Effect of microplastics on aquatic biota: A hormetic perspective[☆]

Tao Sun^{a,d}, Junfei Zhan^{a,d}, Fei Li^{a,c}, Chenglong Ji^{a,b,c}, Huifeng Wu^{a,b,c,*}

^a CAS Key Laboratory of Coastal Environmental Processes and Ecological Remediation, Yantai Institute of Coastal Zone Research (YIC), Chinese Academy of Sciences (CAS); Shandong Key Laboratory of Coastal Environmental Processes, YIC-CAS, Yantai, 264003, PR China

^b Laboratory for Marine Fisheries Science and Food Production Processes, Qingdao National Laboratory for Marine Science and Technology, Qingdao, 266237, PR China

^c Center for Ocean Mega-Science, Chinese Academy of Sciences (CAS), Qingdao, 266071, PR China

^d University of Chinese Academy of Sciences, Beijing, 100049, PR China

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ABSTRACT

As emerging pollutants, microplastics (MPs) have been found globally in various freshwater and marine matrices. This study recompiled 270 endpoints of 3765 individuals from 43 publications, reporting the onset of enhanced biological performance and reduced oxidative stress biomarkers induced by MPs in aquatic organisms at environmentally relevant concentrations (≤ 1 mg/L, median = 0.1 mg/L). The stimulatory responses of consumption, growth, reproduction and survival ranged from 131% to 144% of the control, with a combined response of 136%. The overall inhibitory response of 9 oxidative stress biomarkers was 71% of the control, and commonly below 75%. The random-effects meta-regression indicated that the extents of MPs-induced responses were independent of habitat, MP composition, morphology, particle size and exposure duration. The results implied that the exposure to MPs at low and high concentrations might induce opposite/non-monotonic responses in aquatic biota. Correspondingly, the hormetic dose response relationships were found at various endpoints, such as reproduction, genotoxicity, immunotoxicity, neurotoxicity and behavioral alteration. Hormesis offers a novel perspective for understanding the dose response mode of aquatic organisms exposed to low and high concentrations of MPs, highlighting the necessity to incorporate the hormetic dose response model into the ecological/environmental risk assessment of MPs.

1. Introduction

Plastics products are ubiquitous in our daily life due to their lightweight, inexpensive and durable properties (Pahl et al., 2017). Over the past 70 years, global plastic production has increased exponentially from 5 million tons annually in the 1950s (Thompson, 2015) to over 350 million tons today (PlasticsEurope, 2020). If the current trend continues, the global plastic production is expected to reach 1.1 billion tons in 2050 (Geyer, 2020), leading to an extra 33 billion tons of plastic (Rochman et al., 2013). With high volume manufacturing, intensive use and slow degradation, plastic debris are observed in almost all habitats (Bouwmeester et al., 2015). As an important sink, the aquatic environment is continuously accumulating massive plastic waste (Jambeck et al., 2015; MacArthur, 2017). Nowadays, plastic-caused entanglement, ingestion and potential toxicity pose a serious threat to the health of aquatic biota (Ostle et al., 2019).

Tiny plastic (less than 5 mm in diameter) termed microplastic (MP) is the predominant form of plastic debris in aquatic environments (Galloway et al., 2017). The occurrence of MPs involves both primary (e.g. cosmetic products and synthetic textiles) and secondary sources (mainly the fragmentation of larger plastic debris) (Cole et al., 2011). With small size, large surface and strong hydrophobicity, MPs are easily ingested by aquatic organisms, accumulated in tissues and transferred in food webs (Setälä et al., 2014; Kane et al., 2020). Additionally, MPs can adsorb persistent organic pollutants and trace metals, act as vectors and release these hazardous substances into aquatic environments, causing more damages than large plastics (Brennecke et al., 2016; Wang et al., 2018). As emerging contaminants in aquatic environments, MPs attract considerable public and scientific attention (Fig. 1a), and become a global environmental concern (Burns and Boxall, 2018; de Souza Machado et al., 2018; Klingelhöfer et al., 2020).

Hormesis is a central toxicological concept to account for mild stress-

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* Corresponding author. CAS Key Laboratory of Coastal Environmental Processes and Ecological Remediation, Yantai Institute of Coastal Zone Research (YIC), Chinese Academy of Sciences (CAS); Shandong Key Laboratory of Coastal Environmental Processes, YIC-CAS, Yantai, 264003, PR China.

E-mail address: hfwu@yic.ac.cn (H. Wu).

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Fig. 1. Number of publications about microplastics (MPs) (a) and hormesis (b).

induced beneficial effect (Calabrese and Blain, 2011). The concept of hormesis assumes that low dose of stressor agent can induce an adaptive response and strengthen the biological performance, while high dose may cause an adverse response and weaken the biological resilience (Mattson, 2008; Rattan et al., 2009; Calabrese, 2013; Le Bourg, 2019). This can be displayed in a biphasic dose response relationship. The hormetic effect can be triggered by low to moderate toxicity induction or by overcompensation for homeostasis disruption, which can not only rapidly repair damage and reset the homeostatic setpoint, but also act as a preconditioning stimulus to protect the organism from more serious challenges (Calabrese et al., 2016). Recently, the phenomenon of hormesis has been increasingly documented in publications (Fig. 1b), and the hormetic model has been gradually developed into a fundamental dose response model in toxicology (Calabrese et al., 2016; Costantini and Borremans, 2019).

The potential toxicity of MPs to aquatic organisms is one of the hotspots in global environmental research (Wright et al., 2013; Anderson et al., 2016; de Sá et al., 2018; Franzellitti et al., 2019; Ma et al., 2020). The concentration of MPs in natural aquatic environments is very low (typically below 1 mg/L) (Chen et al., 2020a). However, some negative effects of MPs on aquatic organisms were observed through environmentally unrealistic concentrations (generally 2 to 7 orders of magnitude of the environmental level), which may lead to overreaction or misunderstanding of the risk of MPs (Lenz et al., 2016; Burns and Boxall, 2018; Revel et al., 2020). It is of great significance to evaluate the effect of MPs in aquatic organisms at environmentally relevant concentrations (de Sá et al., 2018). Therefore, this study was conducted, aiming to (i) recompile the data of enhanced biological performance and reduced oxidative stress biomarkers in aquatic biota induced by MPs at environmentally relevant concentrations; (ii) evaluate the characteristics of MPs-induced stimulatory and inhibitory responses; (iii) provide evidence for MPs-induced hormetic dose response relationships. In order to achieve these goals, a systematic literature search was conducted, followed by data extraction and meta-analysis for data integration, and subsequently meta-regression was used to assess the changes in extents of the stimulatory/inhibitory responses.

2. Materials and methods

2.1. Literature retrieval

In order to extensively collect the literature on the toxicity of MPs to aquatic organisms, referring to the Cochrane handbook v.6.1 (Higgins et al., 2020), three databases including *Web of Science Core Collection*, *Medline* and the *Cochrane Library* were systematically searched using the terms and modifiers: *plastic, debris, exposure, toxic*, effect, aquatic,

organism, biota, wildlife, environment, freshwater, marine, sea, ocean, hormone*, dose response, dose-response, biphasic response, acclimation response, adaptive response, preconditioning, conditioning, stimulation, stimulatory, inhibition, inhibitory, without language restriction. Grey literature (e.g. conference papers and dissertations) were also searched via *Index to Scientific and Technical Proceedings* and *Baidu Scholar*. The initial literature search was conducted in July 2020, and supplementary collections were performed in October 2020 and March 2021.

2.2. Inclusion criteria

The titles, abstracts, keywords and full-texts of all retrieved publications (2952 in total) were screened by two researchers for considering inclusion according to the following criteria: (i) original research paper reported the effect of MPs on consumption (e.g. egestion amount, ingestion rate), growth (e.g. body length, change in weight), reproduction (e.g. hatching rate, number of offspring), survival (e.g. mortality rate, survival time), or oxidative stress biomarker (e.g. lipid peroxidation, reactive oxygen species) (Foley et al., 2018; Prokić et al., 2019); (ii) designed at least one control group and one stimulatory/inhibitory group; (iii) the stimulatory/inhibitory response was defined as a difference of 10% or more from the control, also corresponding to the diagnostic threshold among multiple medical/toxicological studies (e.g. Wiesenack et al. (2005), Laffosse et al. (2011), Biais et al. (2017) and Trucco et al. (2018)), or less than 10%, but there was a statistical difference; (iv) the exposure concentration threshold of MPs was set at 1 mg/L (see the review of Yu et al. (2020)) that could cover/overlap/be at the same order of magnitude as the maximum concentrations found in multiple natural environments (e.g. 0.94 mg/L in Amsterdam canals, the Netherlands (Leslie et al., 2017), 1.01 mg/L in Geoje Island, South Korea (Song et al., 2014), 0.62 mg/L in Colombian Caribbean, Colombia (Garcés-Ordóñez et al., 2020), and 1.26 mg/L in Saigon River, Vietnam (Strady et al., 2020), estimated by trawling depth of 0.1 m and/or an average weight of 5 µg/particle proposed by Besseling et al. (2019) where needed) and used in environmentally relevant studies (e.g. O'Donovan et al. (2018), Chen et al. (2020a) and Teng et al. (2021)); (v) the response was induced by MPs only (i.e. not combined exposure with organic pollutants/trace metals); (vi) the mean with standard error (SE) or standard deviation (SD) of each endpoint could be obtained directly or calculated indirectly.

2.3. Data extraction

The following information were extracted from included literature: (i) the first author; (ii) publication year; (iii) freshwater or marine habitat; (iv) the sample size, mean and SD/SE; (v) the mean size,

morphology and composition of MPs; (vi) exposure concentration and duration. Data were extracted directly from tables and full-texts. However, if data were displayed graphically, the Getdata Graph Digitizer v.2.24 software (<http://getdata-graph-digitizer.com/>) was used to measure the values (Sahebkar et al., 2015; Mazidi et al., 2017; Yang et al., 2020). During the data extraction process, any discrepancies between two researchers were resolved by discussion or consultation with the third researcher.

2.4. Data analysis

For the endpoint classified as biological performance indicators (i.e. consumption, growth, reproduction, survival), if an increased response indicating a positive effect (e.g. body length, hatching rate), the stimulatory response to MPs treatment was calculated using Formula (1). However, if a reduced response implied a positive effect (e.g. remaining diet, mortality rate), the stimulatory response was estimated by Formula (2). For the endpoint that was a biomarker of oxidative stress, the inhibitory response was computed via Formula (3).

$$SR = R_t / R_c \times 100 \quad (1)$$

$$SR = R_c / R_t \times 100 \quad (2)$$

$$IR = R_t / R_c \times 100 \quad (3)$$

where *SR* and *IR* were the abbreviations for stimulatory response and inhibitory response, respectively, representing % of the control; R_t and R_c denoted the mean values of MPs-treated group and control group, respectively.

The combined response refers to combing all the same type responses (stimulatory or inhibitory) in individual studies into one response estimator. The combined response was calculated using meta-analysis that is a powerful statistical tool to increase the robustness of the pooled estimator across individual studies with the same topic by reducing or even eliminating (i.e. a given weight of 0) potential sampling error and extreme data (Gurevitch et al., 2018; Higgins et al., 2020). The Stata v.12.0 software (StataCorp, College Station, USA) was used to conduct this meta-analysis. The random-effects model based on the inverse-variance weighted method was used to synthesize the results of each study. This model could adjust the weight of each study by the between-study variance (Formulas (4)–(7)) (DerSimonian and Laird, 1986, 2015).

The between-study variance (τ^2) was computed using:

$$\tau^2 = \left[\sum X_i \left(Y_i - \sum X_i Y_i / \sum X_i \right)^2 - (k - 1) \right] / \left(\sum X_i - \sum X_i^2 / \sum X_i \right) \quad (4)$$

where X_i , Y_i and k were the inverse of variance of i th study, the i th effect estimate and the number of included studies, respectively.

The weight of i th study (W_i) was calculated by the random-effects model, as:

$$W_i = 1 / (V_i + \tau^2) \quad (5)$$

where V_i represented the variance of i th study.

The combined response (R_o) and its variance (V_{Ro}) were then calculated, as:

$$R_o = \sum W_i Y_i / \sum W_i \quad (6)$$

$$V_{Ro} = 1 / \sum W_i \quad (7)$$

The random-effects meta-regression techniques were used via the command **metareg response variable, wsvar(variance) bsest(reml) randomsize** in Stata software to examine whether the extents of the

stimulatory/inhibitory responses vary between different response and exposure variables (Harbord and Higgins, 2008). The statistical uncertainty was quantified in 95% confidence intervals, and the significant level was set at $\alpha = 0.05$.

3. Results and discussion

3.1. Overview of included publications

After final screening, a total of 43 papers, involving 270 endpoints of 3765 individuals, were included in this retrospective analysis (Table S1). Twenty-two studies were conducted on freshwater biota, and 21 studies on marine biota. Polystyrene (PS) was the most frequently selected polymer (28 studies), and sphere (including bead (de Ruijter et al., 2020)) was the most widely used shape (33 studies). The plastic size ranged from 0.05 to 2000 μm , with a median size of 2 μm . The mean and median values of the exposure duration were 13 and 9 days, respectively. The exposure concentrations varied between 0.008 and 1000 $\mu\text{g/L}$, with a median concentration of 100 $\mu\text{g/L}$.

3.2. MPs-induced stimulatory/inhibitory responses at environmentally relevant concentrations

The stimulatory responses of consumption, growth, reproduction and survival of aquatic biota exposed to MPs at environmentally relevant concentrations were significantly higher than the control levels ($p < 0.05$), which were 138%, 144%, 131% and 140% of the control, respectively, with a combined response of 136% (Fig. 2). The stimulation effect suggested that low concentration of MPs might be involved in the adaptive response of aquatic organisms, and act as a conditioning agent to strength biological performance and biological resistance (Guzzetti et al., 2018; Sun et al., 2018; Chen et al., 2020b). A previous meta-analysis of 43 publications conducted by Foley et al. (2018) showed that in many cases, MP administration to aquatic organisms had no significant influence on the biological performance indicators. It should be noted that the exposure concentration of MPs was not considered as a variable/restriction by Foley et al. (2018), meaning that environmentally unrealistic concentrations (e.g. 100 mg/L of MPs used in the included study (Jemec et al., 2016)) were also involved. However, when limited to environmentally relevant concentrations, some potentially positive effects might be observed due to the moderate inducer role of MPs. In addition, the random-effects meta-regression indicated that the extents of MPs-induced stimulatory responses did not differ significantly ($p > 0.05$) among measured endpoint (coefficient of

Fig. 2. The stimulatory response degrees of biological performance indicators. The same letters denoted that there was no statistical difference at $\alpha = 0.05$ level among indicators. The asterisk (*) indicated statistical difference ($p < 0.05$) between control and MPs-treated groups. Data were represented by mean with 95% confidence intervals (CIs).

variation (CV) = 4%) (Fig. 2), habitat (Fig. 3a), MP composition (Fig. 3b), morphology (Fig. 3c), particle size (Fig. 3d), exposure duration (Fig. 3e) and exposure concentration (Fig. 3f), suggesting that aquatic organisms exposed to low concentrations of MPs exhibited generalized stimulation.

The inhibitory responses of oxidative stress biomarkers, including catalase (CAT), superoxide dismutase (SOD), glutathione peroxidase (GPx), glutathione-S-transferase (GST), glutathione (GSH), thiobarbituric acid reactive substances (TBARS), lipid peroxidation (LPO), maleic dialdehyde (MDA) and reactive oxygen species (ROS) were obviously lower than the control levels ($p < 0.05$), which were 69%, 74%, 73%, 73%, 67%, 65%, 75%, 72% and 70% of the control, respectively, with a combined response of 71% (Fig. 4). The inhibition

effect indicated that MP exposure influenced the functioning of the antioxidant system of aquatic organisms. The levels of MDA, TBARS, ROS and LPO were directly related to oxidative stress, among which MDA was the prototype of TBARS that stemmed from the ROS-mediated LPO (Cole et al., 2020; Kamal et al., 2020). Their reductions reflected the enhanced defense response and alleviated oxidative stress, suggesting that the antioxidant system might be dominated in these cases to maintain redox homeostasis (Jia et al., 2013). However, the decrease of other biomarkers did not necessarily mean that the redox maintained at a low steady-state level, but probably meant the imbalance of the antioxidant defense system (e.g. the decrease of GSH might negatively affect the antioxidant capacity), which need to be further explored and clarified (Trestail et al., 2020; Kim et al., 2021). Additionally, the

Fig. 3. Comparisons of the stimulatory response among exposure variables. To improve the statistical power, each variable contained at least three values. The same letter meant no significant difference ($p > 0.05$). Abbreviations: PE, polyethylene; PET, polyethylene terephthalate; PS, polystyrene.

Fig. 4. The inhibitory response extents of oxidative stress biomarkers. The same letters indicated no significant difference among biomarkers ($p > 0.05$). Data were represented by mean with 95% CIs. The asterisk (*) indicated statistical difference ($p < 0.05$) between control and MPs-treated groups. Abbreviations: CAT, catalase; SOD, superoxide dismutase; GPx, glutathione peroxidase; GST, glutathione-S-transferase; GSH, glutathione; TBARS, thiobarbituric acid reactive substances; LPO, lipid peroxidation; MDA, maleic dialdehyde; ROS, reactive oxygen species.

random-effects meta-regression showed that the extents of the inhibitory responses were also independent of measured endpoint ($CV = 5\%$) (Fig. 4), habitat (Fig. 5a), MP composition (Fig. 5b), morphology (Fig. 5c), particle size (Fig. 5d) and exposure duration (Fig. 5e). Intriguingly, at the cellular/molecular level where responses tended to be more sensitive than the individual level (Zhang et al., 2009), a significant concentration-dependent inhibitory response was observed ($p < 0.01$) (Fig. 5f). The concentration-dependent inhibition might be explained by (i) the concentration of MPs did not exceed the threshold of disrupting redox homeostasis; (ii) the increased MP stress could activate the antioxidant system more effectively; (iii) this activation would enhance the defense response and trigger a powerful compensatory reaction to protect against more severe stress (Calabrese, 2001; Jia et al., 2013; Prokić et al., 2019).

In addition, it should be noted that the tested animals at different life stages might have dissimilar accumulation abilities of MPs (Woods et al., 2020), and the enrichment of MPs from the supplement food/prey during the exposure period might occur (Carbery et al., 2018; Hasegawa and Nakaoka, 2021). However, these factors that potentially influence the effect of MPs are easily ignored. Therefore, it is highly recommended that the detailed life stages of the tested animals and the concentration of MPs in food/prey should be measured and reported in future studies to increase the comparability between studies and avoid speculation.

3.3. Evidence of MPs-induced hormetic dose response relationships

The observed effects of MPs on enhancing biological performance and reducing oxidative stress biomarkers challenged our previous understanding of the toxicity of MPs, suggesting that the effects of MPs could not be roughly considered as adverse events, especially at environmentally relevant concentrations. These observations also presented a very interesting hypothesis, that was, with the increase of exposure concentrations, the effects of MPs on aquatic biota might be opposite/non-monotonic. Correspondingly, the hormetic dose response relationships were identified with various endpoints tested (Fig. 6a–i), which provided a novel insight for understanding the complex effects of MPs.

To evaluate the influence of MPs on the biological performance of aquatic biota, Ziajahromi et al. (2017) investigated the effect of an 8-day exposure to polyethylene terephthalate (PET) microfibers (280 μm) on the reproduction of *Ceriodaphnia dubia*. It was shown that the number of

neonates in the second brood of *C. dubia* was significantly stimulated at 62.5 $\mu\text{g/L}$ (196% of the control), but inhibited continuously with the increase of exposure concentrations, presenting an inverted U-shaped hormetic dose response relationship (Fig. 6a).

In terms of oxidative stress biomarkers, after exposure to PS MPs (5 μm) for 21 days, the MDA contents of *Eriocheir sinensis* in MPs-treated groups decreased by 25% and 31% at concentrations of 40 and 400 $\mu\text{g/L}$, respectively, but obviously increased by 80% at 40000 $\mu\text{g/L}$, presenting a J-shaped hormetic relationship (Fig. 6b) (Yu et al., 2018). Moreover, in the study of Yu et al. (2018), an inverted U-shaped hormetic curve of SOD activity was also observed (Fig. 6c). It could be explained that moderate oxidative stress induced by low concentration of MPs could stimulate the activity of SOD, while severe oxidative stress caused by the increased MP concentration exceeded the limit of anti-oxidative capacity, thereby resulting in the disruption/collapse of anti-oxidant system and the inhibition of SOD activity (Trestrail et al., 2020).

To evaluate the potential genotoxicity of MPs, Yu and Chan (2020) investigated the transgenerational effect of PS MPs on *Amphibalanus Amphitrite*. It was shown that parental (F_0) exposure to 19 μm MP at 380 $\mu\text{g/L}$ could decrease the development time of offspring larval (F_1) by 15%. However, when the exposure concentration of F_0 reached 3800 $\mu\text{g/L}$, the development time of F_1 increased to 107% of the control. The transgenerational effect of MPs presented a J-shaped hormetic relationship (Fig. 6d). At molecular level, Revel et al. (2020) showed that the percentages of tailed DNA in *Crassostrea gigas* after exposure to 0.008–100 $\mu\text{g/L}$ polyethylene-polypropylene MPs (<400 μm) were lower than those in the control group, suggesting that environmentally realistic exposure to MPs did not cause DNA damage. However, when exposure to unrealistic concentrations (56, 100, 180 mg/L), significant increases in DNA damage were exhibited, reflected by the number of DNA strand breaks increased up to 2-fold, 11-fold and 15-fold, respectively, compared to the control (Alnajjar et al., 2021).

For the immunotoxicity of MPs, juveniles of *E. sinensis* were exposed to different concentrations of 5 μm MP for 14 days, showing that the activity of lysozyme (LSZ) in hepatopancreas increased significantly at 400 $\mu\text{g/L}$ (138% of the control) and then decreased continuously with the increase of MPs (96% and 90% of the control at 4000 and 40000 $\mu\text{g/L}$, respectively), presenting an inverted U-shaped hormetic curve (Fig. 6e) (Liu et al., 2019). Consistently, other immune parameters in haemolymph of *E. sinensis* were also displayed inverted U-shaped hormetic curves, such as phenoloxidase activity (PO) (Fig. 6f) and acid phosphatase activity (Fig. 6g). Intriguingly, the disappearance of hormesis of PO after 21 days of exposure indicated that the hormetic effect might be temporary at some endpoints (Oberbaum et al., 2010).

To determine the neurotoxicity of MPs, Li et al. (2020) explored whether PS MPs (0.08 μm) could trigger nervous system response of *Corbicula fluminea*. It was shown that after exposure to different concentrations of MPs for 96 h, the activity of acetylcholinesterase (AChE) in gill increased by 17% and decreased by 3% at 100 $\mu\text{g/L}$ and 5000 $\mu\text{g/L}$, respectively, exhibiting an inverted U-shaped hormetic curve (Fig. 6h). At environmentally relevant concentrations (1, 10, 100, 1000 $\mu\text{g/L}$), Gambardella et al. (2017) reported that the activities of AChE in *A. amphitrite* significantly increased at all tested concentrations. However, the neurotoxicity of MPs at high concentrations has also been widely documented (Prokić et al., 2019; Bhagat et al., 2020; Eom et al., 2020).

In terms of behavioral alteration, Gambardella et al. (2018) showed that the swimming speed of *Brachionus plicatilis* changed after exposure to environmentally relevant (1 $\mu\text{g/L}$) and unrealistic (10000 $\mu\text{g/L}$) concentrations of MPs, which were 137% and 68% of the control, respectively, displaying an inverted U-shaped hormetic relationship (Fig. 6i). Moreover, Chen et al. (2020a) reported that zebrafish became hyperactive after exposure to 5 μm MP at 1000 $\mu\text{g/L}$, reflected by the significantly increased moved distance (averaged 163% of the control). However, when exposed to environmentally unrealistic concentrations, the hyperactive behavior of zebrafish did not appear, and was replaced

Fig. 5. Comparisons of the inhibitory response among exposure variables. To improve the statistical power, each variable contained at least three values. The same letters indicated no significant difference ($p > 0.05$). Abbreviations: PE, polyethylene; PE-PP, polyethylene-polypropylene; PET, polyethylene terephthalate; PS, polystyrene.

by reduced activity or even inactivity. For example, Santos et al. (2021) showed that after exposure to 2000 $\mu\text{g/L}$ 1–5 μm MP, the moved distance of zebrafish in MPs-treated group was only 81% of the control.

Taken together, this section provided evidence/examples to indicate that MPs, as a stressor agent, could induce hormetic dose response relationship in aquatic biota, and the shape of the hormetic curve depended on that endpoint.

3.4. Application of hormetic model in risk assessment of MPs

The linear no-threshold (LNT) model, threshold model and hormetic model are the main dose response models used in toxicology and risk

assessment (Agathokleous et al., 2019a). Among them, the LNT model assumes that the response starts linearly from zero dose (Fig. 7a), while the threshold model supposes that the response only appears above a threshold dose (Fig. 7b). However, the hormetic model presumes the occurrence of modest response at low dose and the opposite response at high dose (Fig. 7c) (Hashmi et al., 2014; Agathokleous et al., 2019b).

At present, the hormetic model has attracted considerable interest and has been recommended as a default toxicological model (Sun et al., 2020). The hormetic dose response model appears to be more common than the LNT and threshold models (Calabrese and Baldwin, 2003; Doss, 2013; Cardarelli II and Ulsh, 2018; Costantini and Borremans, 2019), which has been documented in diverse biological models, various agents

Fig. 6. Evidence of MPs-induced hormetic dose response relationships in aquatic biota. Data used in (a), (d), (h) and (i) were extracted from Ziajahromi et al. (2017), Yu and Chan (2020), Li et al. (2020) and Gambardella et al. (2018), respectively. The data in (b) and (c) were obtained from Yu et al. (2018). The data in (e), (f) and (g) were extracted from Liu et al. (2019). Hormesis was determined according to Agathokleous et al. (2019b) and Calabrese et al. (2019). The asterisk (*) indicated statistical difference ($p < 0.05$) between control and MP exposure groups in the original paper, and the pound (#) denoted the maximum hormetic response. Abbreviations: AChE, acetylcholinesterase; ACP, acid phosphatase; MDA, maleic dialdehyde; PO, phenoloxidase; SOD, superoxide dismutase.

Fig. 7. The dose response models of linear no-threshold model (a), threshold model (b) and hormetic model (c).

and numerous endpoints (Calabrese and Blain, 2011; Viebahn-Hänsler et al., 2012; Rattan et al., 2013; Vandenberg, 2014; Le Bourg, 2015; Mytych et al., 2016; Pennisi et al., 2017; Shibamoto and Nakamura, 2018; Calabrese et al., 2019; Campos et al., 2019; Santoro et al., 2020). The current study provided various evidence for the occurrence of hormetic dose response relationships in aquatic organisms exposed to

MPs (see Fig. 6 for examples). These dose response relationships (i.e. J-shaped or inverted U-shaped) highlighted the insufficiency of applying LNT/threshold model to predict the toxicity of MPs at low concentrations, while the hormetic model could provide more accurate prediction in the zone below the threshold (Calabrese, 2012). Therefore, MPs-induced hormesis needs to be considered in future MP toxicity

studies, and the hormetic model should be applied to the ecological/environmental risk assessment of MPs.

4. Conclusions

The present study provided substantial evidence for the onset of enhanced biological performance and reduced oxidative stress biomarkers in aquatic biota induced by MPs at environmentally relevant concentrations (≤ 1 mg/L, median = 0.1 mg/L). The extents of the stimulatory responses (131%–144% of the control) and inhibitory responses (65%–75% of the control) were typically generalizable, independent of measured endpoint, habitat, MP composition, morphology, particle size and exposure duration. However, the inhibitory response of oxidative stress biomarkers exhibited a significant concentration-dependent manner. In addition, various endpoints presented J-shaped or inverted U-shaped hormetic dose response relationships, highlighting that the hormetic model should be considered in the risk assessment of MPs.

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.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.envpol.2021.117206>.

Credit author contribution statement

Tao Sun: Methodology, Formal analysis, Writing – original draft. Junfei Zhan: Formal analysis., Fei Li: Writing – review & editing. Chengloung Ji: Writing – review & editing. Huifeng Wu: Supervision, Writing – review & editing, Project administration.

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