levels of nonionic surfactants, $OPEO_n$, in leachates of plastic packaging bags under different weathering scenarios; (D–L) numbers of MPAs in individual categories released from three studied plastic types under different weathering scenarios. Foam: floating foam; Net: fishing nets; Bag: plastic bags. Letters a and b represent the significant difference based on the one-way ANOVA test. Data are representative of three replicates ($n = 3$). Error bars indicate the s.e.m.

slow the oxidation process of polymers [15,51,52]. Additionally, the antioxidants accounted for the largest proportions of detected MPAs in terms of their numbers (23–35 %) and responses (29–54 %) for all three types of plastics (Table S7). Plasticizers can increase the flexibility of polymers by reducing the glass transition temperature [53] and alleviate the friction between polymers as lubricants by breaking hydrogen bonds or van der Waals forces [54,55]. As expected, a host of commonly-used plasticizers, such as phthalic acid esters, epoxy hydrocarbons, fatty acid methyl ester, and phenyl alkylsulfonate, were also consistently found in the leachates, comprising 4–9 % of the detected MPA numbers and 4–28 % of the MPAs' responses for the plastic packaging bags, floating foam, and fishing nets (Table S7).

It is also worth noting that each plastic had distinct MPA profiles. For example, an antistatic agent (Armostat 400) and a curing agent [hexakis (methoxymethyl) melamine] were exclusive to the leachates of plastic bags and foam, respectively (Table S6), both of which were intentionally incorporated according to their application requirements. Plastic bags possess high resistance to moisture and can easily accumulate static electricity, which may severely affect the use of packaged products; therefore, the application of antistatic agents is highly necessary [56]. Curing agents can improve the mechanical properties of plastic foam materials, and gain their resistance to heat, water, and corrosion [57].

Moreover, the weathering of plastic bags was prone to produce smaller particles and even microplastics (Fig. S3), which may have resulted in the substantial release of MPAs from plastics due to the enlarged specific surface areas. In particular, a group of MPAs, i.e., $OPEO_n$, were present in the leachates of plastic bags with a very high instrumental response and elevated toxicity (predicted fathead minnow $LC_{50} = 2.65$ mg/L; Fig. 3 C). Alkylphenol ethoxylates, such as $NPEO_n$ and $OPEO_n$, have been widely used as surfactant additives in the manufacture of plastic products. $NPEO_n$ has been banned in some regions due to their documented endocrine-disruption effects (e.g., the EU has restricted the use of $NPEO_n$ in clothing and textile). In contrast, only a few countries, e.g., Switzerland, have restricted the use of $OPEO_n$ [58], and most countries worldwide have no regulations implemented to control $OPEO_n$. It is possibly making them become "handy" alternatives to $NPEO_n$ and consequently even more abundant in plastic items manufactured in recent years. This also explains their significant levels in the plastic bag leachates and also indicates the utmost importance to explore their toxicity.

3.4. Toxic effects of plastic leachates and prioritization of MPAs

Risks posed by plastic leachates to aquatic organisms largely depend on their chemical concentrations/composition and associated toxicity [59]. No obvious dose-effect relationship was observed on fish survival rate for any of the plastic leachates (probably because of the large intra-group differences caused by complex mixture compounds in leachates). According to the multi-factor variance analysis, none of the factors (concentration [$F = 1.122$, degree of freedom (df) = 5, $p = 0.353$], weathering scenario [$F = 1.908$, $df = 2$, $p = 0.153$], plastic type [$F = 1.619$, $df = 2$, $p = 0.203$]) had an obvious influence on the survival rate. However, all factors (concentration [$F = 3.262$, $df = 5$, $p = 0.009$], weathering scenario [$F = 20.825$, $df = 2$, $p = 0.000$], and plastic type [$F = 14.425$, $df = 2$, $p = 0.000$]) exhibited a significant influence on the heartbeat rate. Fish exhibited abnormal heartbeat rates after exposure to all three types of plastics' leachates, suggesting that the leachate-associated MPAs would negatively impact the cardiovascular system and development of zebrafish; moreover, the MPA cocktail from packaging bags appeared to be more toxic than those from the other two plastic products (Fig. S5). Additionally, no significant perturbation in the transcription expression of vitellogenin genes was noticed for all the exposed fish larvae (Fig. S6) and either the leachate concentration [$F = 1.285$, $df = 5$, $p = 0.292$] or the plastic type [$F = 2.814$, $df = 2$, $p = 0.073$] exhibited obvious influence according to the multi-factor variance analysis, which could be ascribed to sexual immaturity of fish larvae [60].

To prioritize key MPAs in the complex plastic leachates, we comprehensively considered the responses of MPAs and their potential toxicity predicted using the TEST program [61], and dug out a suite of noteworthy substances with considerable responses (> 30 M) and high toxicity ($LC_{50} < 5$ mg/L), the criteria based on previous studies [62,63] with minor modifications, for further chemical and biological analyses: $OPEO_n$ migrated from the plastic bags under the wave scenario (Fig. 4).

Fig. S7 demonstrates the mass spectrum of $OPEO_n$ in the authentic material (top), which satisfactorily matched that in the leachate of plastic bags under the wave scenario (bottom; $\Delta m/z < 10$ ppm for all characteristic ions). Both spectra are dominated by m/z 532.40, 576.43, 493.33, 449.30, and 620.45, corresponding to $[OPEO_7 + NH_4]^+$, $[OPEO_8 + NH_4]^+$, $[OPEO_6 + Na]^+$, $[OPEO_5 + Na]^+$, and $[OPEO_9 + NH_4]^+$, respectively. In terms of these ions, we determined the $OPEO_n$ concentrations in leachates of packaging bags under the wave (0.150 ± 0.050 mg/L), UV (0.031 ± 0.003 mg/L), and shoal (0.001 ± 0.0004 mg/L) weathering scenarios (see Fig. 3C). Meanwhile, the ions representing $[OPEO_4 + Na]^+$, $[OPEO_{10} + NH_4]^+$, $[OPEO_{11} + NH_4]^+$, $[OPEO_{12} + NH_4]^+$, and $[OPEO_{13} + NH_4]^+$ at m/z 405.27, 664.47, 708.50, 752.55, and 796.56, respectively, were also visible but with lower mass intensities. Therefore, our identification of $OPEO_n$ in the leachates was of the highest confidence, and using the technical mixture we purchased that had $OPEO_n$ congener profiles of environmental relevance for the following *in vivo* toxicity test can well reflect exposure of aquatic organisms to $OPEO_n$ in the Yangtze River Estuary. Alkylphenol polyethoxylates, a family of non-ionic surfactants mainly composed of $OPEO_n$ and nonylphenol polyethoxylates ($NPEO_n$), are highly cost-efficient non-ionic surfactants with excellent performance; their technical mixtures, each of which contains a series of homologs, have been commonly applied as emulsifiers, detergents, and wetting and dispersing agents in numerous consumer products, like plastic polymers and textiles [64,65]. Previous studies have documented the ubiquity of $OPEO_n$ in assorted plastics [66,67] as well as various environmental compartments, including sediments, water, and sewage [68]. The theoretical monoisotopic masses of $NPEO_n$ were also extracted on the mass spectra for our plastic leachates, but their intensities were relatively faint, which might result from the regulation on $NPEO_n$ and nonylphenols in many countries worldwide due to their recognized

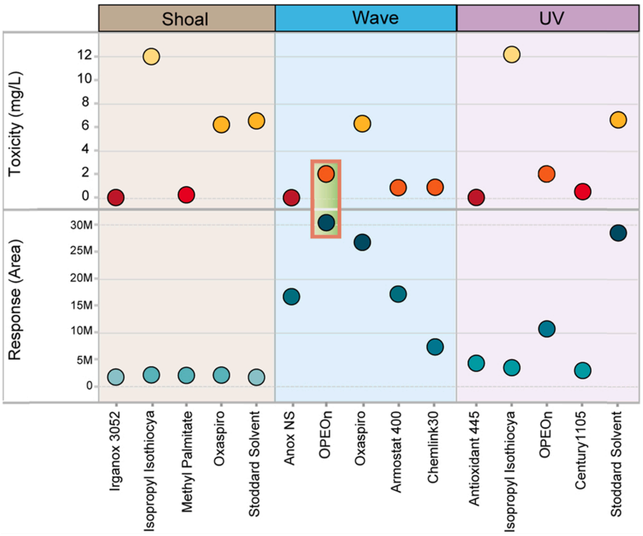

Fig. 4. Top five MPAs with the highest response values under the three weathering scenarios and their toxicity to the fathead minnow (LC_{50}, 96-hour exposure duration) predicted by the TEST program. $OPEO_n$ highlighted in the box simultaneously have high toxicity ($LC_{50} < 5$ mg/L) and substantial responses (> 30 M). Response data represent the mean values of three independent replicates ($n = 3$).

threats to aquatic biota and human health [69,70].

To illustrate the toxicity of $OPEO_n$, a series of concentrations for the $OPEO_n$ was established including 0.004, 0.02, 0.1, 0.5, and 2.5 mg/L. Within this wide concentration gradient, the environmentally relevant concentration (Fig. 3C) magnitude of $OPEO_n$ was covered. The endpoints of survival rate, heartbeat rate, and hatching rate of zebrafish were all negatively correlated with the $OPEO_n$ concentrations, with $r = -0.706$ ($p = 0.001$), $r = -0.593$ ($p = 0.000$), and $r = -0.766$ ($p = 0.000$), respectively. Additionally, these endpoints also showed a linear relationship with $OPEO_n$ concentrations for the endpoints of survival rate ($R^2 = 0.498$, $p = 0.010$), heartbeat rate ($R^2 = 0.352$, $p = 0.000$), and hatching rate ($R^2 = 0.587$, $p = 0.000$).

Of note, $OPEO_n$ could cause obvious acute lethal toxicity to fish embryos at environmentally-relevant concentrations (≥ 0.1 mg/L; Fig. 5A and 3C). The survival rate at 2.5 mg/L was 57 % for zebrafish, which was quite consistent with the predicted LC_{50} (2.65 mg/L) for fathead minnow. Moreover, sublethal toxicity can be observed even at 0.004 mg/L $OPEO_n$, triggering a significant increase in embryonic heartbeat rates (Fig. 5B, SI video). The hatching rate of zebrafish embryos decreased significantly for the groups treated with ≥ 0.1 mg/L $OPEO_n$, and it reduced by 1.8-fold for the subjects exposed to 2.5 mg/L $OPEO_n$ relative to the control (Fig. 5C). Moreover, the hatched zebrafish larvae after $OPEO_n$ exposure exhibited appreciable morphological distortions (i.e., spinal column curvature compared to the control; Fig. 5E–F) and abnormal swimming behaviors in their early life stage. However, the impact of $OPEO_n$ on the body length of hatched fish was non-significant according to the correlation analysis (with $r = 0.142$, $p = 0.573$), and no obvious linear relationship was observed between the $OPEO_n$ concentration and the body length ($R^2 = 0.02$, $p = 0.573$) (Fig. 5D).

Collectively, although no estrogenic effects of the plastic leachates were found on zebrafish, which might be confounded by the immaturity of endocrine systems in the survived fish, the significant acute and subacute toxicities of $OPEO_n$ to the embryonic and larval fish at

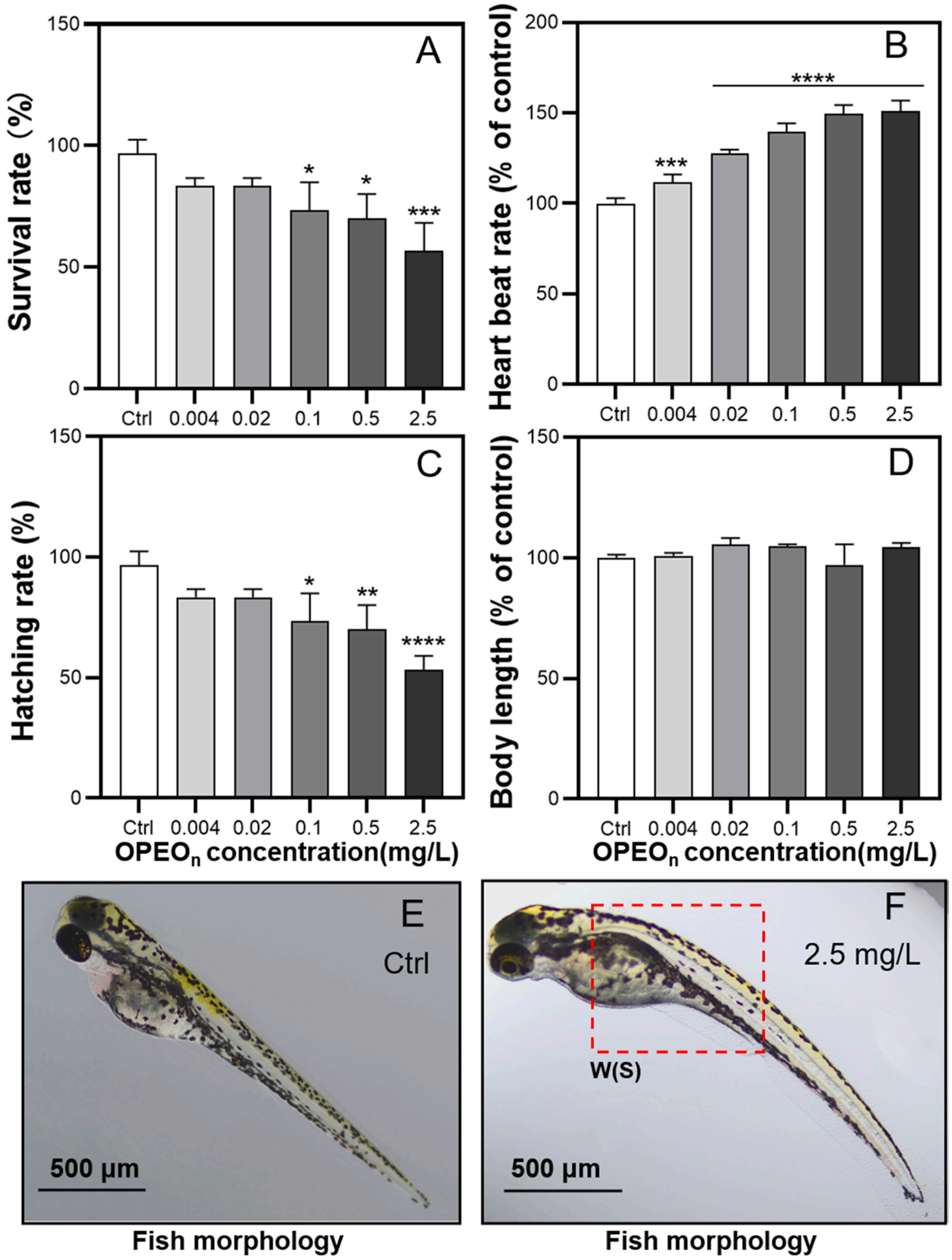

Fig. 5. Alterations in growth and development biomarkers of zebrafish after exposure to $OPEO_n$ covering environmentally relevant concentrations. (A) survival rate at 24 hpf; (B) heartbeat rate at 48 hpf; (C) hatching rate at 72 hpf; and (D) body length at 96 hpf. Morphological effects of $OPEO_n$ on zebrafish were monitored at 96 hpf for (E) the control group and (F) the exposure group (in 2.5 mg/L $OPEO_n$). The red dotted box indicates the bending deformation of the fish spine. The estuarine relevant concentration of $OPEO_n$ was within the range of 0.001–0.21 mg/L as suggested by Fig. 3C. Data are representative of three independent replicates ($n = 3$). Asterisk symbols * represents $p < 0.05$, ** represents $p < 0.01$, *** represents $p < 0.001$, and **** represents $p < 0.0001$.

environmentally relevant concentrations are cause for concern, indicating that the leached nonionic surfactant $OPEO_n$ from plastic bags could cause severe ecotoxic outcomes in the estuarine environment. We would like to point out that the chemical leaching may be of even greater complexity in the natural milieu since here we screened for limited numbers of industrial additives, but there always be previously unsuspected compounds that are either intentionally added to or sorbed on plastics from the surrounding estuarine environment [71–73]. Moreover, only the aqueous exposure route for MPAs entering aquatic organisms was evaluated in the present study; however, fish would ingest fragmented plastics directly into their gastrointestinal tracts [74], where the acidic condition may aggravate the release of additives and thus exert badly higher toxicity [75].

4. Conclusions

In conclusion, we demonstrated that plastic debris had very high abundance in the estuarine environment and various kinds of MPAs can leach out under different weathering scenarios. Among the MPAs, a series of non-ionic surfactants are noteworthy given their outstanding concentrations in the leachates of plastic bags, and high aquatic toxicity as well, even at environmentally relevant concentrations. Our findings strongly call for the need for continuous investigations of plastics-driven pollution in the previously neglected estuarine environment and the resultant risk to aquatic ecosystem. This study also emphasizes that we need to have stringent control over the types and quantities of additives that are incorporated in plastic products, and we need to curtail the applications of additives that have potential high levels of toxicity. Meanwhile, the recycling strategy of plastic debris commonly found in the estuary, such as fishing nets, floating foam, and plastic bags, should be established, as it is currently severely lacking.

Environmental implication

The specific hydrodynamic conditions have created the estuary as a plastic pollution hotspot. Moreover, the additives migrated from plastics would be very complicated in the estuarine area because of specific environmental conditions. Field investigation indicates that floating foam, fishing nets, and plastic bags are representative plastic debris, and they are subjected to severe weathering in typical estuarine conditions. Lab simulation reveals that more plastic additives can leach out under the wave scenario and from the plastic bags than other weathering scenarios and plastic types. Particularly, a suite of nonionic surfactants, octylphenol polyethoxylates, exhibit high response and toxicity, and deserve our special attention.

CRediT authorship contribution statement

Qiqing Chen: Conceptualization, Methodology, Investigation, Visualization, Toxicity analysis, Additives information collection and analysis, Writing – original draft, Writing – review & editing. **Zhuo Gao:** Fish exposure, Investigation, Additives information collection, Chemical quantification, Writing – original draft, Writing – review & editing. **Yan Wu:** Conceptualization, Chemical data analysis, Writing – original draft, Writing – review & editing. **Haifeng Li:** Methodology, Chemical quantification. **Jing Jiang:** Investigation, Writing – review & editing. **Yan Yang:** Fish exposure, Investigation. **Li Xu:** Chemical quantification. **Huahong Shi:** Writing – review & editing.

Declaration of Competing Interest

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

Data Availability

Data will be made available on request.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jhazmat.2023.130861.

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