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Micro(nano)plastics as a vector of pharmaceuticals in aquatic ecosystem: Historical review and future trends

Andreza Martins de Souza[a,b], Andressa Liberal Santos[a], Danielle Silva Araújo[b], Rosana Rodrigues de Barros Magalhães[b], Thiago Lopes Rocha[a,*]

[a] Laboratory of Environmental Biotechnology and Ecotoxicology, Institute of Tropical Pathology and Public Health, Federal University of Goiás, Goiânia, Goiás, Brazil
[b] Faculdade Unida de Campinas, Goiânia, Goiás, Brazil

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ABSTRACT

Pharmaceuticals can be adsorbed by microplastics (MPs) and nanoplastics (NPs) in the aquatic environment. The interaction between these emerging pollutants can induce several effects on environmental and human health. Thus, the current study aimed to summarize and discuss the literature on the interactions and ecotoxicity of MP/NPs with pharmaceuticals in the aquatic environment. A scientometric and systematic review was conducted, and the data were summarized and discussed. The historical analysis indicated that the first article on the interactive effects between MP/NPs and pharmaceuticals was published in 2016. Scientific production is emerging in fourteen countries. Several types of MP/NPs (n = 13) and pharmaceuticals (n = 65) were studied, while the toxicity was evaluated in 30 articles (37.04 %). The interaction of MP/NPs with several pharmaceutical groups was confirmed, mainly antibiotics. In general, results confirmed the Trojan horse effects and indicated that MP/NPs changed the bioaccumulation and ecotoxicity of pharmaceuticals. The data reviewed demonstrated that future studies under environmentally relevant conditions are necessary for a better understanding of the mechanisms of action and toxicity of pharmaceuticals adsorbed to MP/NPs, especially mixtures with NPs. This study confirms that MP/NPs can alter the bioaccumulation and ecotoxicity of pharmaceuticals in aquatic organisms, indicating their potential toxicological risk.

1. Introduction

The rapid growth of the human population has been associated with the increase in the production and consumption of plastics in the world. The term plastic is used generically to designate synthetic and semi-synthetic polymeric material, commonly derived from petroleum, and which exhibits high molecular mass and plasticity (da Costa et al., 2016). The increasing production and use of plastics lead to the release of micro(nano)particles into aquatic ecosystems (Nguyen et al., 2019). Microplastics (MPs) are plastic particles with a dimension of 100 nm to

Abbreviations: 4MBC, 4- methyl benzylidene camphor; 5-FU, 5-fluorouracil; ABS, acrylonitrile butadiene tyrene; Abt, antibiotic; Acs, anticonvulsant; ACT, acetaminophenol; Adb, antidiabetic; Adp, antidepressant; Afg, antifungal; Aht, antihistamine; AML, amlodipine; AMP, ampicillin; AMT, amitriptyline; AMX, amoxicillin; Ang, analgesics; Anp, antineoplastics; Ans, anesthetic; Apl, antihyperlipidemic; ASA, acetylsalicylic acid; Ask, antismoking; Atf, anti-inflammatory; ATN, atenolol; ATR, atorvastatin; Ayp, antihypertensive; AZI, azithromycin; CBZ, carbamazepine; Cci, cyclooxygenase-2 inhibitors; CCP, cyclophosphamide; CFN, caffeine; CFX, cephalexin; CFZ, cefazolin; CLA, clarithromycin; CLO, chloramphenicol; CTC, chlortetracycline; CTL, citalopram; CTR, cetirizine; DCF, diclofenac; Drt, diuretic; DXC, doxycycline; EE2, 17α-ethinyl estradiol; ENR, enrofloxacin; EPps, persistent organic pollutantsemerging pollutants; ERT, arythromycin; ETR, etoricoxib; FCZ, fluconazole; FEN, fenbendazole; FLO, florfenicol; FLU, flubendazole; FRS, furosemide; FXT, fluoxetine; GFB, gemfibrozil; IBU, ibuprofen; KCZ, ketoconazole; LEV, levofloxacin; LSR, losartan; MET, methotrexate; MPs, microplastics; MTF, metformin; MTN, metronidazole; NAD, nadolol; NCT, nicotine; NIL, nylon; NOR, norfloxacin; NPs, nanoplastics; NPX, naproxen; OTC, oxytetracycline; PA, polyamide; PAC, paracetamol; PCN, procainamide; PE, polyethylene; PEPP, post-exposure predatory performance; PET, polyethylene terephthalate; PLA, polylactic acid; PMM, polymethyl methacrylate; POM, polyoxymethylene; POPs, persistent organic pollutantsemerging pollutants, PP, polypropylene; PCPs, personal care products; PRP, propranolol; PRX, paraxanthine; PS, polystyrene; PVC, polyvinyl chloride; ROX, roxithromycin; SDZ, sulfadiazine; SER, sertraline; SMR, sulfamerazine; SMX, sulfamethoxazole; STZ, sulfamethazine; SVT, simvastatin; TAM, tamoxifen; TC, tetracycline; TCS, triclosan; TIL, tylosin; TMP, trimethoprim; TRS, torasemide; USA, United States of America; VAC, vancomycin; VFX, venlafaxine; VSR, valsartan; WWTP, wastewater treatment plants.

* Corresponding author at: Universidade Federal de Goiás, Instituto de Patologia Tropical e Saúde Pública, Rua 235, Setor Universitário, Goiânia, Goiás, Brasil CEP: 74605050.

E-mail address: thiagorochabio20@ufg.br (T.L. Rocha).

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5 mm, while nanoplastics (NPs) have a diameter <100 nm (Ng et al., 2018; Thompson et al., 2009).

The plastic particles can be synthesized with micro or nano scale, being called primary MP/NPs. For example, primary MPs have been used as exfoliants in personal care products and NPs in facial cleansers stand out (Hernandez et al., 2017). Furthermore, these particles can originate from the degradation of larger plastics, called secondary MP/NPs, such as particles derived from car tires, agricultural plastic cover, fabric microfiber, plastic bags, and nets (Cole et al., 2011). Degradation of plastics can occur due to mechanical factors, biological, thermal and/or photo-oxidative degradation (Singh and Sharma, 2008).

MP/NPs are present in different environmental compartments (air, soil, and water) (González-Pleiter et al., 2020a; Zhang et al., 2020b), where they can interact with different contaminants and pollutants, such as metals (Brennecke et al., 2016), persistent organic pollutants (POPs) (Yu et al., 2019) and pharmaceuticals (Huang et al., 2021c). Thus, MP/NPs can act as vectors of pollutants or pathogens (Huang et al., 2021b; Rochman et al., 2013; Zettler et al., 2013; Zhang et al., 2020b).

In the aquatic environment, MP/NPs can interact with pharmaceuticals, which are considered emerging pollutants (EPs). Pharmaceuticals were detected in various environmental matrices, such as surface water, groundwater, wastewater treatment plants (WWTP), and even in polar regions (Fick et al., 2009; González-Alonso et al., 2017; Homem and Santos, 2011; Watkinson et al., 2009). Environmental pollution by pharmaceuticals can occur due to: (1) intense growth of the pharmaceutical industry; (2) lack of efficient methodologies for the removal, storage, and disposal of pharmaceutical waste; (3) human and veterinary drug use, often uncontrolled and used in fish farming; (4) environmental routes of pharmaceutical products and their persistent residues.

More than 600 pharmaceuticals have been detected in environmental matrices in 71 countries (aus der Beek et al., 2016). The main classes of pharmaceuticals identified in the aquatic environment were antibiotics, analgesics, and estrogens (aus der Beek et al., 2016). In addition to the effects of isolated pharmaceuticals on aquatic organisms (Nogueira et al., 2019), recent studies indicate that these pollutants can be adsorbed by MP/NPs, with adsorption varying according to the type of pharmaceuticals and plastic particles (Li et al., 2018b; Shen et al., 2018; Almeida et al., 2019; Feng et al., 2020; Zhou et al., 2020a; Barreto et al., 2021; Guo et al., 2021; Magri et al., 2021).

Although several studies indicate the interaction of MP/NPs with pharmaceuticals and personal care products (PCPs) (Qu et al., 2018; Zhang et al., 2019a; Feng et al., 2020; Xu et al., 2020; Zhou et al., 2020a), knowledge about their interactive effects and mixture toxicity to aquatic organisms is still scarce. Thus, the current study aimed to summarize and discuss the literature concerning the interactive effects and ecotoxicity of MP/NPs and pharmaceuticals in the aquatic environment. Furthermore, a scientometric and systematic review was conducted, and the data concerning the number of studies, geographical distribution, type of MP/NPs and pharmaceuticals, experimental conditions (concentrations, exposure time, and environmental factors), species, and ecotoxicological effects were summarized and discussed. In this sense, the hypothesis that MP/NPs alter the bioaccumulation and ecotoxicity of pharmaceuticals in aquatic organisms was tested. Besides, knowledge gaps were identified, as well as recommendations for future studies.

2. Methodology

The review was carried out in the “Web of Science”, “Science Direct”, “Scopus” and “PubMed” databases using the following keywords: “microplastics” or “nanoplastics” in combination with “pharmaceuticals” or “mixing toxicity” (Fig. 1). The survey was conducted until January 2022, encompassing articles from 2016 to 2021. Initially, 6491 articles were found. Experimental articles written in English, covering MP/NPs with pharmaceuticals in the aquatic environment were selected. Next, records, reviews, technical reports, protocols, non-English articles, and gray literature (academic abstracts and theses) were excluded. Thus, a total of 81 articles was selected and summarized according to the following parameters: (*i*) year of publication; (*ii*) geographical location (mailing address of the corresponding author); (*iii*) types of MP/NPs; (*iv*) types of pharmaceuticals; (*v*) environmental conditions; (*vi*) model organisms; (*viii*) bioaccumulation and toxicity; and (*ix*) interaction between MP/NPs and pharmaceuticals. Plastic particles were classified as MPs and NPs according to their diameter (MPs: 100 nm to 5 mm; NPs: <100 nm) (Ng et al., 2018; Thompson et al., 2009). The graphics were made using the Prism 8 GraphPad® software.

3. Results and discussion

3.1. Historical and geographical overview

The first study describing the interaction of MPs with pharmaceuticals was published in 2016 (Wu et al., 2016) (Fig. 2A). This study demonstrated the interaction of polyethylene (PE) MPs (250-280 μm) with pharmaceutical and PCPs, including carbamazepine (CBZ) of the antiepileptic class, 4-methyl benzylidene camphor (4MBC), triclosan (TCS) and 17α-ethinyl estradiol (EE2). The interaction was demonstrated through linear sorption coefficients, increasing salinity, and dissolved organic matter. The results showed that sorption was dependent on the hydrophobicity of the pharmaceutical or PCPs (Wu et al., 2016). Therefore, MPs can play an important role in the transport and fate of pharmaceuticals, especially hydrophobic ones (Wu et al., 2016). In the same year, the first ecotoxicological study was published (Fonte et al., 2016), which described the interactive effects of PE MPs (1-5 μm in diameter) and cephalexin (CFX), from the antibiotic class, for epibenthic and euryhaline fish *Pomatoschistus microps* juveniles. This interaction increased the toxicity of the CFX and decreased predatory performance; also, the increased temperature elevated the toxic effects of the mixture. After 2018, there was a rapid development of research when 28.85% of articles were published. This growth may be due to the increasing interest in the environment and discussions present in various sectors, including governmental ones. In 2021, there was a significant increase in the number of articles, representing 49.40% of all publications concerning the interaction of MP/NPs with drugs in the aquatic environment (Fig. 2A), confirming that this topic is recent in the scientific literature.

Studies concerning the interactive effects of MP/NPs and pharmaceuticals were conducted in fourteen countries (Fig. 2B). China stands out (n = 51; 62.96 % of the studies), following by Spain (n = 7; 8.64 %), Portugal (n = 6; 7.41 %), USA (n = 5; 6.17 %), Germany (n = 4; 4.94 %), Greece, Italy, Japan, Poland, Republic of Korea, Singapore, Sri Lanka, Taiwan and Tunisia (n = 1 each; 1.23 % each). These data confirm that China lead the ranking in the number of world publications of scientific articles (NATIONAL SCIENCE BOARD, 2019). The revised data showed that only one country (USA) is from the American and Africa (Tunisia) continent (n = 1 each; 7.14 % each), 6 countries (China, Japan, Republic of Korea, Singapore, Sri Lanka and Taiwan) are from Asia (n = 6; 42.86 %), and 6 (Germany, Greece, Italy, Poland, Portugal, and Spain) from Europe (n = 6; 42.86 %), indicating that future studies on the interactive effects of MP/NPs with pharmaceuticals are needed in countries in the Global South, such as Brazil, countries of the Oceania, among others (Fig. 2B).

3.2. Types of MPs/NPs

Reviewed data showed that 11 types of MPs and 2 types of NPs were evaluated for their interaction with pharmaceuticals (Fig. 3A). The most studied type of MP was polystyrene (PS) (n = 37, 28.03 %), followed by PE (n = 36; 27.27 %), polyvinyl chloride (PVC) MPs (n = 22; 16.67 %), polypropylene (PP) (n = 14; 10.11 %), polyethylene terephthalate (PET) (n = 9; 6.82 %), polylactic acid (PLA) (n = 5; 3.79 %), nylon (NIL) and polyamide (PA) (n = 2 each; 1.52 % each), acrylonitrile butadiene styrene (ABS), polymethyl methacrylate (PMMA), and polyoxymethylene (POM) (n = 1; 0.76 %). However, 2 articles (1.51 %) did not spec-

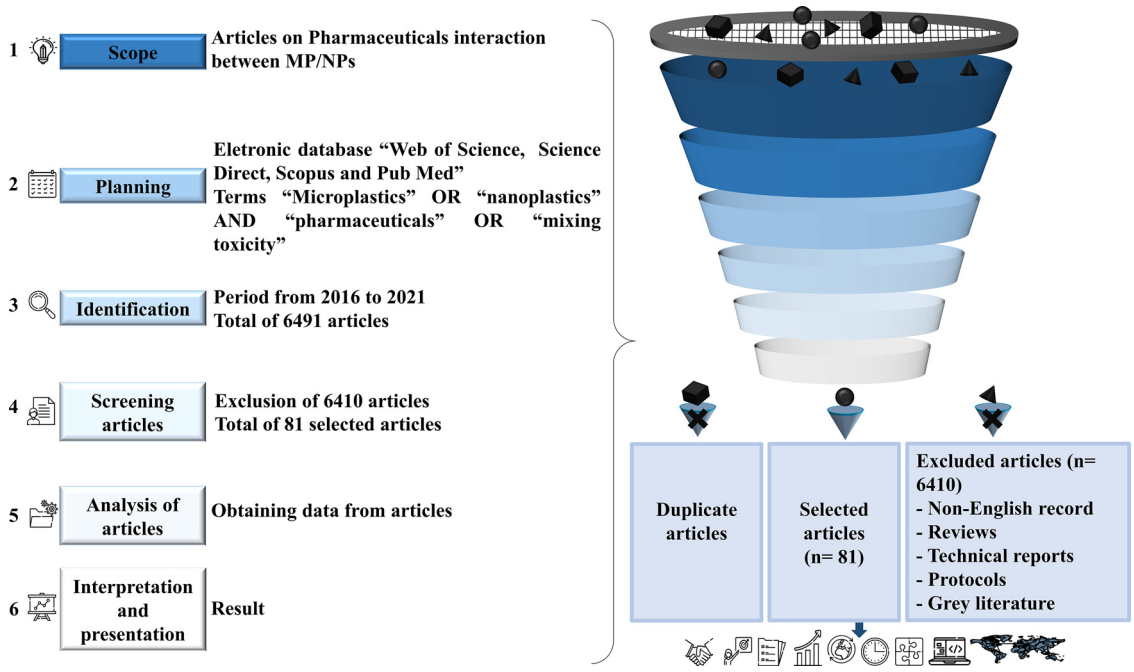

Fig. 1. Systematic review methodology.

ify which composition of MPs was used. Furthermore, only PS (92.86 %) and PET (7.14 %) NPs were studied by 13 and 1 articles, respectively, indicating the need to study the interaction of pharmaceuticals with other types of NPs. Similar research trends with isolated MPs were reported by de Sá et al. (2018), which showed that the types of MPs most commonly reported across field and laboratory studies include PE, PS, PP, and PES MPs. Furthermore, these MPs are widely used and used around the world (Chen et al., 2021; Zheng and Suh, 2019).

The type of MP/NPs as well as their size and chemical characteristics was shown to interfere with the adsorption of pharmaceuticals and the toxicity to aquatic organisms (González-Pleiter et al., 2020b; Shi et al., 2020). They may have different effects due to their different chemical compositions (Lee et al., 2021). The different chemical chains of each type of MP/NPs can interfere in the type of chemical bond, in the strength of this bond, and consequently in the adsorption of pharmaceuticals (Lee et al., 2021). Therefore, it is necessary to describe and study these chemical interactions between the pollutants.

3.3. Types of pharmaceuticals

In total, 65 different pharmaceuticals were studied (Table 1), which belong to 15 different pharmacological classes (Fig. 3B), mainly antibiotics (n = 26; 40 %), antihypertensives (n = 6; 9.23 %); antidepressants (n = 5; 7.69 %); analgesics, antifungals, antihyperlipidemic and antineoplastics (n = 4 each; 6.15 % each); anti-inflammatory (n = 3; 4.61 %); anesthetic and diuretics (n = 2; 2.08 %); anticonvulsant, antidiabetic, antihistamine, anti-smoking and cyclooxygenase inhibitors (n = 1 each; 1.54 %). On the other hand, further studies with the pharmaceuticals acebutolol (anti-hypertensive), salbutamol (bronchodilator), alprazolam (benzodiazepine), budesonide (antiallergic), bupropion (antidepressant), cimetidine (antihistamine), clonazepam (benzodiazepine), clofibric acid (lipid lowering drugs metabolite), clopidogrel (antiplatelet drugs), diazepam (benzodiazepine), diltiazem (antihypertensive) among others are needed, since that they are the most used pharmaceutical products (Patel et al., 2019).

The pharmaceutical product tetracycline (TC) (antibiotic) was the most studied (n = 19), followed by ciprofloxacin (CIP) and sulfamethoxazole (SMX) (antibiotic; n = 9 each). The class of antibiotics and their metabolites pose a potential risk to the environment, as together with MP/NPs they can cause toxicity to microorganisms, leading to microbial resistance (Santos et al., 2022; Sharma et al., 2021). With adsorption on MP/NPs, antibiotics can be carried over long distances and can cause toxic effects throughout the environment (Feng et al., 2020; You et al., 2021). The type of pharmaceutical product also influences the effects it may have on aquatic organisms (Bhagat et al., 2021; Hanslik et al., 2021). Therefore, it is essential to monitor and study for better understanding and remediation of the problems caused by pharmaceuticals in the aquatic environment.

3.4. Experimental conditions

Revised data showed that the interaction of MP/NPs with pharmaceuticals depends on experimental design and environmental conditions, such as pH, temperature, exposure time, aging factors, hydrophobicity, salinity, type of bond, among others. Besides, an increase in adsorption can occur according to the increase in salinity, or vice versa depending on the case. As demonstrated, PS NPs (80.05; 79.96 and 86.05 nm) (500 mg/L) with TC (3 - 30 mg/L), an antibiotic, had increased sorption capacity with increased salinity (0 - 35 practical salinity units) (Feng et al., 2020; Wang et al., 2020b). Aged MPs, in general, showed a higher level of sorption, due to their larger surface area created from their irregular shape, with greater quantity and depth of pores.

The interaction of MP/NPs with pharmaceuticals was analyzed in a natural environment or in laboratory conditions (Table 2). The ecotoxicity was studied by *in vitro* (6.67 %) or *in vivo* tests (93.33 %) (Almeida et al., 2019; Zhang et al., 2019a; Zhang et al., 2019b). For example, increasing temperature improved the synergistic effects of MP/NPs and pharmaceuticals, as reported for CFX (antibiotic class) and PE MPs (1-5 μm) in *P. microps* (Fonte et al., 2016). After 96 h of exposure to CFX (1.3-10 mg/L) with MPs (0.184 mg/L) at 20 and 25°C, it can be observed that there was an increase in mortality at the highest temperature, in addition to an increase in the toxicity curve for fish relative to the post-exposure predatory performance (PEPP) (Fonte et al., 2016). Furthermore, aged MPs can increase the biochemical response (i.e., acetylcholinesterase - AChE) in *Oreochromis niloticus* after 14 days of exposure (Huang et al., 2021c).

As for the ecotoxicological studies, the concentrations of MP/NPs ranged from 0.001 - 600 mg/L (Zhang et al., 2019a; Zhang et al., 2019b).

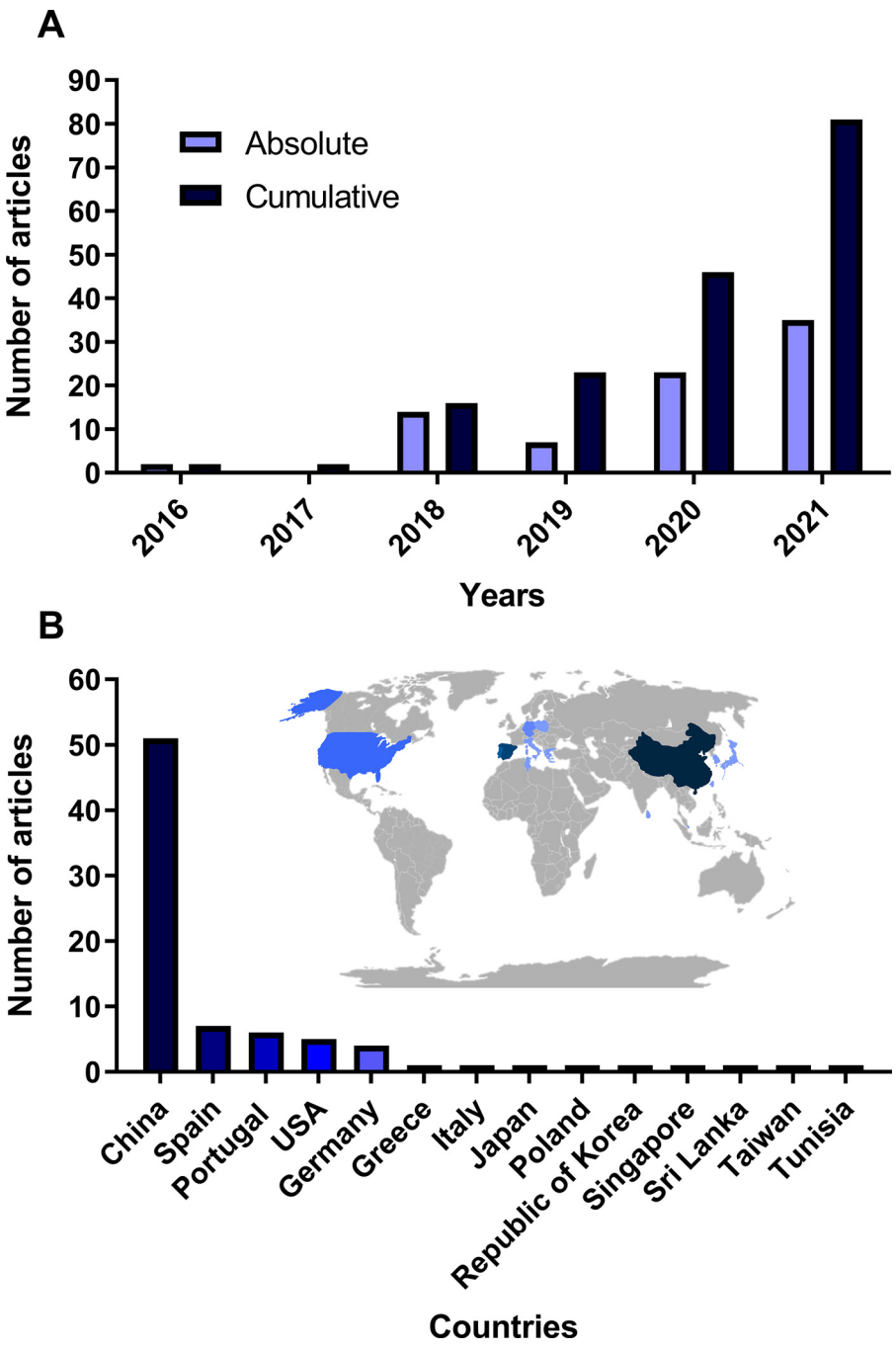

Fig. 2. Absolute and cumulative number of articles per year (A). Number of articles per country (B).

For the PS NPs the range of concentrations was 0.005 - 200 mg/L. For the PS MPs the range was 0.001 - 600 mg/L, and the PE MPs had a concentration of 0.184 mg/L. Environmental concentrations for MP/NPs range from almost zero to more than 1 million particles per m^3 in aquatic environments (Li et al., 2018a; Lu et al., 2021), and commonly detected concentrations in the ng/L range. About pharmaceuticals concentrations in the ecotoxicological studies, they also varied widely from 0.0063 to 1000 mg/L. With TC ranging from 3 - 300 mg/L and SMX had a concentration of 0.05 mg/L, for example. Pharmaceutical concentrations in aquatic systems are constantly detected in the µg/L range. Therefore, one must take into consideration the environmentally relevant concentrations of each pharmaceutical, exposure methods (static, semi-static, or continuous flow), exposure period (i.e., acute or chronic), and whether the model organism is a suitable monitor for the investigation.

3.5. Model organisms, bioaccumulation, and toxicity

The toxic effects of MP/NPs with pharmaceuticals were investigated in 30 papers, with 21 different organisms (Fig. 4). Studies were conducted with 10 freshwater organisms, these being: *Danio rerio* (zebrafish) (14.29 %), *Corbicula fluminea* (clam) (9.52 %), *Daphnia magna* (crustacean) (9.52 %), *O. niloticus* (red tilapia fish) (9.52 %), *Anabaena* sp. (cyanobacteria) (4.76 %), *Chorella pyrenoidosa* (algae) (4.76 %), *Cyprinus carpio* (fish common carp) (4.76 %), *Misgurnus anguillicaudatus* (fish) (4.76 %), *Salmo trutta f. Fario* (fish) (4.76 %) and *Synechocystis* (cyanobacteria) (4.76 %). Therefore, 9 marine organisms were studied, these being: *Tegillarca granosa* (clam) (14.29 %), *Mytilus galloprovincialis* (mussel) (9.52 %), *Skeletonema costatum* (diatom) (9.52 %), *Vibrio fischeri* (bacterium) (9.52 %), *Artemia salina* (crustacean) (4.76 %), *Mytilus coruscus* (clam) (4.76 %), nematodes (4.76 %), *P. microps* (fish) (4.76 %),

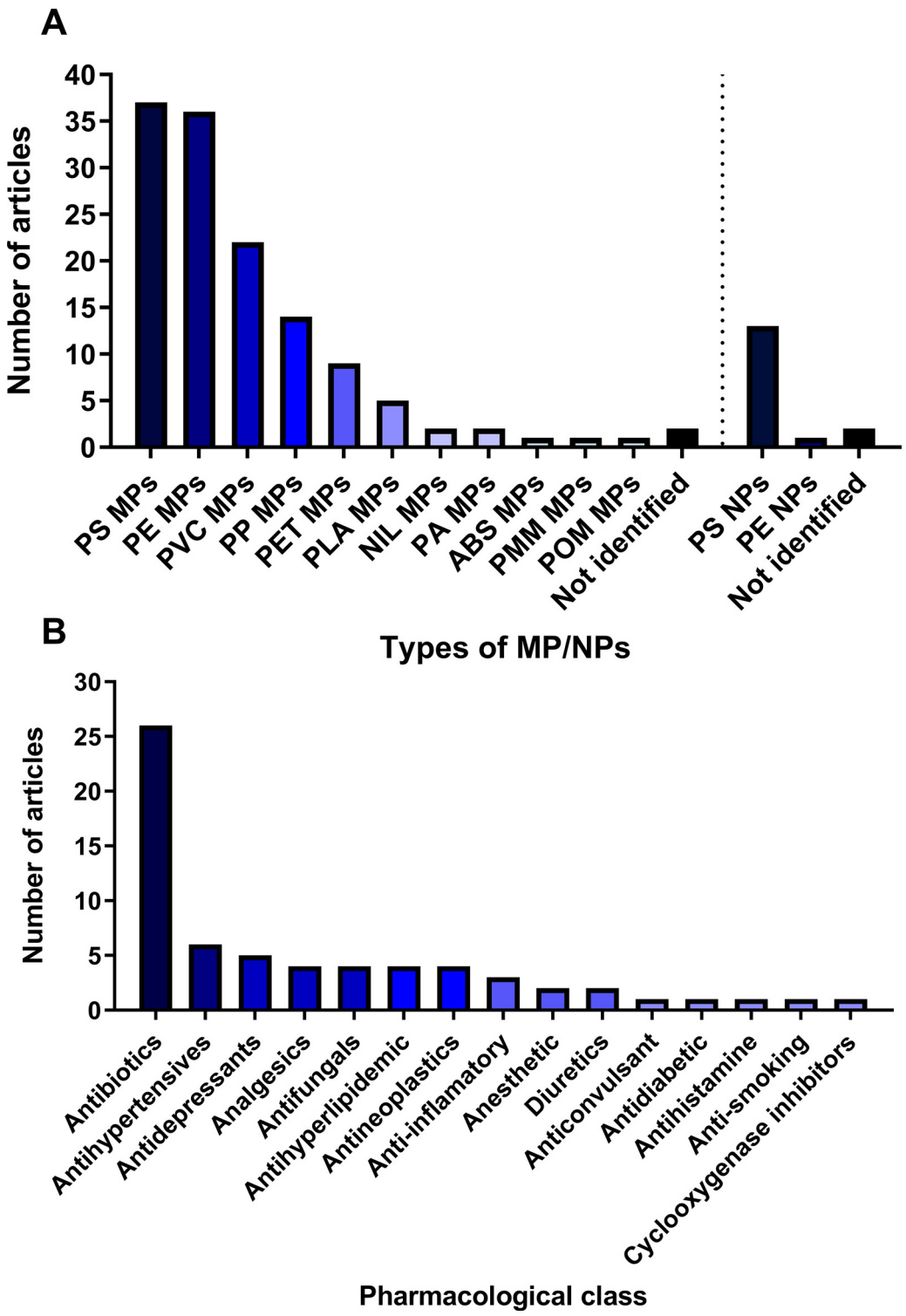

Fig. 3. Number of articles according to type of microplastics (MPs) and nanoplastics (NPs) (A). Pharmacological class with respect to the number of drugs (B).

and *Tetraselmis chii* (microalgae) (4.76 %). In addition, two cell lines (DLB-1 and SAF-1; 4.76 % each) derived from marine fish were also used.

The most studied species were *D. rerio* and *T. granosa* (n = 3 each; 14.29%). *D. rerio* is a teleost fish originally from Asia, of the *Cyprinidae* family. It has been widely used in ecotoxicological research due to its great genetic advantages and applicability of the 10Rs ethical principles in research (Canedo et al., 2022; Pereira et al., 2019). *T. granosa* is a marine bivalve of the *Arcidae* family, found mainly in the Indo-Pacific region (Rosani et al., 2021). We can observe that more studies with different model organisms and standardization of organisms are needed for comparable results of different MP/NPs and pharmaceuticals.

There was one *in vitro* study, using two fish cell lines, being SAF-1 (ECACC-00122301; derived from *Sparus aurata L.*, known as sea bream)

Table 1
Number of studies according to pharmaceuticals.

Pharmaceuticals	Number of studies	Relative frequency (%)
Tetracycline	19	12.58
Ciprofloxacin	9	5.96
Sulfamethoxazole	9	5.96
Carbamazepine	7	4.64
Oxytetracycline	6	3.97
Diclofenac	5	3.31
Ibuprofen	5	3.31
Atorvastatin	4	2.65
Florfenicol	4	2.65
Propranolol	4	2.65
Tylosin	4	2.65
Amlodipine	3	1.99
Amoxicillin	3	1.99
Atenolol	3	1.99
Cephalexin	3	1.99
Norfloxacin	3	1.99
Simvastatin	3	1.99
Ampicilin	2	1.99
Chortetracycline	2	1.99
Erythromycin	2	1.99
Gemfibrozil	2	1.99
Levofloxacin	2	1.99
Nicotine	2	1.99
Paracetamol	2	1.99
Roxithromycin	2	1.99
Sertraline	2	1.99
Trimetoprim	2	1.99
Venlafaxine	2	1.99
Acetamidophenol	1	0.66
Acetyl salicylic acid	1	0.66
Amitriptyline	1	0.66
Azythromycin	1	0.66
Caffeine	1	0.66
Cefazolin	1	0.66
Cetirizine	1	0.66
Citalopram	1	0.66
Clarithromycin	1	0.66
Chloramphenicol	1	0.66
Cyclophosphamide	1	0.66
Doxycycline	1	0.66
Enrofloxacin	1	0.66
Etoricoxib	1	0.66
Fluconazole	1	0.66
Fluoxetine	1	0.66
Furosemide	1	0.66
Ketoconazole	1	0.66
Lidocaine	1	0.66
Losartan	1	0.66
Metformin	1	0.66
Metronidazole	1	0.66
Naproxen	1	0.66
Paraxanthine	1	0.66
Procainamide	1	0.66
Sulfadiazine	1	0.66
Sulfamerazine	1	0.66
Sulfamethazine	1	0.66
Tamoxifen	1	0.66
Torasemide	1	0.66
Valsartan	1	0.66
Vancomycin	1	0.66

from the caudal fin, and DLB-1 (Neuronal line from *Dicentrarchus labrax L.*, known as European sea bass). This study demonstrated that FXT (Antidepressant) and PRP (Antihypertensive) (pharmaceutical concentration: 2.56 10^{-6} – 1 g/L) among other pharmaceuticals, associated with 100 nm PS NPs (0.001-10 mg/L) were the most toxic drugs for both cell lines, due to the decreased viability curve and LD_{50} after exposure for 24 h (Almeida et al., 2019). We can take into account that there was a suppression of genes encoding GST, UGT, MRP2, CYP1A2, and CYP2U1, which are responsible for detoxification in *T. granosa* after exposure during 4 weeks, of PS MPs (500 nm; 0.26 mg/L) with the pharmaceutical OTC and FLO (both antibiotics, at concentrations of 270 and 42 ng/L, respectively) (Zhou et al., 2020b). There was also altered expression of genes associated with gill biotransformation and immune function in *M. galloprovincialis* following 96h exposure to MP PS (0.05 mg/L, mean diameter 110 ± 6.9 nm) associated with CBZ (Antiepileptic) at 6.3 µg/L. For example, CYP 32 (biotransformation gene) mRNA levels were downregulated in the gills, and the transcriptional levels of GST and p53 (detoxification and DNA repair gene, respectively) decreased, indicating a decrease in phase II biotransformation processes, and impairment of the DNA damage repair capacity (Brandts et al., 2018).

The bioaccumulation of pharmaceuticals, such as VFX (antidepressant, at 0.5 mg/L) was observed in the liver of *M. anguillicaudatus* through the "Trojan horse" effect of PVC MPs (1 - 10 µm, at 1 - 50 m/L), as well as the bioaccumulation factor increased 10-fold in the presence of PVC MPs after 90 - day exposure (Qu et al., 2018). Furthermore, MPs increased the bioaccumulation of ROX (antibiotic) in the gut, gills, brain, and liver of red tilapia (Huang et al., 2021c; Zhang et al., 2019b). Furthermore, co-exposure of MPs associated with TC leads to increased bioaccumulation in the tissues of *E. crypticus* (Ma et al., 2020; W. Zhou et al., 2020).

Shi et al. (2020) analyzed the immunotoxicity of the PS NPs (500 nm; 0.29 mg/L) and the antidepressant class SER (100 ng/L) in the clam *T. granosa* after 14 days of co-exposure. Results showed that the co-exposure increase the immunotoxicity of the SER by inducing hemocyte apoptosis, reducing total hemocyte count, restricting energy availability for phagocytosis, and hindering detoxification of SER in the clam (Shi et al., 2020). In addition, PS NPs also supported the idea of a "Trojan horse" by acting as drug carriers and increasing their toxicity (Almeida et al., 2019).

3.6. Interactions and effects between MP/NPs and pharmaceuticals in the aquatic environment

It has already been noted that PS and PE MP/NPs, in general, showed high sorption; PE adsorbed even nonsteroidal anti-inflammatory drugs (NSAIDs), which have low adsorption under environmentally relevant conditions (Table 3) (Elizalde-Velázquez et al., 2020; Wang et al., 2020). PA MPs showed high adsorption of antibiotics (Li et al., 2018b). MPs associated with pharmaceuticals may increase the adverse effects on living organisms of both contaminants, that is, they had synergistic action (Prata et al., 2018; Qu et al., 2018).

The antibiotics AZI and CLA showed sorption on PET, PLA, POM, and PS MPs (1 g of MPs incubated in 20 mL of Milli-Q water, together with 100 – 10000 mg/L of AZI and CIP during 0 – 6 h). AZI showed a higher proportion of sorption (sorption concentrations of AZI: 0.00178 ± 0.00078 and 0.00270 ± 0.00018 mg/g; sorption concentrations of CLA: 0.00487 ± 0.00018 mg/g) because it is more hydrophobic. Both antibiotics were desorbed in contact with water and the joint exposure showed higher toxicity for *Anabaena* sp. Thus, MPs can be vectors of antibiotics in aquatic systems, affecting the trophic level of microorganisms (González-Pleiter et al., 2020b). Regarding SMX, it can be highlighted that it underwent irreversible sorption to PE MPs (45-48 µm) after 96h of mixing. Again, the sorption was dependent on the hydrophobicity of the pharmaceutical and also, on electrostatic interactions (Razanajatovo et al., 2018).

On the other hand, PRP showed higher toxicity when exposed to PS NPs (100 nm), for 24h. The LC_{50} was altered in the combined exposure, being more toxic towards fish cells, of the DLB-1 and SAF-1 lineages. PRP with PS NPs demonstrated the ability to alter enzymatic activities, suggesting that they may compromise cellular responses to other stressors (Almeida et al., 2019). AMP, from the antidepressant class, affected the development of *Salmo trutta f. fario* by increasing cholinesterase activity and inhibiting two carboxylesterases. The two carboxylesterases are involved in the detoxification of pollutants and are presumed to act by protecting against acetylcholinesterase inhibiting pesticides. And there was an alteration in the swimming and resting behavior of trout; however the effects of AMP were not modulated by MPs

Table 2
Interaction of microplastics (MPs) and nanoplastics (NPs) with pharmaceuticals in aquatic organisms.

Types of MP/NPs	Characterization of MP/NPs	Pharmaceuticals	Experiment and model organism	Concentrations	Main effects	References
PE MPs	Fluorescent red microspheres, 1-5 μm in diameter	Antibiotic (Abt): CFX	Laboratory. Model: *Pomatoschistus microps*	MPs: 0.184 mg/L and CFX: 1 - 10 mg/L	At 20°C MPs + CFX ↓ Post-Exposure Predatory Performance (PPPE). At 25°C ↑ CFX toxicity curves. The ↑ of temperature is toxicity	Fonte et al. (2016)
MPs	Fluorescent red polymer microspheres 1-5 μm in diameter	Abt: florfenicol (FLO)	Laboratory. Model: *Corbicula fluminea*	FLO of 1.8 - 7.1 mg/L and MPs of 0.2 - 0.7 mg/L	Inhibition of feeding (57-83%), significant inhibition of ChE (44-57%) and ↑ of the antioxidant enzymes. *C. fluminea* absorbs MPs and FLO from water and accumulates or at least retains it in your body	Guilhermino et al. (2018)
MPs	Fluorescent red polymer microspheres, 1-5 μm in diameter	Anesthetic (Ans) = procainamide (PCN). Abt = Doxycycline (DXC)	Laboratory. Model: *Tetraselmis chiii*	MPs: 0.75 - 48 mg/L; co-exposure with 1.5 mg/L pharmaceuticals. PCN: 4 - 256 mg/L. DXC: 4 - 128 mg/L	Co-exposure of MPs + drugs ↑ toxicity	Prata et al. (2018)
PVC MPs	<10 μm in diameter	Antidepressant (Adp): venlafaxine (VFX)	Laboratory. Model: *Misgurnus anguillicaudatus*	Sorption: 50 - 500 mg/L of MPs in 100 mL vials, 500 μg/L of VFX were added. Oxidative stress tests: VFX from 0 - 500 μg/ together with 50 mg/L MPs. Bioaccumulation: 50 mg/L of fluorescent MPs. Exposure and bioaccumulation: VFX 500 μg/L with 50 mg/L of MPs	↑ adverse effects. [] of VFX ↓ in water with MPs. Bioaccumulation of contaminants in the liver through MP. Bioaccumulation factor ↑ 10X in the presence of MPs	Qu et al., (2018)
PS NPs	Diameter of 110 ± 6.9 nm	Anticonvulsant (Acs): CBZ	Laboratory. Model: *Mytilus galloprovincialis*	0.05 mg/L PS combined with 6.3 μg/L CBZ	↑ mRNA in digestive glands and gills. Co-exposure induced significant ↓ regulation in gene expression. Hemocyte genotoxicity	Brandts et al. (2018)
NPs NPs	0.1 μm green fluorescent microspheres	Abt: roxithromycin (ROX)	Laboratory. Model: *Oreochromis niloticus*	ROX alone and with MPs: 50 μg/L. MPs: 1 - 100 μg/L	MPs ↑ ROX bioaccumulation in tilapia intestine, gills, brain and liver. ↓ Neurotoxicity with ROX + MPs. CIP450 activities after exposure to ROX + MPs	Zhang et al. (2019b)
PS NPs		Antihyperlipidemic (Apl): Gemfibrozil (GFB). Antihypertensive (Ayp): propranolol (PRP). Diuretic (Drt): furosemide (FRS). Adp: fluoxetine (FXT). Antidiabetic (Adb): metformin (MTF). Antismoking (Ask): nicotine (NCT). Analgesics (Ang): paracetamol (PAC) and acetylsalicylic acid (ASA)	Laboratory. Fish cells	NPs 10 mg/L; pharmaceuticals $2.56 .10^{-6}$ up to 1 g/L (↑ 5X)	Alters pharmaceutical toxicity, LD50 ↑	Almeida et al. (2019)

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Table 2 (*continued*)

Types of MP/NPs	Characterization of MP/NPs	Pharmaceuticals	Experiment and model organism	Concentrations	Main effects	References
PS MPs	1 and 10 μm	Abt: ROX	Laboratory. Model: *Daphnia magna*	Acute toxicity: 0.1 - 150 mg/L of ROX; 0.1 - 600 mg/L PS 1 μm; and 0.005 - 40 mg/L PS 10 μm. Sublethal toxicity: 0.01 mg/L ROX, PS 1 and 10 μm	ROX, MPS PS ↑ acute toxicity. LC_{50} of 22.03 (ROX), 87.83 (MPs PS 1 μm) and 291.69 mg/L (MPs PS 10 μm). EC50 of 20.28 (ROX), 66.97 (MPs PS 1 μm) and 199.94 mg/L (MPs PS 10 μm). ROX and MPs ↑ oxidative stress	Zhang et al. (2019a)
PS MPs	<50 μm, irregular shape	Adp: amitriptyline (AMT)	Laboratory. Model: *Salmo trutta f. Fario*	1st experiment: 100 - 105 particles/L. 2nd experiment: 105 - 106 particles/L. (for AMT or blends)	AMT had a significant effect on development, ↑ cholinesterase activity and ↓ carboxylesterase. Altered swimming and resting behavior. Effects not modulated by MPs	Schmieg et al. (2020)
PS MPs	500 nm	Abt: oxytetracycline (OTC) and FLO	Laboratory and field. Model: *Tegillarca granosa*	270 ng/L OTC, 42 ng/L FLO and 0.26 mg/L MPs	↑ Bioaccumulation due to Co exposure. GST activity and expression of suppressed detox genes	Shi et al. (2020)
PET, PLA, POM and PS MPs		Abt: azithromycin (AZI) and clarithromycin (CLA)	Laboratory. Model: *Anabaena sp*	Sorption kinetics: MPs (1 g in 20 mL) loaded with 500 mg/L of AZI or 1000 mg/L of CLA. Sorption analysis: CLA 100 - 10000 mg/L and AZI 100 - 10000 mg/L	All antibiotics were siphoned into all MPs. AZI (↑ hydrophobic) had ↑ adsorption. Both antibiotics were desorbed from the MPs	González-Pleiter et al. (2020b)
PS MP/NPs	500 nm and 30 μm microspheres	Adp: sertraline (SER)	Laboratory. Model: *Tegillarca granosa*	MPs 0.29 mg/L; BE 100 ng/L	NPs and MPs + SER inhibited *T. granosa* immune responses. NPs ↑ SER immunotoxicity, as it induces apoptosis of hemocytes and THC, restricts energy availability for phagocytosis, and hinders SER detoxification	Shi et al. (2020)
PS NPs	Fluorescent red with 600 nm	Anti-inflammatory (Atf): ibuprofen (IBU)	Laboratory. Model: *Chlorella pyrenoidosa*	Growth inhibition: 1 mg/L of NPs and 5 - 100 mg/L of IBU. Accumulation and degradation: 0.5 mg/L rac-/R-/S-IBU; 1 mg/L of NPs	Inhibitory effect of IBU on growth was ↓ in the presence of NPs. Co-exposure ↑ T-AOC and ↓ ERROR and MDA. Treatment with NPs ↓ bioaccumulation and accelerated biodegradation of the IBU and ↑ removal from the medium. Enantioselective toxicity, bioaccumulation and biodegradation of IBU was observed both in the absence and in the presence of NPs	Wang et al. (2020a)
PS, PS-SO3H, PS-NH2 NPs	PS-SO3H 80.05 nm; PS 79.69 nm; PS-NH2 86.05 nm.	Abt: TC	Laboratory. Model: *Skeletonema costatum*	Sorption isotherms: 500 mg/L of NPs PS; and 3 - 30 mg/L of TC. Aggregation of NPs: 100 mg/L of NPs PS. Water toxicity for: 200, 200 and 20 mg/L for PS, PS-SO3H and PS-NH2; and TC same [] of its saturated sorption for the NPs, calculated by the Langmuir model	↑ adsorption with ↑ of salinity	Feng et al. (2020)

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Table 2 (*continued*)

Types of MP/NPs	Characterization of MP/NPs	Pharmaceuticals	Experiment and model organism	Concentrations	Main effects	References
PLA and PVC MPs	Virgin and aged PLA, virgin PVC	Abt: TC and CIP	Laboratory. Model: *Skeletonema. costatum*	Absorption: 20 mg of MPs and 50 ml of antibiotic in 100 ml. Adsorption isotherms: 0.5 - 10 mg/L (Abt), 20 mg MPs in 50 mL of antibiotic solution in 100 mL	Both original and aged PLA showed better vectorial effects for antibiotics than PVC. The aging factor is the adsorption capacity on PLA 1.18 - 2.19 times. The amount of desorption of antibiotics in MPs in the simulated intestinal fluid was ↑ that in Milli-Q water. The desorption capacity of antibiotics with PLA was better than that of PVC, which proved that the potential negative impact of PLA in the aquatic environment and organisms could be more severe	Fan et al. (2021a)
PS MPs	Green fluorescent microspheres, dry powder with a size of 5 μm	Abt: SMX. Ayp: PRP	Laboratory. Model: *Oreochromis niloticusas*	Virgin or aged MPs: 10 μg/L; PRP or SMX: 50 μg/L	↑ [] of PRP in brain tissues combined with aged MPs. Aged MPs ↑ biochemical response under. Aged MPs + PRP ↓ neurotoxicity. Aged MPs + SMX = stress	Huang et al. (2021c)
PS MPs	500 nm	Abt: OTC and FLO	Laboratory. Model: *T. granosa*	MPs: 0,26 mg/L. OTC: 270 ng/L. FLO: 42 ng/L	↑ inducing ROS production, lipid peroxidation, DNA damage and increased by the copresence of MPs. ↓ in lectin content in serum, hemocyte viability	Zhou et al. (2021)
PS NPs	100 nm	Abt: sulfamethazine (STZ)	Laboratory. Model: *Oryzias melastigma*	STZ: 0,5 – 5 mg/g. PS: 5 mg/g	The presence of PS might alleviate the intestinal toxicity of STZ in a scenario of dietary co-exposure	Zhang et al. (2021c)
PE, PS, PP, PVC MPs		Antihistamine (Aht): Cetirizine (CTR). Adp: citalopram (CTL). Atf: diclofenac (DCF) etc	Laboratory. Model: *Danio rerio*	MPs: 5 – 100 mg/L	MPs most likely do not transfer elevated amounts of environmental pollutants to biota	Hanslik et al. (2021)
PS NPs	50 nm. Hydrodynamic diameter: 57 ± 4 nm	Antifungal (Afg): ketoconazole (KCZ), fluconazole (FCZ)	Laboratory. Model: *Danio rerio*	PS NPs, KCZ, FCZ: 1 mg/L	↑ malformation rate, CAT activity, ROS, LPO. ↓ hatching rate, survival rate, heart rate	Bhagat et al. (2021)
MPs		Atf: DCF. Cyclooxygenase-2 inhibitors (Cci): Etoricoxib (ETR)	Laboratory. Model: *M. galloprovincialis*	10 μg/L	MPs worked as a vector for the accumulatio of the pharmaceuticals	Álvarez-Ruiz et al. (2021)

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Table 2 (*continued*)

Types of MP/NPs	Characterization of MP/NPs	Pharmaceuticals	Experiment and model organism	Concentrations	Main effects	References
PE white microbeads (W) and fluorescent blue microbeads (FB) MPs	250 - 300 μm	Atf: IBU	Laboratory. Model: *Vibrio fischeri*	MPs: 0.4 mg/L; IBU: 15 nM	MPs exhibited a potential role as contaminant vectors	Martín et al. (2021)
PS MPs	500 nm	Abt: OTC, FLO, SMX	Laboratory. Model: *Mytilus coruscus*	OTC: 270 ng/L. FLO: 42 ng/L. SMX: 140 ng/L. PS: 0.26 mg/L	↑ synergistic immunotoxicity, intracellular ROS. ↓ cytoskeleton, cell viability of hemocytes, cytoskeleton and immune related genes. MPs ↑ biacumulation	Han et al. (2021)
PS MP/NPs	80 nm and 6 μm	Abt: CIP	Laboratory. Model: *C. fluminea*	MP/NPs: 10 μg/g. CIP: 0.409 – 7.81 μg/g.	MP/NPs ↓ CIP toxicity because it is less bioavailable	Guo et al. (2021)
PVC MPs		Acs: CBZ. Apl: simvastatin (SVT)	Laborator. Model: *Artemia salina*	PVC: 0.26 mg/dm^3. SVT: 5.80 – 12.03 mg/dm^3. CBZ: 52.08 mg/dm^3	LC_{50} SVT + PVC = 10.29 mg/dm^3. LC_{50} CBZ + PVC = 46.50 mg/dm^3	Albendín et al. (2021)
PS NPs	60 nm	Apl: SVT	Laboratory. Model: *D. rerio*	PS: 0 – 150 μg/L. SVT: 0 – 150 μg/L	↑ mortality, hatching and heartbeat	Barreto et al. (2021)
PVC MPs	>40 μm	Apl: Atorvastatin (ATR) and SVT	Laboratory. Model: nematodes	ATR and SVT: 0.6 – 6 mg/Kg. PVC: 20 mg/Kg	↓ abundance of the species. ↑ toxicity	Allouche et al. (2021)
PE, PVC and PET MPs	PE: 475.8 μm. PVC: 159.3 μm. PET: 172.7 μm	Ayp: Atenolol (ATN)	Laboratory. Model: *D. magna* and *V. fischeri*	Toxicity: ATN 0.5 – 0.06 mg/L and PVC 0.05 g/L. Ozonation: ATN 100 mg/L and MPs 0.05 – 0.50 g. Adsorption: ATN 0.1 – 4 mg/L and MPs 0.05 – 0.50 g	↑ ATN removal in the presence of MPs. PVC ↑ adsorption. MPs adsorbed ATN cannot affect acute toxicity	Lee et al. (2021)
PS MPs	5 μm	Abt: TC	Laboratory. Model: *Cyprinus carpio*	TC: 1 μg/L. PS: 700 μg/L	↓ oxidative damage	Zhang et al. (2021a)
PS MP/NPs	MPs: 0.5, 5 and 50 μm. NPs: 0.05 μm	Abt: CIP	Laboratory. Model: *Synechocystis*	MP/NPs: 5 - 100 mg/L. CIP: 40 μg/L	CIP + MP/NPs = antagonistic effect	You et al. (2021)

Table 3
Interaction of microplastics (MPs) and nanoplastics (NPs) with pharmaceuticals.

Types of MP/NPs	Characterization of MP/NPs	Pharmaceuticals	Concentrations	Interactions	References
PE MPs	Pellets 250 - 280 μm	Acs: CBZ	Kinetics: 10 - 50 mg MPs in 60 mL vials filled with 50 mL; and CBZ at 1 mg/L. Sorption: CBZ [] of 10 - 200 μg/L. Salinity: CBZ 100 μg/L	Hydrophobicity-related sorption. AH does not ↓ CBZ sorption on MPs	Wu et al. (2016)
PE, PS, PP, PA and PVC MPs	90%= 75 - 180 μm	Abt: sulfadiazine (SDZ), amoxicillin (AMX), TC, CIP, and trimethoprim (TMP)	MPs: 0.02 g per vial. Drugs: 0.5 - 15 mg/L	PA MPs ↑ adsorption capacity for antibiotics. Adsorption of the 5 antibiotics in MPs decreased in the order of CIP>AM>TMP>SDZ>TC.Seawater ↓ adsorption	Li etal. (2018b)
PVC MPs	Virgin PVC MPs of 1 - 10 μm	Adp: VFX	MPs: 1 - 50 μg/mL(sorption); 1 - 50 mg/L (ecosystem influence tests). VFX: 50 μg in 100 mL of MPs solutions	Up to 80% sorption. ↑ levels of PMs accumulated + VFX. VFX exposed to 50 mg/L of MPs ↑ their amount in sediment	Qu et al. (2018)
PS MPs	Microspheres of ~ 0.88 μm	Abt: TC		↓ amounts of emerging MPs slightly improved the removal of TC-HCl	Wang et al. (2018)
PE MPs	MPs average size: 150 μm, surface area 0.2341 m2/g	Abt: SMX	MPs: 100 mg in 40 mL. SMX: 1 mg/L (sorption kinetics, salinity and pH); 0.2 - 5 mg/L (isotherms)	Sorption equilibrium in 24h. pH and salinity had no significant effect	Xu et al. (2018a)
PE, PP and PS MPs	Virgin PE, PP from centrifuge tubes, PS from disposable petri dishes. Size: PE 150 μm, PP and PS < 280 μm.	Abt: TC	Batch sorption: 0.2 - 5 mg/L TC; 100 mg MPs + 20 mL basal solution of TC placed in 40 mL virdro	Hydrophobic, electrostatic interactions are important in sorption. PS had ↑ sorption capacity, followed by PS>PP>PE. pH-dependent sorption, ↑ gradually peaked at pH 6.0, then ↓. ↑ of [] of MOD inhibited sorption of TC in 3 MPs	Xu et al. (2018b)
PE MPs	45 - 48 μm	Abt: SMX. Ayp: PRP. Adp: SER	MPs: 50 - 500 mg/L. Pharmaceuticals: 100 μg/L (SMX); 60 μg/L (PRP); 10 - 100 μg/L (SER)	Drugs were sorbed to the MPs. PRP and SER were desorbed, SMX had irreversible sorption	Razanajatovo et al. (2018)
PE MPs	Size 150 - 250 μm. They were aged under different conditions such as pH, temperature, ionic strength	Abt: TC	Adsorption: 2 g of MPs were added and 250 mL flask containing 200 mL of TC solution (10 mg/L)	Aging factors, with pH, ionic strength, and temeprature, had little impact on asdorption of MPs to TC. MPs aged in solution with AH (humic acid) exhibited ↓ in adsorption capacity. AH may coat the surface of MPs and change their hydrophobicity, there may be electrostatic repulsion between AH and TC, and competitiveness to adsorb onto MPs, which ↓ adsorption affinity of MPs to TC	Shen et al. (2018)
PE and PS MPs	PE 260 μm, non-porous. PS 250 μm mesoporous with an average pore size of ~ 195 Å	Acs: CBZ. Atf: DCF and IBU. Drt: torasemide (TRS)	100 mg of MPs in 100 mL of solution (0.001 Kg/L)	PE: CBZ is acidic and had ↓ sorption at pH 4, 7, and 10; DIC and IBU are acidic and had sorption only at pH 4; TRS is acidic and had ↓ sorption at H 4 and 7. PS: CBZ, DIC, and IBU had similar sorption to PE; TRS had no sorption	Seidensticker et al. (2018)
PE, PP, PS and PVC MPs	PE, PP and PVC are light yellow and PS is white. PE contains many tiny irregular particles. PP has more of a layered structure. PS has ship-shaped protrusions and an irregular surface. PVC has raised surface that is looser and contains folded structures	Abt: tylosin (TIL)	Isotherms: To each glass tube were added 25 mL of TIL solutions with dferent concentrations (1 - 30 ppm) and the amounts of MPs were 0.005 - 0.03 g	Sorption equilibrium at 36h. Sorption capacity of TIL followed the order PE<PP<PS<PVC. Sorption dominated by electrostatic intteraction, surface complexation, and hydrophobic interaction. Ionic strength has a dual effect on sorption, as ionic concentration ↑ the sorption of TIL on MPs ↑ slightly and subsequently ↓. Sorption ↓ with the ↑ of pH	Guo et al. (2018)
PS MPs	Virgin and ambient, from 0.45 - 1.0 mm.	Abt: OTC	Kinetics: 50 mg MPs + 30 mL stock solution containing 20 mg/L OTC in 50 mL tubes. Isotherms: 2 - 50 mg/L of OTC	Maximum adsorption at pH 5. Adsorption promoted more in the presence of humic acid (HA) than fulvic acid	Zhang et al. (2018)
PS and PVC MPs	Purchased, virgin, diameter ~ 75 μm	Abt: CIP	Kinetics: 10 mg MPs (0.4 g/L) added to a 50 mL flask filled with 25 mL of 10 mg/L CIP. Isotherms: 2-25 mg/L CIP, MPs was the same mass as kinetics. Influence factors: 10 mg/L of CIP and 10 mg of MPs	Aged MPs exhibit ↑ sorption capacity. Original MPs ↓ sorption capacity according to ↑ the degree of crystallinity, while aged ones ↑ sorption. Adsorption suppressed the salinity	Liu et al. (2019)

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Table 3 (*continued*)

Types of MP/NPs	Characterization of MP/NPs	Pharmaceuticals	Concentrations	Interactions	References
PA, PE, PET, PS, PVC and PP MPs	Purchased, sieved at 100 - 150 μm. PA: 100 - 150 μm. PE: 100 - 150 μm. PET: 100 - 150 μm. PS: amorphous. PVC: 100 - 150 μm. PP: 100 - 150 μm	Abt: SMX	20 mg MPs + 10 mL of SMX solutions in 20 mL tubes. Kinetics: initial 2.4 mg/L of SMX, 24h. Isotherms: 0 - 12 mg/L SMX	Sorption equilibrium in 16h. External mass transfer was sorption slower. PA had ↑ sorption capacity. Sorption capacity of SMX ↓ with ↑ of pH	Guo et. al (2019)
PS MPs	Spherical with diameter 300 - 400 nm	Abt: TC	0.2 g/L of TC	Mg2+ significantly inhibited TC adsorption at pH> 5.0. ↑ adsorption in the presence of humic acid than at pH 6.0. Adsorption more favorable at neutral pH	Wan et al. (2019)
PE MPs	PE (protective bag) was bought from supermarket and cut into pieces <5 mm	Abt: sulfamerazine (SMR), TC, chloramphenicol (CLO) and TIL	5 L beaker containing 4 L of 5 μg/L (being added weekly, reaching 20 μg/L) antibiotic solution, 1 g of PE MPs were added	MPs can enrich antibiotics. Salinity ↑ can ↓ adsorption	Wang et al. (2019)
PP, low-density PE(LD-PE) high density PE (HD-PE) and PVC MPs	LD-PE: diameter 63-125 μm. HD-PE: density 0.94 g cm^{-3}, surface area 0.3548 m^2 g^{-1}. PP: density of 0.90 g cm^{-3}, surface area 0.4836 m2 g^{-1}. PVC: density of 1.4 g cm^{-3}, 0.6929 m2 g^{-1}	Abt: enrofloxacin (ENR), CIP, and norfloxacin (NOR). Antineoplastics (Anp): 5-fluorouracil (5-FU) and methotrexate (MET). Afg: flubendazole (FLU) and fenbendazole (FEN). Ayp: PRP and nadolol (NAD)	MPs: 100 mg in 1 ml. Pharmaceutical: 0.5 mg/L	Variant sorption capacity between drugs, type of plastic, and environmental conditions. ↑ sorption potential in ionic solution. Equilibrium partition coefficient ↑ for hydrophobic substances and ↓ for less hydrophobic substances. pH can influence + the interaction strength of polar compounds	Puckowski et al. (2020)
PS MPs	Aged. Early PS MPs possessed smooth surface, aged ones possessed cracks and pits. Compared to the originals, the average size of aged MPs was decreased from 50.4 ± 11.9 μm pristine to 18.2 ± 10.6 μm	Apl: ATR. Ayp: amlodipine (AML)	Simulated desorption: 130 mL of 80 mg/L pharmaceuticals in 170 mL of water containing 1.5 g PS MPs. Sorption kinetics: 8 mL and digestive fluids added to a vial containing 0.064 g PS MPs loaded with pharmaceuticals. Desorption mechanisms: pure PS MPs 2.5 g/L; pharmaceuticals 1.0 - 10 mg/L	↑ of drug desorption dependent on competition and solubilization. Aging of MPs suppressed desorption due ↓ to interactions. MPs + pharmaceuticals = risks ↓ to organisms according to ↓ concentrations	Liu et al. (2020b)
PS, ultra-high molecular weight PE (UHMWPE), medium molecular weight density PE (AMWPE), and PP MPs	PP (~ 1 mm) rough surface; PS (600-800 μm) irregular shape with sharp edges. AMWPE (300 - 400 μm) non-spherical, with sharp edges, smooth surface; and UHMWPE (2-10 μm) had irregular shapes and edges less than 10 μm	Atf: IBU, naproxen (NPX), and DCF	Sorption kinetics: 0.6 g of MPs in 100 mL vials, which were filled with 60 mL of 2.5 mg/L solution of each pharmaceuticals	↓ sorption between pharmaceuticals and PMs under environmentally relevant conditions. pH-dependent sorption. acidic pH pharmaceuticals ↑ absorption. DCF and PE MPs exhibit ↑ sorption coefficient	Elizalde-Velázquez et al. (2020)
PS and PE MPs	Aged PS MPs making rough surface, cracking and corrosion. MPs: PE -~45 μm and PP -~50 μm	Apl: ATR. Ayp: AML	Adsorption: 50 mg/L stock solution of pharmaceuticals; MPs: 0.1 g aged PS MPs + 16 mL ultrapure water; then 4 mL stock solution of pharmaceuticals was added to the suspension of MPs. Pre-loading experiment: 1 mL of aged added to the suspension of MPs 5 g/L before adding the pharmaceuticals 10 mg/L. Evaluation of the real effect of the aged intermediates: aged intermediates 0.1 mg.L, PS 0.5 g/L and pharmaceuticals 1 mg/L	Adsorption of PS MPs and pharmaceuticals depended on hydrophobicity and π-π interaction, for aged PS electrostatic interaction and hydrogen bonding. Intermediates released in the aging process at high [] ↓ ATV adsorption on PS MPs and ↑ AML adsorption. These intermediates at environmental concentration (0.1 mg/L) had ↓ adsorption of pharmaceuticals on MPs. Impact dependent on electrostatic interaction between MPs and aged intermediates	Liu et al. (2020a)
PE MPs	Pure ~100 μm. Different sizes and shapes, rough surface with irregular folds, ↓ degree of crystallinity, ↑ proportion of amorphous region	Abt: CIP	Effect of pH, MOD: 2 g/L MPs and 10 mg/L CPX. Adsorption kinetics: 25 mg/L CPX and 2 g/L MPs. Adsorption isotherms: 30 to 500 mg/L and 2 g/L MPs	Adsorption of CPX ↑ gradually with increasing pH, ↓ with increasing ionic strength	Atugoda et al. (2020)
NYL MPs	Obtained from nylon ropes from a fishing boat (35 strand twisted ropes, 0.5 mm, used for 7 years, rough surface), they were cut at 1, 5 and 10 mm	Abt: TC	Sorption equilibrium: 0.25 g of 1 mm MPs in 150 mL bottle with 100 mL, at concentration 5 ml/L. Surface area effects: 1, 5 and 10 mm nylon ropes. Isotherm: 0.25 g of 1 mm nylon cords in 100 mL of various TC concentrations 3 - 30 mg/L. Desorption: 0.25 g of nylon ropes	Sorption process was spontaneous, exothermic and with decreasing randomness of nature. Sorption was pH dependent. Ionic strength played a limited role. Sorption predominated by van der Waals forces. ↑ desorption on gut surfactant	Lin et al. (2020)

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Table 3 (*continued*)

Types of MP/NPs	Characterization of MP/NPs	Pharmaceuticals	Concentrations	Interactions	References
PE, PET, PS and PVC MPs	MPs derived from waste plastics.PE: 3.5 ± 0.3 mm, PET: 2.7 ± 0.2 mm, PS: 3.1 ± 0.3 mm, PS: 3.4 ± 0.3 mm, PVC: 4.3 ± 0.5 mm	Abt: AMX and vancomycin (VAC). Ang: PAC	MPs: 0.1g in 100 mL. Pharmaceuticals: preliminary and kinetic tests 1mg/L; equilibrium tests 1 - 16 mg/L; desorption tests initial 16 mg/L	AMX-bearing MPs. Sorption takes more than 28 days (AMX) to reach equilibrium. Temperature and pH dependent release of contaminants	Godoy et al. (2020)
PE, PP, PET, PS, ABS, PMMA and NYL MPs	Virgin products or shredded recycled plastics. Pure PE 75 - 90 μm. PMMA 27 - 45 μm. PEHD plastic desacoles were in thin film state, pure PE had 75 μm and were spherical particles with smooth surface. Distinct PP samples, were found to be composed with talc and glass fiber; others in bead shape with larger size (400 μm) and less regular geometry. PA samples, composed of nylon and others of glass fiber. PP, PE, PS are highly hydrophobic. PA has polar portions	Ang: acetaminophenol (ACT-paracetamol)		Pure polymers have ↓ absorption than real MPs. MPs + MON have ↑ absorption	Ateia et al. (2020)
PVC MPs. PS NPs	MPs: PS of 74 μm; PVC of 1 μm and 74 μm. NPs: synthesized by styrene monomer emulsion polymerization; size of 40.1 ± 9.1 nm	Abt: CFX	Adsorption: 10 mg MPs/NPs + 20 mL CIP solution in 30 mL vials. Isotherms: CIP 2 - 50 mg/L, pH 3 - 11, salinity 5 - 35%	NPs have ↑ adsorption to hydrophobic organic pollutants. Electrostatic interactions and hydrogen bonds dominate adsorption of CIP. Proposed electrosorption for removal of NPs from water	Xiong et al. (2020)
PS NPs	500 nm and 200 nm diameter	Abt: CIP	Batch sorption: 100 mg/L of 500 nm PS-COOH + CIP solution. Kinetics: CIP 0.2 - 0.8 mg/L. Isotherm: CIP 0.2 - 1.2 mg/L with 200 nm and 500 nm PS-COOH. 100 mg/L of NPs in all of the above. pH: 4.5 - 8.5; CIP 0.4 mg/L; 500 nm PS-COOH 100 mg/L	Adsorption of PS-COOH + CIP was a spontaneous exothermic reaction. ↑ toxicity on C.elegans survival	Yilimulati et al. (2021)
PS NPs	PS of 50 nm. PS-COOH of 55 nm	Abt: NOR and levofloxacin (LEV)	3 mg PS or PS-COOH NPs in 50 mL, 6 mg PS or 3 mg PS-COOH. 30 mL of solution with varying initial concentrations (1 - 14 mg/L in 50 mL); 30 mL of 1 - 16 mg/L	Sorption capacity of NOR and LEV on PS-COOH NPs were ↑. The ↑ of pH ↑ sorption of the 2 FQs and then ↓ because NOR and LEV had reverse charge at different pH values. Salinity and organic matter inhibited the sorption process. NPs with or without surface functionalization have different behavior	Zhang et al. (2020a)
PET, HDPE, PVC, LDPE and PP MPs	MPs all virgin, plus LDPE from chopped-up shopping bags and PP from chopped-up plastic straws.Diameter 2.3-5 μm and chopped-up pieces = or <35	Ayp: ATN. Atf: IBU. Abt: SMX	ATN 0.84 μg/L, IBU 1.09 μg/L, SMX 0.77 μg/L	Target drugs found adsorbed on all MPs tested	Magadini et al. (2020)
PE, PS and PVC MPs	PE with average diameters of 28 - 590 μm. PS and PVC with an average diameter of 75 μm. PVC irregular spherical shape with large bumps on surface, small folds on surface. PS irregular sheet shape with irregular edges on a single particle, flat surface	Abt: TC	Adsorption: 10 mg PE and 20 mL of TC solution (5 mg/L) in 50 mL Erlenmeyer flask. Isothermal: 10 mg of MPs + 20 mL of TC (1 - 35 mg/L)	PE showed ↑ adsorption capacity, coefficient, and strength. With the ↑ of PE size the adsorption and coefficient ↓. Presence of Pb^{2+}, Cr^{3+}, Cd^{2+} and Zn^{2+} ↑ adsorption. Cu^{2+} ↑ adsorption	Yu et al. (2020)

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Table 3 (*continued*)

Types of MP/NPs	Characterization of MP/NPs	Pharmaceuticals	Concentrations	Interactions	References
PET MPs	MPs of mariculture system	Abt: TC, SMX, CIP, CLO and erythromycin (ERT)	3 water samples and 3 samples of MPs. Multi-antibiotic resistant bacteria (BMRA) were tested for antibiotic susceptibility	↑ resistance to penicillin, sulfamatoxazole, erythromycin, and tetracycline. The dominant multiple antibiotic resistance profile was TET-SFX-ERY-PEN, which accounted for 25.4% in the microplastic samples and 23.9% in the water samples	Zhang et al. (2020c)
PVC MPs		Abt: TC and ampicillin (AMP)	Abt: 0.5 mg/L. 0.25 g MPs in 500 mL bottles	Presence of Zn, TC, and AMP inhibited shriveling for a short period of time (28 days)	Zhao et al. (2020)
PVC MPs		Abt: TC	0.1; 10 and 100 mg/L of TC and 0 and 0.25 g/L of PVC	Proteobacteria ↑ with the increment of TC. TC removal was ↑ with sludge adsorption. MPs + TC ↑ nitrosation	Li et al. (2020)
PS MPs	Iron infused, microspheres with surface carboxyl and amine functional groups	Ayp: AML. Acs: CBZ		AMP has a preference for surfaces with a carboxylic group. CBZ tends to pH-dependent surfaces	Williams et al. (2020)
PS MPs	MPs PS irregular surface with bumps	Abt: TIL	Single system: PS MPs with different amounts of 0.005 - 0.03 g and 20 mL of TYL with different concentrations (1 - 30 mg/L) added to a tube. Sorption isotherms: TYL 1 - 30 mg/L ; 0.01 - 0.04 g PS MPs; 20 mL sorption solution added	When TYL and Cd (II) coexist, Cd (II) can inhibit the sorption of TYL on PS MPs. Complexation of Cd (II) and TYL ↑ sorption in PS MPs. pH and ionic strength essential in sorption	Huang et al. (2021a)
PVC MPs	1 μm	Abt: CFX and cefazolin (CFZ)	PVC: 10 mg/10 mL CFZ: 1 – 104.9 μm/10 mL	Aged PVC ↑ hydrolysis of CFZ, adsorption capacity	Wang et al. (2021a)
MPs		Anp: cyclophosphamide (CCP), tamoxifen (TAM). Ask: NCT. Ang: caffeine (CFN). Apl: paraxanthine (PRX) and GFB. Ayp: ATN. Acst: CBZ. Abt: TMP and ERT	MPs: 300 mg/L. Pharmaceuticals detected: 24 – 111 ng/g	All target drugs were detected in the analyzed samples	Santana-Viera et al. (2021)
PS, PET, PP and HDPE MPs	Obtained from macroplastics and commercially. 100-250 μm. PS: 20 – 1000 μm	Atf: DCF. Abt: metronidazole (MTN)	Pharmaceuticals: 0.5 – 15 mg/L. MPs: 10 mg/1.5 mL	DCF ↑ adsorption. Smaller size has ↑ adsorption. Aged MPs ↑ adsorb hydrophili compounds. ↑ pH and salinity ↑ desorption. Dissolved organic matter ↓ sorption	Munoz et al. (2021)
PE MPs	0.15 to 0.425 mm	Abt: TC, chlortetracycline (CTC) and OTC	PE: 0.25 g / 25 mL.Pharmaceuticals: 0 – 50 mg/L	Adsorption capacities of Pharmaceuticals onto PE: OTC>CTC>TC	Chen et al. (2021)
PE MPs and tire wear particles (TWP)	TWP: 63 – 149 μm passed through the 74 μm sieve	Abt: CTC, AMX	Pharmaceuticals: 0.5 – 8 mg/L	Adsorption capacity ↑ after aging. Desorption amount and rate from TWP ↑	Fan et al. (2021b)
PS MPs	33,27 ± 11,85 μm	Apl: ATR		PS facilitated the phototransformation of ATR	Wang et al. (2021b)
PLA MPs	75 – 150 μm	Abs: OTC	OTC: 1 – 12 mg/L.PLA: 0.03 g / 50 mL	PLA coatedwith oxygen-containing groups ↑ OTC adsorption	Sun et al. (2021)
PVC and PE MPs		Abs: TC and AMP	MPs: 0.5 g /L. Pharmaceuticals: 0.5 mg/L	Adsorption capacity on MPs: AMP>TC. PE ↑ conducive to microbial. PE + TC ↑ risks of spreading of antibiotc resistance genes and mobile genetic elements	Wang et al. (2021d)
PE MPs	300 μm	Acs: CBZ	CBZ: 10 mg/L. PE: 2 – 20 g/L	Adsorption of CBZ by carbono nanotubes ↓ in the presence of MPs	Sheng et al. (2021)
PE MPs	75 – 140 μm	Abt: TC	TC: 0 - 15 mg/L. PE: 0.1 g/20 mL	MPs exposed to the environment adsorbed ↑ TC	Wang et al. (2021c)
PS MPs	Cylindrical	Abt: TC	MPs: 0.6 g/100 mL. TC: 0.01 – 0.2 mM/100mL	In the presence os hexabbromocyclodecane0.6 g MPs ↑ TC adsorption	Lin et al. (2021)
PLA, PET and PP MPs	150 – 250 μm	Abt: SMX	MPs: 40 mg/ 60 mL. SMX: 20 mL/ 60 mL or 0.5 – 10 mg/L	↑ adsorption as the MPs age. PLA ↑ adsorption. ↑ adsorption acidic conditions	Kong et al. (2021)
PE, PP, PS and PVC MPs		Abt: NOR		Adsorpiton: PVC>PS>PE>PP	Zhang et al. (2021b)
HDPE MPs	45 μm	Abt: TC	MPs: 1 mg/mL. TC: 1 – 10 mg/L	TC adsorption onto PE was rapid	Nguyen et al. (2021)
PS and PE MPs	PS: 53 – 500 μm. PE: 500 – 1000 μm	Abt: SMX. Ayp: valsartan (VSR) and losartan (LSR)	MPs: 1000 mg/L. Pharmaceuticals: 500 μg/L	VSR and LSR were adsorbed to MPs	Arvaniti et al. (2021)
PS MPs	1 μm	Abt: TC	TC: 0 - 20 mg/L. PS: 5.69 – 107 particles/mL	K^+ solutions TC ↓ the mobility of PS	Zhao et al. (2021a)
PET NPs	30 nm	Abt: LEV	NPs: 30 mg/L. LEV: 10 mM	PS form complexes with LEV	Magrì et al. (2021)

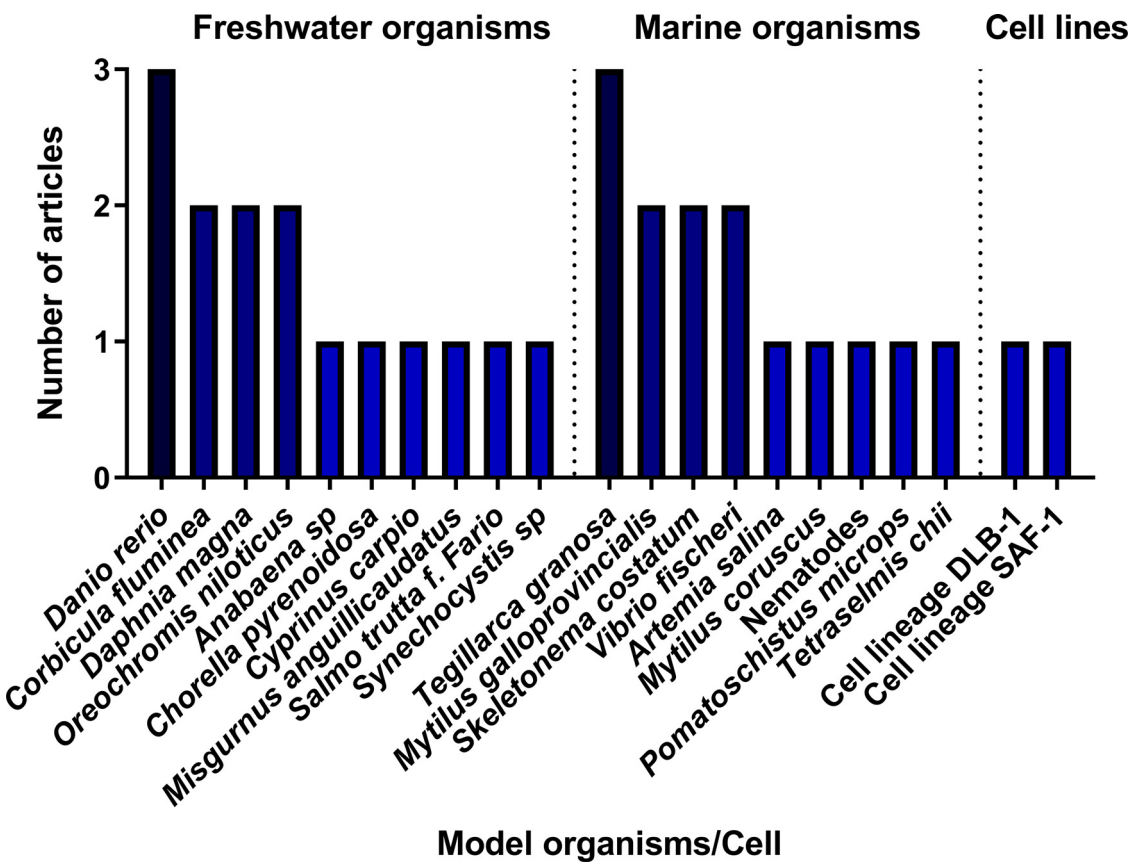

Fig. 4. Number of studies according to model organisms and cell lines.

(Schmieg et al., 2020). Overall, the pharmaceuticals showed adsorption to the MP/NPs, causing a "Trojan horse" effect, demonstrating the importance of studying their interactions at various levels of biological organization.

4. Conclusions and perspectives

The current review summarized the data available in the literature concerning the interaction and toxicity MP/NPs with pharmaceuticals. Results showed the interaction of MP/NPs with several pharmaceuticals groups, mainly antibiotics, antihypertensives, antidepressants, analgesics and antifungals. This interaction and their ecotoxicity to aquatic organisms depend on experimental design and environmental conditions. The small size of the MP/NPs and the high hydrophobicity of the pharmaceuticals have been shown to be key points in the interaction. Studies were conducted mainly with *in vivo* approach and freshwater species. To summarize, several research gaps that deserve further attention are highlighted, such as:

a) Ecotoxicological assessment of MP/NPs and pharmaceuticals mixture in environmentally relevant conditions, such as mesocosms, multispecies exposure, global changes, among others;
b) Analysis of tissue and subcellular distributions, and detoxification mechanisms;
c) Investigate the interaction of MP/NPs and pharmaceuticals with sediments and their ecotoxicity to organisms living in sediment;
d) Analysis of ecotoxicity after long-term exposure period and multigenerational effects.
e) Investigate the interaction and ecotoxicity of pharmaceuticals with MP/NPs isolated from environmental matrices, especially under environmentally relevant conditions.

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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References

Albendín, M.G., Aranda, V., Coello, M.D., González-Gómez, C., Rodríguez-Barroso, R., Quiroga, J.M., Arellano, J.M., 2021. Pharmaceutical products and pesticides toxicity associated with microplastics (Polyvinyl chloride) in *Artemia salina*. Int. J. Environ. Res. Public Health 18. doi:10.3390/ijerph182010773.

Allouche, M., Ishak, S., Nasri, A., Hedfi, A., Ben Ali, M., Albogami, B., Almalki, M., Pacioglu, O., Boufahja, F., 2021. What is the impact of microplastics and lipid regulators on marine meiofauna? Case study of polyvinyl chloride, atorvastatin, and simvastatin. Sustain 13. doi:10.3390/su132313190.

Almeida, M., Martins, M.A., Soares, A.M.V., Cuesta, A., Oliveira, M., 2019. Polystyrene nanoplastics alter the cytotoxicity of human pharmaceuticals on marine fish cell lines. Environ. Toxicol. Pharmacol. 69, 57–65. doi:10.1016/j.etap.2019.03.019.

Álvarez-Ruiz, R., Picó, Y., Campo, J., 2021. Bioaccumulation of emerging contaminants in mussel (*Mytilus galloprovincialis)*: Influence of microplastics. Sci. Total Environ. 796. doi:10.1016/j.scitotenv.2021.149006.

Arvaniti, O.S., Antonopoulou, G., Tsagkogianni, D., Stasinakis, A.S., 2021. Screening on the sorption of emerging contaminants to polystyrene and polyethylene and use of coagulation – flocculation process for microplastics' removal. Glob. Nest J. 23, 303–308. doi:10.30955/gnj.003854.

Ateia, M., Zheng, T., Calace, S., Tharayil, N., Pilla, S., Karanfil, T., 2020. Sorption behavior of real microplastics (MPs): Insights for organic micropollutants adsorption on a large set of well-characterized MPs. Sci. Total Environ. 720. doi:10.1016/j.scitotenv.2020.137634.

Atugoda, T., Wijesekara, H., Werellagama, D.R.I.B., Jinadasa, K.B.S.N., Bolan, N.S., Vithanage, M., 2020. Adsorptive interaction of antibiotic ciprofloxacin on polyethylene microplastics: Implications for vector transport in water. Environ. Technol. Innov. 19, 100971. doi:10.1016/j.eti.2020.100971.

Barreto, A., Santos, J., Amorim, M.J.B., Maria, V.L., 2021. Polystyrene nanoplastics can alter the toxicological effects of simvastatin on *Danio rerio*. Toxics 9, 1–15. doi:10.3390/toxics9030044.

aus der Beek, T., Weber, F.A., Bergmann, A., Hickmann, S., Ebert, I., Hein, A., Küster, A., 2016. Pharmaceuticals in the environment-Global occurrences and perspectives. Environ. Toxicol. Chem. 35, 823–835. doi:10.1002/etc.3339.

Bhagat, J., Zang, L., Nakayama, H., Nishimura, N., Shimada, Y., 2021. Effects of nanoplastic on toxicity of azole fungicides (ketoconazole and fluconazole) in zebrafish embryos. Sci. Total Environ. 800. doi:10.1016/j.scitotenv.2021.149463.

Brandts, I., Teles, M., Gonçalves, A.P., Barreto, A., Franco-Martinez, L., Tvarijonaviciute, A., Martins, M.A., Soares, A.M.V.M., Tort, L., Oliveira, M., 2018. Effects of nanoplastics on *Mytilus galloprovincialis* after individual and combined exposure with carbamazepine. Sci. Total Environ. 643, 775–784. doi:10.1016/j.scitotenv.2018.06.257.

Brennecke, D., Duarte, B., Paiva, F., Caçador, I., Canning-Clode, J., 2016. Microplastics as vector for heavy metal contamination from the marine environment. Estuar. Coast. Shelf Sci. 178, 189–195. doi:10.1016/j.ecss.2015.12.003.

Canedo, A., Saiki, P., Santos, A. L., Carneiro, K.S., Souza, A. M., Qualhato, G., Brito, R. S., Mello-Andrade, F., Rocha, T. L., 2022. Zebrafish (Danio rerio) meets bioethics: the 10Rs ethical principles in research. Ciência Animal Brasileira 23, e70884.

Chen, Y., Awasthi, A.K., Wei, F., Tan, Q., Li, J., 2021. Single-use plastics: production, usage, disposal, and adverse impacts. Sci. Total Environ. 752, 141772. doi:10.1016/j.scitotenv.2020.141772.

Cole, M., Lindeque, P., Halsband, C., Galloway, T.S., 2011. Microplastics as contaminants in the marine environment: a review. Mar. Pollut. Bull. 62, 2588–2597. doi:10.1016/j.marpolbul.2011.09.025.

da Costa, J.P., Santos, P.S.M., Duarte, A.C., Rocha-Santos, T., 2016. (Nano)plastics in the environment - Sources, fates and effects. Sci. Total Environ. 566–567, 15–26. doi:10.1016/j.scitotenv.2016.05.041.

Elizalde-Velázquez, A., Subbiah, S., Anderson, T.A., Green, M.J., Zhao, X., Cañas-Carrell, J.E., 2020. Sorption of three common nonsteroidal anti-inflammatory drugs (NSAIDs) to microplastics. Sci. Total Environ. 715, 136974. doi:10.1016/j.scitotenv.2020.136974.

Fan, X., Gan, R., Liu, J., Xie, Y., Xu, D., Xiang, Y., Su, J., Teng, Z., Hou, J., 2021a. Adsorption and desorption behaviors of antibiotics by tire wear particles and polyethylene microplastics with or without aging processes. Sci. Total Environ. 771, 145451. doi:10.1016/j.scitotenv.2021.145451.

Fan, X., Zou, Y., Geng, N., Liu, J., Hou, J., Li, D., Yang, C., Li, Y., 2021b. Investigation on the adsorption and desorption behaviors of antibiotics by degradable MPs with or without UV ageing process. J. Hazard. Mater. 401, 123363. doi:10.1016/j.jhazmat.2020.123363.

Feng, L.J., Shi, Y., Li, X.Y., Sun, X.D., Xiao, F., Sun, J.W., Wang, Y., Liu, X.Y., Wang, S.G., Yuan, X.Z., 2020. Behavior of tetracycline and polystyrene nanoparticles in estuaries and their joint toxicity on marine microalgae *Skeletonema costatum*. Environ. Pollut. 263, 114453. doi:10.1016/j.envpol.2020.114453.

Fick, J., Söderström, H., Lindberg, R.H., Phan, C., Tysklind, M., Larsson, D.G.J., 2009. Contamination of surface, ground, and drinking water from pharmaceutical production. Environ. Toxicol. Chem. 28, 2522–2527. doi:10.1897/09-073.1.

Fonte, E., Ferreira, P., Guilhermino, L., 2016. Temperature rise and microplastics interact with the toxicity of the antibiotic cefalexin to juveniles of the common goby (*Pomatoschistus microps)*: Post-exposure predatory behaviour, acetylcholinesterase activity and lipid peroxidation. Aquat. Toxicol. 180, 173–185. doi:10.1016/j.aquatox.2016.09.015.

Godoy, V., Martín-Lara, M.A., Calero, M., Blázquez, G., 2020. The relevance of interaction of chemicals/pollutants and microplastic samples as route for transporting contaminants. Process Saf. Environ. Prot. 138, 312–323. doi:10.1016/j.psep.2020.03.033.

González-Alonso, S., Merino, L.M., Esteban, S., López de Alda, M., Barceló, D., Durán, J.J., López-Martínez, J., Aceña, J., Pérez, S., Mastroianni, N., Silva, A., Catalá, M., Valcárcel, Y., 2017. Occurrence of pharmaceutical, recreational and psychotropic drug residues in surface water on the northern Antarctic Peninsula region. Environ. Pollut. 229, 241–254. doi:10.1016/j.envpol.2017.05.060.

González-Pleiter, M., Edo, C., Velázquez, D., Casero-Chamorro, M.C., Leganés, F., Quesada, A., Fernández-Piñas, F., Rosal, R., 2020a. First detection of microplastics in the freshwater of an antarctic specially protected area. Mar. Pollut. Bull. 161, 1–6. doi:10.1016/j.marpolbul.2020.111811.

González-Pleiter, M., Pedrouzo-Rodríguez, A., Verdú, I., Leganés, F., Marco, E., Rosal, R., Fernández-Piñas, F., 2020b. Microplastics as vectors of the antibiotics azithromycin and clarithromycin: effects towards freshwater microalgae. Chemosphere doi:10.1016/j.chemosphere.2020.128824.

Guilhermino, L., Vieira, L.R., Ribeiro, D., Tavares, A.S., Cardoso, V., Alves, A., Almeida, J.M., 2018. Uptake and effects of the antimicrobial florfenicol, microplastics and their mixtures on freshwater exotic invasive bivalve *Corbicula fluminea*. Sci. Total Environ. 622–623, 1131–1142. doi:10.1016/j.scitotenv.2017.12.020.

Guo, X., Cai, Y., Ma, C., Han, L., Yang, Z., 2021. Combined toxicity of micro/nano scale polystyrene plastics and ciprofloxacin to *Corbicula fluminea* in freshwater sediments. Sci. Total Environ. 789, 147887. doi:10.1016/j.scitotenv.2021.147887.

Guo, X., Chen, C., Wang, J., 2019. Sorption of sulfamethoxazole onto six types of microplastics. Chemosphere 228, 300–308. doi:10.1016/j.chemosphere.2019.04.155419, 418.

Guo, X., Pang, J., Chen, S., Jia, H., 2018. Sorption properties of tylosin on four different 420 microplastics. Chem 209, 240–245. doi:10.1016/j.chemosphere.2018.06.100.

Han, Y., Zhou, W., Tang, Y., Shi, W., Shao, Y., Ren, P., Zhang, J., Xiao, G., Sun, H., Liu, G., 2021. Microplastics aggravate the bioaccumulation of three veterinary antibiotics in the thick shell mussel *Mytilus coruscus* and induce synergistic immunotoxic effects. Sci. Total Environ. 770, 145273. doi:10.1016/j.scitotenv.2021.145273.

Hanslik, L., Huppertsberg, S., Kämmer, N., Knepper, T.P., Braunbeck, T., 2021. Rethinking the relevance of microplastics as vector for anthropogenic contaminants: Adsorption of toxicants to microplastics during exposure in a highly polluted stream - Analytical quantification and assessment of toxic effects in zebrafish (*Danio rerio*). Sci. Total Environ. 151640. doi:10.1016/j.scitotenv.2021.151640.

Hernandez, L.M., Yousefi, N., Tufenkji, N., 2017. Are there nanoplastics in your personal care products? Environ. Sci. Technol. Lett. 4, 280–285. doi:10.1021/acs.estlett.7b00187.

Homem, V., Santos, L., 2011. Degradation and removal methods of antibiotics from aqueous matrices - a review. J. Environ. Manage. 92, 2304–2347. doi:10.1016/j.jenvman.2011.05.023.

Huang, D., Xu, Y., Yu, X., Ouyang, Z., Guo, X., 2021a. Effect of cadmium on the sorption of tylosin by polystyrene microplastics. Ecotoxicol. Environ. Saf. 207, 111255. doi:10.1016/j.ecoenv.2020.111255.

Huang, W., Song, B., Liang, J., Niu, Q., Zeng, G., Shen, M., Deng, J., Luo, Y., Wen, X., Zhang, Y., 2021b. Microplastics and associated contaminants in the aquatic environment: A review on their ecotoxicological effects, trophic transfer, and potential impacts to human health. Journal of Hazardous Materials. Elsevier doi:10.1016/j.jhazmat.2020.124187.

Huang, Y., Ding, J., Zhang, G., Liu, S., Zou, H., Wang, Z., Zhu, W., Geng, J., 2021c. Interactive effects of microplastics and selected pharmaceuticals on red tilapia: role of microplastic aging. Sci. Total Environ. 752, 142256. doi:10.1016/j.scitotenv.2020.142256.

Kong, F., Xu, X., Xue, Y., Gao, Y., Zhang, L., Wang, L., Jiang, S., Zhang, Q., 2021. Investigation of the adsorption of sulfamethoxazole by degradable Microplastics artificially aged by chemical oxidation. Arch. Environ. Contam. Toxicol. 81, 155–165. doi:10.1007/s00244-021-00856-w.

Lee, H., Im, S.J., Kim, Y., Lee, G., Jang, A., 2021. Effects of microplastics on the removal of trace organic compounds during ozonation: Oxidation and adsorption of trace organic compounds and byproducts. Environ. Pollut. 280, 116878. doi:10.1016/j.envpol.2021.116878.

Li, Jingyi, Liu, H., Paul Chen, J., 2018a. Microplastics in freshwater systems: a review on occurrence, environmental effects, and methods for microplastics detection. Water Res 137, 362–374. doi:10.1016/j.watres.2017.12.056.

Li, Jia, Zhang, K., Zhang, H., 2018b. Adsorption of antibiotics on microplastics. Environ. Pollut. 237, 460–467. doi:10.1016/j.envpol.2018.02.050.

Li, L., Liu, D., Li, Z., Song, K., He, Y., 2020. Evaluation of microplastic polyvinylchloride and antibiotics tetracycline co-effect on the partial nitrification process. Mar. Pollut. Bull. 160. doi:10.1016/j.marpolbul.2020.111671.

Lin, L., Tang, S., Wang, X., Sun, X., Liu, Y., 2021. Sorption of tetracycline onto hexabromocyclododecane/polystyrene composite and polystyrene microplastics: Statistical physics models, influencing factors, and interaction mechanisms. Environ. Pollut. 284, 117164. doi:10.1016/j.envpol.2021.117164.

Lin, L., Tang, S., Wang, X.S., Sun, X., Han, Z., Chen, Y., 2020. Accumulation mechanism of tetracycline hydrochloride from aqueous solutions by nylon microplastics. Environ. Technol. Innov. 18, 100750. doi:10.1016/j.eti.2020.100750.

Liu, G., Zhu, Z., Yang, Y., Sun, Y., Yu, F., Ma, J., 2019. Sorption behavior and mechanism of hydrophilic organic chemicals to virgin and aged microplastics in freshwater and seawater. Environ. Pollut. 246, 26–33. doi:10.1016/j.envpol.2018.11.100.

Liu, P., Lu, K., Li, J., Wu, X., Qian, L., Wang, M., Gao, S., 2020a. Effect of aging on adsorption behavior of polystyrene microplastics for pharmaceuticals: Adsorption mechanism and role of aging intermediates. J. Hazard. Mater. 384, 121193. doi:10.1016/j.jhazmat.2019.121193.

Liu, P., Wu, X., Liu, H., Wang, H., Lu, K., Gao, S., 2020b. Desorption of pharmaceuticals from pristine and aged polystyrene microplastics under simulated gastrointestinal conditions. J. Hazard. Mater. 392, 122346. doi:10.1016/j.jhazmat.2020.122346.

Lu, H.C., Ziajahromi, S., Neale, P.A., Leusch, F.D.L., 2021. A systematic review of freshwater microplastics in water and sediments: recommendations for harmonisation to enhance future study comparisons. Sci. Total Environ. 781, 146693. doi:10.1016/j.scitotenv.2021.146693.

Ma, J., Sheng, G.D., Chen, Q.L., O'Connor, P., 2020. Do combined nanoscale polystyrene and tetracycline impact on the incidence of resistance genes and microbial community disturbance in *Enchytraeus crypticus*? J. Hazard. Mater. 387, 122012. doi:10.1016/j.jhazmat.2019.122012.

Magadini, D.L., Goes, J.I., Ortiz, S., Lipscomb, J., Pitiranggon, M., Yan, B., 2020. Assessing the sorption of pharmaceuticals to microplastics through in-situ experiments in New York City waterways. Sci. Total Environ. 729, 138766. doi:10.1016/j.scitotenv.2020.138766.

Magrì, D., Veronesi, M., Sánchez-Moreno, P., Tolardo, V., Bandiera, T., Pompa, P.P., Athanassiou, A., Fragouli, D., 2021. PET nanoplastics interactions with water contaminants and their impact on human cells. Environ. Pollut. 271. doi:10.1016/j.envpol.2020.116262.

Martín, C., Fajardo, C., Costa, G., Sánchez-Fortún, S., San Andrés, M.D., González, F., Nande, M., Mengs, G., Martín, M., 2021. Bioassays to assess the ecotoxicological impact of polyethylene microplastics and two organic pollutants, simazine and ibuprofen. Chem 274. doi:10.1016/j.chemosphere.2021.129704.

Munoz, M., Ortiz, D., Nieto-Sandoval, J., de Pedro, Z.M., Casas, J.A., 2021. Adsorption of micropollutants onto realistic microplastics: role of microplastic nature, size, age, and NOM fouling. Chem 283, 131085. doi:10.1016/j.chemosphere.2021.131085.

NATIONAL SCIENCE BOARD, 2019. Publications output: U.S. trends and international comparisons. Sci. Eng. Indicators 2020 Nsb-2020-6 35.

Ng, E.L., Huerta Lwanga, E., Eldridge, S.M., Johnston, P., Hu, H.W., Geissen, V., Chen, D., 2018. An overview of microplastic and nanoplastic pollution in agroecosystems. Sci. Total Environ. 627, 1377–1388. doi:10.1016/j.scitotenv.2018.01.341.

Nguyen, B., Claveau-Mallet, D., Hernandez, L.M., Xu, E.G., Farner, J.M., Tufenkji, N., 2019. Separation and analysis of microplastics and nanoplastics in complex environmental samples. Acc. Chem. Res. 52, 858–866. doi:10.1021/acs.accounts.8b00602.

Nguyen, T.B., Ho, T.B.C., Huang, C.P., Chen, C.W., Hsieh, S.L., Tsai, W.P., Dong, C.Di, 2021. Adsorption characteristics of tetracycline onto particulate polyethylene in dilute aqueous solutions. Environ. Pollut. 285, 117398. doi:10.1016/j.envpol.2021.117398.

Nogueira, A.F., Pinto, G., Correia, B., Nunes, B., 2019. Embryonic development, locomotor behavior, biochemical, and epigenetic effects of the pharmaceutical drugs paracetamol and ciprofloxacin in larvae and embryos of *Danio rerio* when exposed to environmental realistic levels of both drugs. Environ. Toxicol. 34, 1177–1190. doi:10.1002/tox.22819.

Patel, M., Kumar, R., Kishor, K., Mlsna, T., Pittman, C.U., Mohan, D., 2019. Pharmaceuticals of emerging concern in aquatic systems: chemistry, occurrence, effects, and removal methods. Chem. Rev. 119, 3510–3673. doi:10.1021/acs.chemrev.8b00299.

Pereira, A.C., Gomes, T., Ferreira Machado, M.R., Rocha, T.L., 2019. The zebrafish embryotoxicity test (ZET) for nanotoxicity assessment: from morphological to molecular approach. Environ. Pollut. 252, 1841–1853. doi:10.1016/j.envpol.2019.06.100.

Prata, J.C., Lavorante, B.R.B.O., Maria da, M.da C., Guilhermino, L., 2018. Influence of microplastics on the toxicity of the pharmaceuticals procainamide and doxycycline on the marine microalgae *Tetraselmis chuii*. Aquat. Toxicol. 197, 143–152. doi:10.1016/j.aquatox.2018.02.015.

Puckowski, A., Cwięk, W., Mioduszewska, K., Stepnowski, P., Białk-Bielińska, A., 2021. Sorption of pharmaceuticals on the surface of microplastics. Chem 263. doi:10.1016/j.chemosphere.2020.127976.

Qu, H., Ma, R., Wang, B., Zhang, Y., Yin, L., Yu, G., Deng, S., Huang, J., Wang, Y., 2018. Effects of microplastics on the uptake, distribution and biotransformation of chiral antidepressant venlafaxine in aquatic ecosystem. J. Hazard. Mater. 359, 104–112. doi:10.1016/j.jhazmat.2018.07.016.

Razanajatovo, R.M., Ding, J., Zhang, S., Jiang, H., Zou, H., 2018. Sorption and desorption of selected pharmaceuticals by polyethylene microplastics. Mar. Pollut. Bull. 136, 516–523. doi:10.1016/j.marpolbul.2018.09.048.

Rochman, C.M., Hoh, E., Kurobe, T., Teh, S.J., 2013. Ingested plastic transfers hazardous chemicals to fish and induces hepatic stress. Sci. Rep. 3, 1–7. doi:10.1038/srep03263.

Rosani, U., Bortoletto, E., Bai, C.M., Novoa, B., Figueras, A., Venier, P., Fromm, B., 2021. Digging into bivalve miRNAomes: Between conservation and innovation. Philos. Trans. R. Soc. B Biol. Sci. 376. doi:10.1098/rstb.2020.0165.

Santana-Viera, S., Montesdeoca-Esponda, S., Torres-Padrón, M.E., Sosa-Ferrera, Z., Santana-Rodríguez, J.J., 2021. An assessment of the concentration of pharmaceuticals adsorbed on microplastics. Chem 266, 129007. doi:10.1016/j.chemosphere.2020.129007.

Santos, A.L., Rodrigues, C.C., Oliveira, M., Rocha, T.L., 2022. Microbiome: A forgotten target of environmental micro(nano)plastics? Sci. Total Environ. 822, 153628. doi:10.1016/j.scitotenv.2022.153628.

Schmieg, H., Burmester, J.K.Y., Krais, S., Ruhl, A.S., Tisler, S., Zwiener, C., Köhler, H.R., Triebskorn, R., 2020. Interacting effects of polystyrene microplastics and the antidepressant amitriptyline on early life stages of brown trout (*Salmo trutta f. fario*). Water (Switzerland) 12. doi:10.3390/W12092361.

Seidensticker, S., Grathwohl, P., Lamprecht, J., Zarfl, C., 2018. A combined experimental and modeling study to evaluate pH-dependent sorption of polar and non-polar compounds to polyethylene and polystyrene microplastics. Environ. Sci. Eur. 30, 1–12. doi:10.1186/s12302-018-0155-z.

Sharma, L., Siedlewicz, G., Pazdro, K., 2021. The toxic effects of antibiotics on freshwater and marine photosynthetic microorganisms: State of the art. Plants 10, 1–15. doi:10.3390/plants10030591.

Shen, X.C., Li, D.C., Sima, X.F., Cheng, H.Y., Jiang, H., 2018. The effects of environmental conditions on the enrichment of antibiotics on microplastics in simulated natural water column. Environ. Res. 166, 377–383. doi:10.1016/j.envres.2018.06.034.

Sheng, X., Wang, J., Zhang, W., Zuo, Q., 2021. The potential for pe microplastics to affect the removal of carbamazepine medical pollutants from aqueous environments by multiwalled carbon nanotubes. Toxics 9. doi:10.3390/toxics9060139.

Shi, W., Han, Y., Sun, S., Tang, Y., Zhou, W., Du, X., Liu, G., 2020. Immunotoxicities of microplastics and sertraline, alone and in combination, to a bivalve species: size-dependent interaction and potential toxication mechanism. J. Hazard. Mater. 396, 122603. doi:10.1016/j.jhazmat.2020.122603.

Singh, B., Sharma, N., 2008. Mechanistic implications of plastic degradation. Polym. Degrad. Stab. 93, 561–584. doi:10.1016/j.polymdegradstab.2007.11.008.

Sun, Y., Wang, X., Xia, S., Zhao, J., 2021. New insights into oxytetracycline (OTC) adsorption behavior on polylactic acid microplastics undergoing microbial adhesion and degradation. Chem. Eng. J. 416, 129085. doi:10.1016/j.cej.2021.129085.

Thompson, R.C., Moore, C.J., Saal, F.S.V., Swan, S.H., 2009. Plastics, the environment and human health: current consensus and future trends. Philos. Trans. R. Soc. B Biol. Sci. 364, 2153–2166. doi:10.1098/rstb.2009.0053.

Wan, T., Lu, S., Cheng, W., Ren, J., Wang, M., Hu, B., Jia, Z., Li, Y., Sun, Y., 2019. A spectroscopic and theoretical investigation of interaction mechanisms of tetracycline and polystyrene nanospheres under different conditions. Environ. Pollut. 249, 398–405. doi:10.1016/j.envpol.2019.03.049.

Wang, C., Liang, S., Bai, L., Gu, X., Jin, X., Xian, Z., Wu, B., Ok, Y.S., Li, K., Wang, R., Zhong, H., Gu, C., 2021a. Structure-dependent surface catalytic degradation of cephalosporin antibiotics on the aged polyvinyl chloride microplastics. Water Res 206, 117732. doi:10.1016/j.watres.2021.117732.

Wang, F., Wang, B., Qu, H., Zhao, W., Duan, L., Zhang, Y., Zhou, Y., Yu, G., 2020a. The influence of nanoplastics on the toxic effects, bioaccumulation, biodegradation and enantioselectivity of ibuprofen in freshwater algae *Chlorella pyrenoidosa*. Environ. Pollut. 263, 114593. doi:10.1016/j.envpol.2020.114593.

Wang, H., Liu, P., Wang, M., Wu, X., Shi, Y., Huang, H., Gao, S., 2021b. Enhanced phototransformation of atorvastatin by polystyrene microplastics: critical role of aging. J. Hazard. Mater. 408, 124756. doi:10.1016/j.jhazmat.2020.124756.

Wang, H., Wu, Y., Feng, M., Tu, W., Xiao, T., Xiong, T., Ang, H., Yuan, X., Chew, J.W., 2018. Visible-light-driven removal of tetracycline antibiotics and reclamation of hydrogen energy from natural water matrices and wastewater by polymeric carbon nitride foam. Water Res 144, 215–225. doi:10.1016/j.watres.2018.07.025.

Wang, S., Xue, N., Li, W., Zhang, D., Pan, X., Luo, Y., 2020b. Selectively enrichment of antibiotics and ARGs by microplastics in river, estuary and marine waters. Sci. Total Environ. 708, 134594. doi:10.1016/j.scitotenv.2019.134594.

Wang, Y., Wang, X., Li, Y., Li, J., Liu, Y., Xia, S., Zhao, J., 2021c. Effects of exposure of polyethylene microplastics to air, water and soil on their adsorption behaviors for copper and tetracycline. Chem. Eng. J. 404, 126412. doi:10.1016/j.cej.2020.126412.

Wang, Z., Gao, J., Zhao, Y., Dai, H., Jia, J., Zhang, D., 2021d. Plastisphere enrich antibiotic resistance genes and potential pathogenic bacteria in sewage with pharmaceuticals. Sci. Total Environ. 768, 144663. doi:10.1016/j.scitotenv.2020.144663.

Watkinson, A.J., Murby, E.J., Kolpin, D.W., Costanzo, S.D., 2009. The occurrence of antibiotics in an urban watershed: From wastewater to drinking water. Sci. Total Environ. 407, 2711–2723. doi:10.1016/j.scitotenv.2008.11.059.

Williams, T., Walsh, C., Murray, K., Subir, M., 2020. Interactions of emerging contaminants with model colloidal microplastics, C60 fullerene, and natural organic matter-effect of surface functional group and adsorbate properties. Environ. Sci. Process. Impacts 22, 1190–1200. doi:10.1039/d0em00026d.

Wu, C., Zhang, K., Huang, X., Liu, J., 2016. Sorption of pharmaceuticals and personal care products to polyethylene debris. Environ. Sci. Pollut. Res. 23, 8819–8826. doi:10.1007/s11356-016-6121-7.

Xiong, Y., Zhao, J., Li, L., Wang, Y., Dai, X., Yu, F., Ma, J., 2020. Interfacial interaction between micro/nanoplastics and typical PPCPs and nanoplastics removal via electrosorption from an aqueous solution. Water Res 184, 116100. doi:10.1016/j.watres.2020.116100.

Xu, B., Huang, D., Liu, F., Alfaro, D., Lu, Z., Tang, C., Gan, J., Xu, J., 2020. Contrasting effects of microplastics on sorption of diazepam and phenanthrene in soil. J. Hazard. Mater. 124312. doi:10.1016/j.jhazmat.2020.124312.

Xu, B., Liu, F., Brookes, P.C., Xu, J., 2018a. The sorption kinetics and isotherms of sulfamethoxazole with polyethylene microplastics. Mar. Pollut. Bull. 131, 191–196. doi:10.1016/j.marpolbul.2018.04.027.

Xu, B., Liu, F., Brookes, P.C., Xu, J., 2018b. Microplastics play a minor role in tetracycline sorption in the presence of dissolved organic matter. Environ. Pollut. 240, 87–94. doi:10.1016/j.envpol.2018.04.113.

Yilimulati, M., Wang, L., Ma, X., Yang, C., Habibul, N., 2021. Adsorption of ciprofloxacin to functionalized nano-sized polystyrene plastic: Kinetics, thermochemistry and toxicity. Sci. Total Environ. 750, 142370. doi:10.1016/j.scitotenv.2020.142370.

You, X., Cao, X., Zhang, X., Guo, J., Sun, W., 2021. Unraveling individual and combined toxicity of nano/microplastics and ciprofloxacin to *Synechocystis* sp. at the cellular and molecular levels. Environ. Int. 157, 106842. doi:10.1016/j.envint.2021.106842.

Yu, F., Yang, C., Huang, G., Zhou, T., Zhao, Y., Ma, J., 2020. Interfacial interaction between diverse microplastics and tetracycline by adsorption in an aqueous solution. Sci. Total Environ. 721, 137729. doi:10.1016/j.scitotenv.2020.137729.

Yu, F., Yang, C., Zhu, Z., Bai, X., Ma, J., 2019. Adsorption behavior of organic pollutants and metals on micro/nanoplastics in the aquatic environment. Sci. Total Environ. 694, 133643. doi:10.1016/j.scitotenv.2019.133643.

Zettler, E.R., Mincer, T.J., Amaral-Zettler, L.A., 2013. Life in the "plastisphere": microbial communities on plastic marine debris. Environ. Sci. Technol. 47, 7137–7146. doi:10.1021/es401288x.

Zhang, C., Wang, Q., Zuo, Z., Ding, J., Xu, G., Zou, J., 2021a. Interactive effects of microplastics and tetracycline on bioaccumulation and biochemical status in Jian carp (*Cyprinus carpio var. Jian*). Front. Environ. Sci. 9, 1–9. doi:10.3389/fenvs.2021.764344.

Zhang, H., Wang, J., Zhou, B., Zhou, Y., Dai, Z., Zhou, Q., Chriestie, P., Luo, Y., 2018. Enhanced adsorption of oxytetracycline to weathered microplastic polystyrene: kinetics, isotherms and influencing factors. Environ. Pollut. 243, 1550–1557. doi:10.1016/j.envpol.2018.09.122.

Zhang, M., Xu, L., 2020a. Transport of micro- and nanoplastics in the environment: trojan-Horse effect for organic contaminants. Crit. Rev. Environ. Sci. Technol. 0, 1–37. doi:10.1080/10643389.2020.1845531.

Zhang, P., Yan, Z., Lu, G., Ji, Y., 2019a. Single and combined effects of microplastics and roxithromycin on *Daphnia magna*. Environ. Sci. Pollut. Res. 26, 17010–17020. doi:10.1007/s11356-019-05031-2.

Zhang, Q., Xu, E.G., Li, J., Chen, Q., Ma, L., Zeng, E.Y., Shi, H., 2020b. A review of Microplastics in table salt, drinking water, and air: direct human exposure. Environ. Sci. Technol. 54, 3740–3751. doi:10.1021/acs.est.9b04535.

Zhang, S., Ding, J., Razanajatovo, R.M., Jiang, H., Zou, H., Zhu, W., 2019b. Interactive effects of polystyrene microplastics and roxithromycin on bioaccumulation and biochemical status in the freshwater fish red tilapia (*Oreochromis niloticus*). Sci. Total Environ. 648, 1431–1439. doi:10.1016/j.scitotenv.2018.08.266.

Zhang, Y., Lu, J., Wu, J., Wang, J., Luo, Y., 2020c. Potential risks of microplastics combined with superbugs: Enrichment of antibiotic resistant bacteria on the surface of microplastics in mariculture system. Ecotoxicol. Environ. Saf. 187, 109852. doi:10.1016/j.ecoenv.2019.109852.

Zhang, Ye, Ni, F., He, J., Shen, F., Deng, S., Tian, D., Zhang, Yanzong, Liu, Y., Chen, C., Zou, J., 2021b. Mechanistic insight into different adsorption of norfloxacin on microplastics in simulated natural water and real surface water. Environ. Pollut. 284, 117537. doi:10.1016/j.envpol.2021.117537.

Zhang, Y.T., Chen, H., He, S., Wang, F., Liu, Y., Chen, M., Yao, G., Huang, Y., Chen, R., Xie, L., Mu, J., 2021c. Subchronic toxicity of dietary sulfamethazine and nanoplastics in marine medaka (*Oryzias melastigma*): insights from the gut microbiota and intestinal oxidative status. Ecotoxicol. Environ. Saf. 226, 112820. doi:10.1016/j.ecoenv.2021.112820.

Zhao, P., Cui, L., Zhao, W., Tian, Y., Li, M., Wang, Y.Y., Chen, Z., 2021a. Cotransport and deposition of colloidal polystyrene microplastic particles and tetracycline in porous media: the impact of ionic strength and cationic types. Sci. Total Environ. 753, 142064. doi:10.1016/j.scitotenv.2020.142064.

Zheng, J., Suh, S., 2019. Strategies to reduce the global carbon footprint of plastics. Nat. Clim. Chang. 9, 374–378. doi:10.1038/s41558-019-0459-z.

Zhou, R., Lu, G., Yan, Z., Jiang, R., Bao, X., Lu, P., 2020a. A review of the influences of microplastics on toxicity and transgenerational effects of pharmaceutical and personal care products in aquatic environment. Sci. Total Environ. 732, 139222. doi:10.1016/j.scitotenv.2020.139222.

Zhou, W., Han, Y., Tang, Y., Shi, W., Du, X., Sun, S., Liu, G., 2020b. Microplastics aggravate the bioaccumulation of two waterborne veterinary antibiotics in an edible bivalve species: potential mechanisms and implications for human health. Environ. Sci. Technol. 54, 8115–8122. doi:10.1021/acs.est.0c01575.

Zhou, W., Tang, Y., Du, X., Han, Y., Shi, W., Sun, S., Zhang, W., Zheng, H., Liu, G., 2021. Fine polystyrene microplastics render immune responses more vulnerable to two veterinary antibiotics in a bivalve species. Mar. Pollut. Bull. 164, 111995. doi:10.1016/j.marpolbul.2021.111995.