Sorption and Risk Assessment of Pharmaceuticals sorbed to Microplastics

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Outline

- **Emerging pollutants: what are they?**
- **Plastic pollution**
- **Microplastics and plastic litter in the environment**
- **Pharmaceuticals as emerging pollutants**
- **Sources and fate of pharmaceuticals and microplastics**
- **Interaction of microplastics with pharmaceuticals**
- **Adsorption of pharmaceuticals in plastic litter**
- **Environmental implications of the interaction of microplastics and pharmaceuticals**
  - ✓ **impact on the bioaccumulation**
  - ✓ **impact on the toxicity**
- **Interaction of microplastics with pharmaceuticals – impact on aquatic and terrestrial organisms (some laboratory studies)**

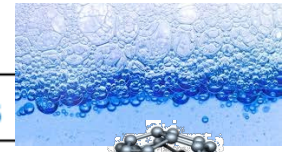
Examples of emerging pollutants

1. Pharmaceuticals

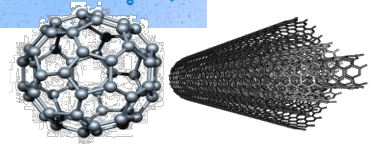
- Antibiotics
- Anti-inflammatory
- Hormones
- Psychiatric drugs
- Illicit drugs
- Veterinary medicine

2. Personal care products and cosmetics

- Cosmetic ingredients: bisphenols, parabens, triclosan
- UV filters
- Disinfectants
- Biocides



3. Industrial substances



- Surfactants
- Alkylphenols
- Perfluorinated compounds
- Nanoparticles

4. Other substances/issues

- Rare earth elements
- ~~Metalloids: Se~~
- Microplastics
- ~~Radionuclides~~
- Food packaging end containers
- Corrosion inhibitors

Emerging contaminants and issues of concern

5. Pesticides

- Fungicides: triazoles
- Herbicides
- Insecticides: neonicotinoids
- Bactericides
- Rodenticides
- Nematicides

6. Biological agents

- Pathogenic bacteria
- Multi-drug resistant microbes
- Antifungal resistance
- Antibiotic resistance genes

7. Unintentional persistent organic pollutants

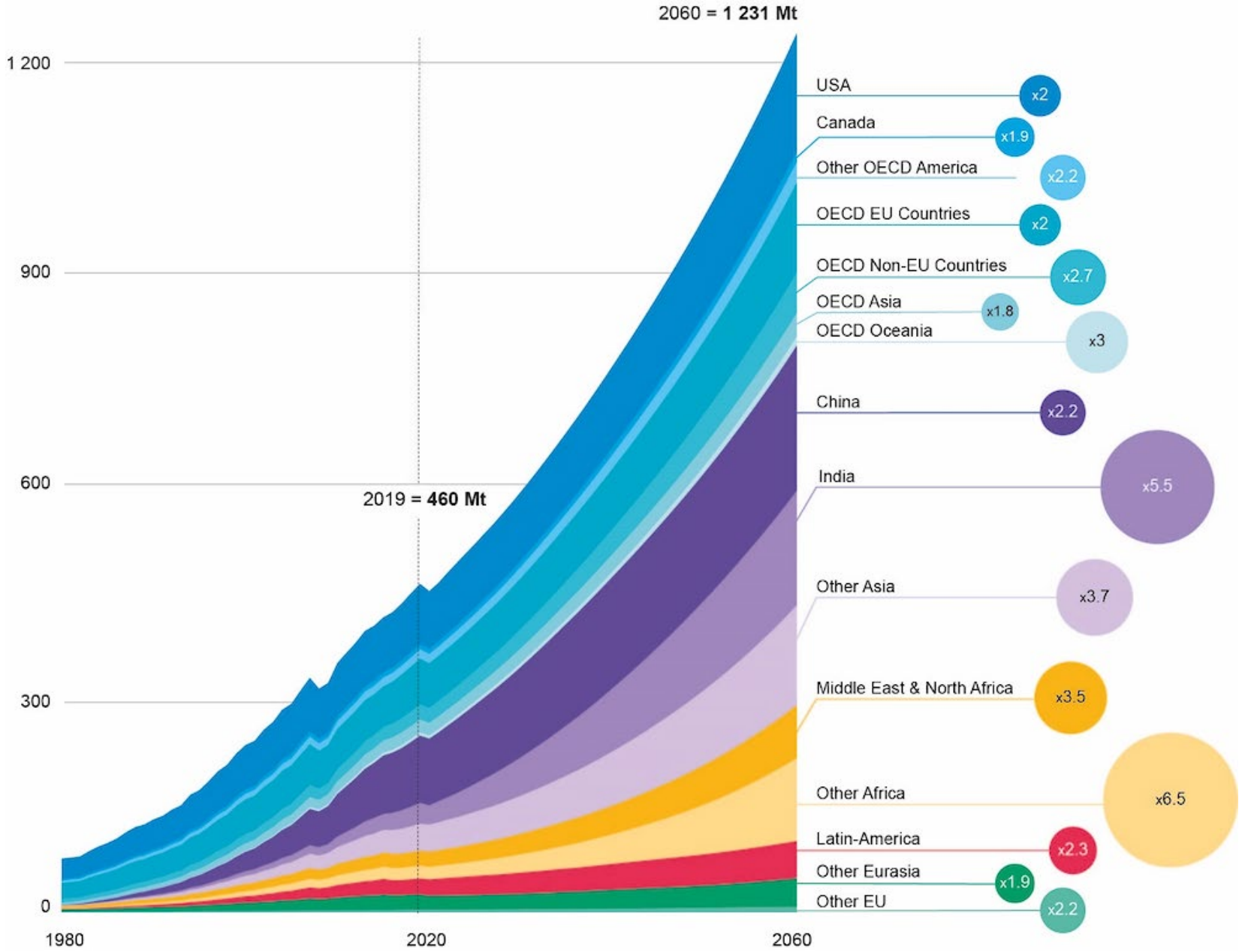
- Dioxins
- Brominated dioxins
- Halogenated polycyclic aromatic hydrocarbon
- Polychlorinated naphthalenes
- Environmentally persistent free radicals

Adapted from: Morin-Crini et al., Environ. Chem. Lett. 20 (2022) 2311

Plastic pollution

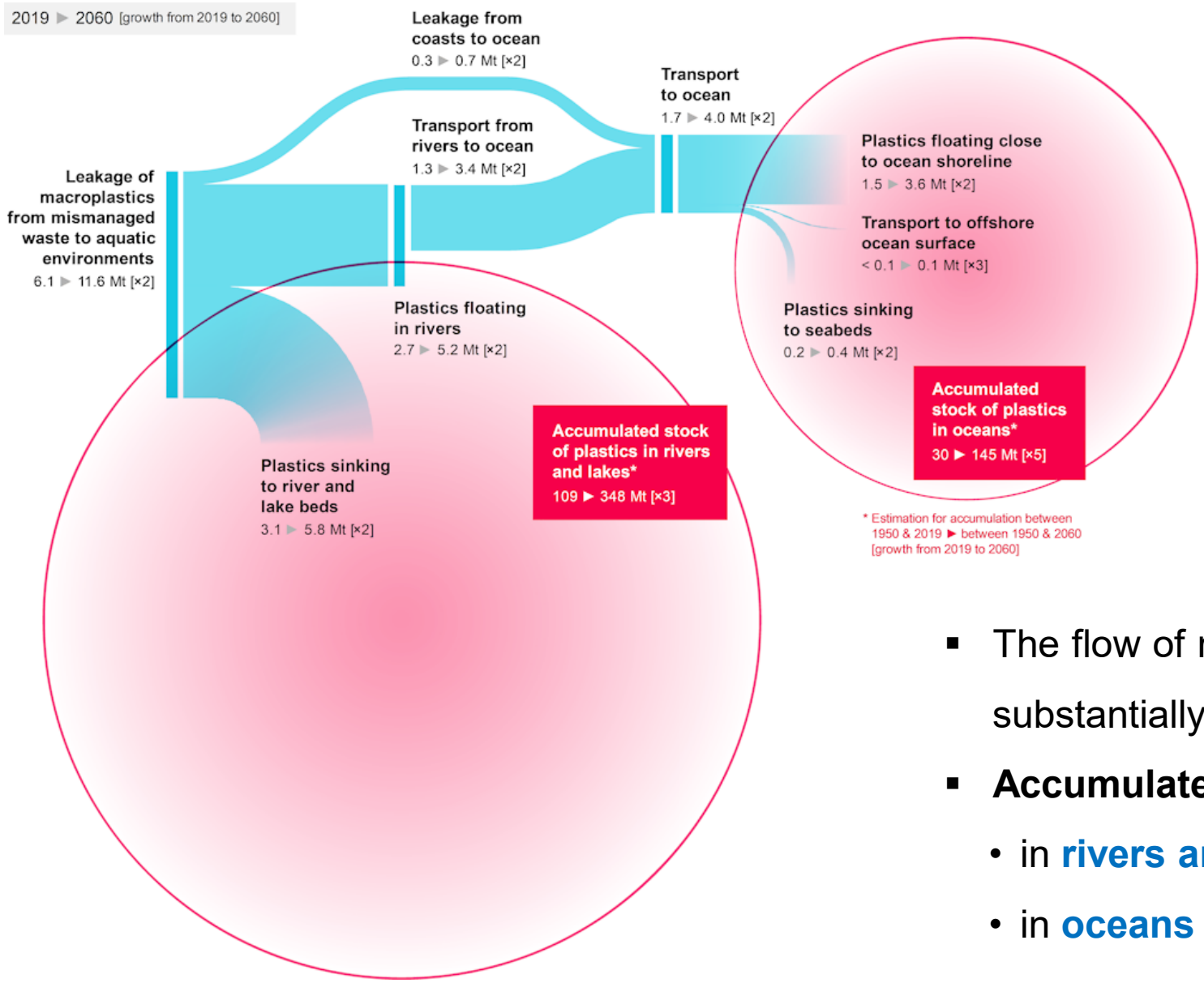
- **Plastic use** is projected to almost **triplicate from 460 Mt in 2019 to 1231 Mt in 2060**

- **Plastic use** will **grow fast in developing and emerging economies** in Africa and Asia



Source: OECD, 2022 – Global Plastics Outlook: Policy Scenarios to 2060

Plastic pollution



- **Leakage of plastics** into the aquatic environment is projected to **double between 2019 and 2060**

- The flow of macroplastics into rivers and lakes is substantially larger than outflows to the oceans
- **Accumulated stock of plastics in 2060**:
  - in **rivers and lakes** will **increase 3x** (348 Mt)
  - in **oceans** will **increase 5x** (145 Mt)

Source: OECD, 2022 – Global Plastics Outlook: Policy Scenarios to 2060

Ocean plastic a 'planetary crisis' - UN

BBC NEWS

5 December 2017 · Comments

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The Guardian

More than 170tn plastic particles afloat in oceans, say scientists

'Cleanup is futile' if production continues at current rate, amid rapid rise in marine pollution

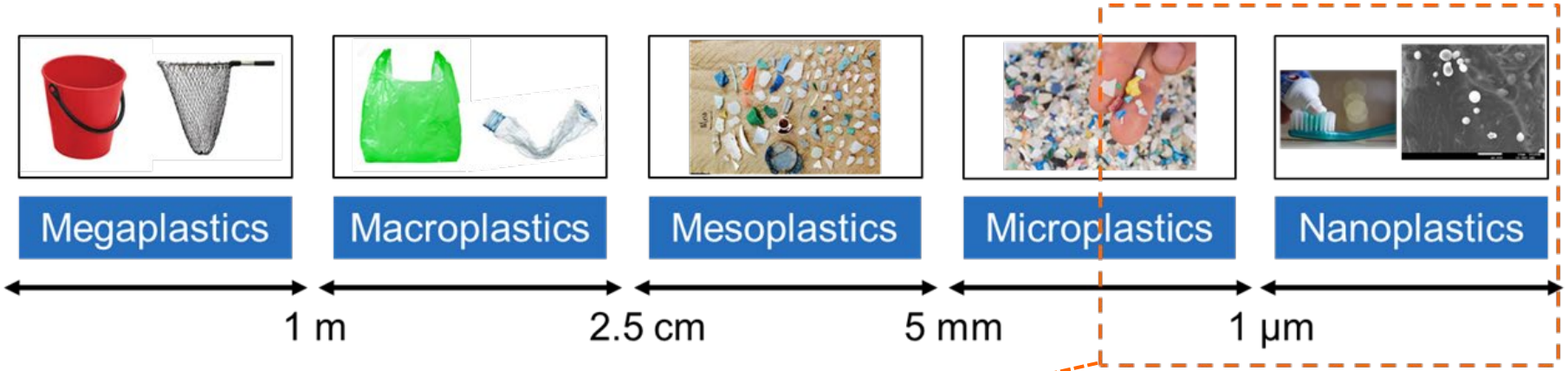
Helena Horton *and* Damian Carrington

Wed 8 Mar 2023 20.00 CET

Vultures scavenge for food among rubbish, including plastic waste, strewn on Costa del Este neighbourhood of Panama City. Photograph: Luis Acosta/AFP/Get

Microplastics in the environment

Plastic litter is mainly classified based on the size (Marine Strategy Framework Directive (MFSD, 2008/56/EC)):



Major environmental sources

Primary MPLs/NPLs

- Resin pellets for plastic production and maintenance
- Cosmetics and other personal care products

Secondary MPLs/NPLs

- From erosion and degradation processes of plastics debris

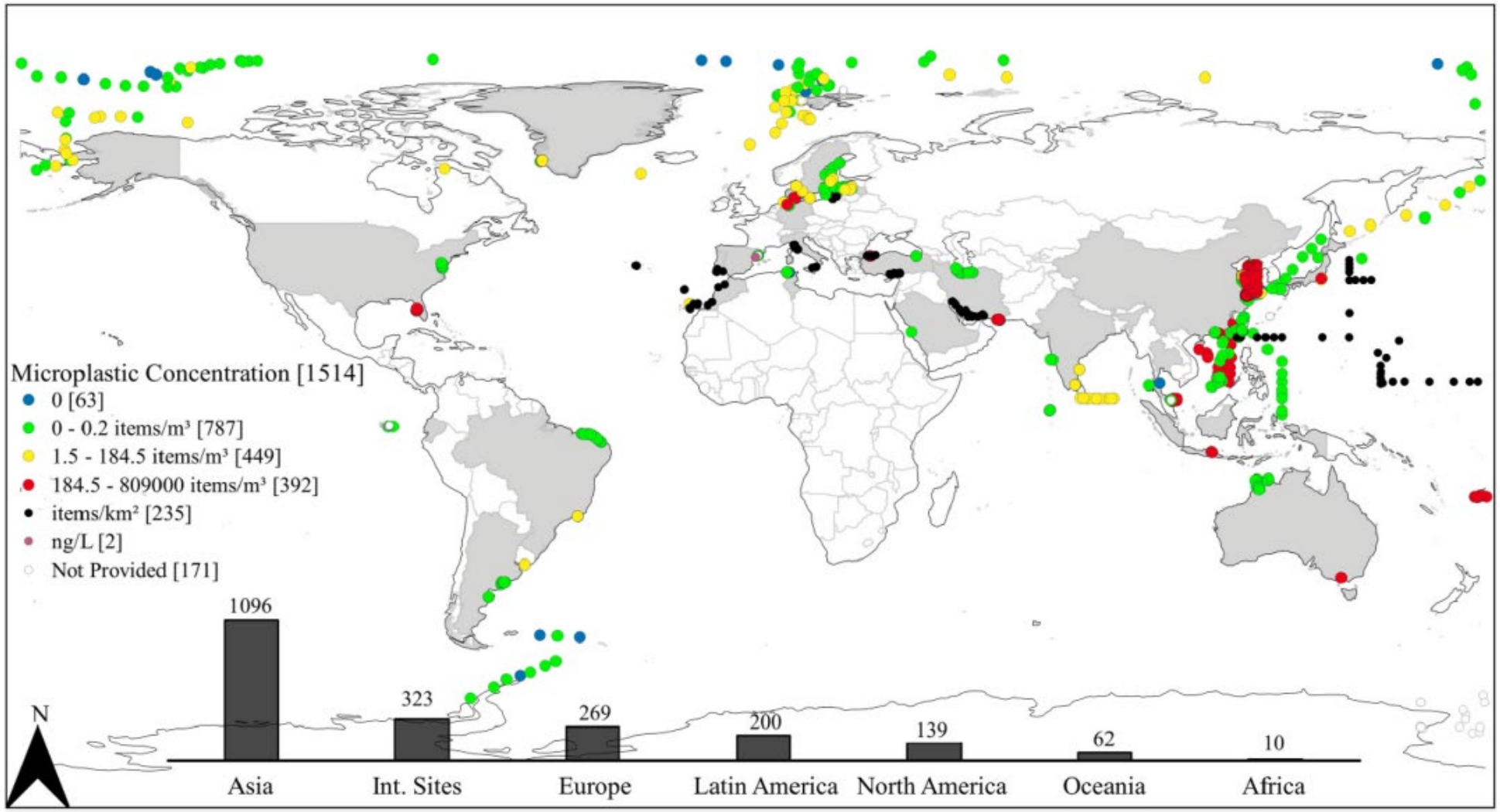
- Independently of the size, plastic results as **persistent debris**, because of its **durability** and **slow degradation** in the environment
- **Most common MPs found in the environment:** *polyethylene terephthalate (PET), polyester, polyethylene (PE), polyvinylchloride (PVC), polypropylene (PP), polyamide (PA), polystyrene (PS)…*

Source: Picó & Barceló, ACS Omega 4 (2019) 6709

Microplastics in the environment

- **Microplastics** are **worldwide distributed** along coastal and maritime zones of all continents
- **Asia, Europe** and **Latin America** with a high number of studies

Occurrence of MPs in **marine and coastal waters**

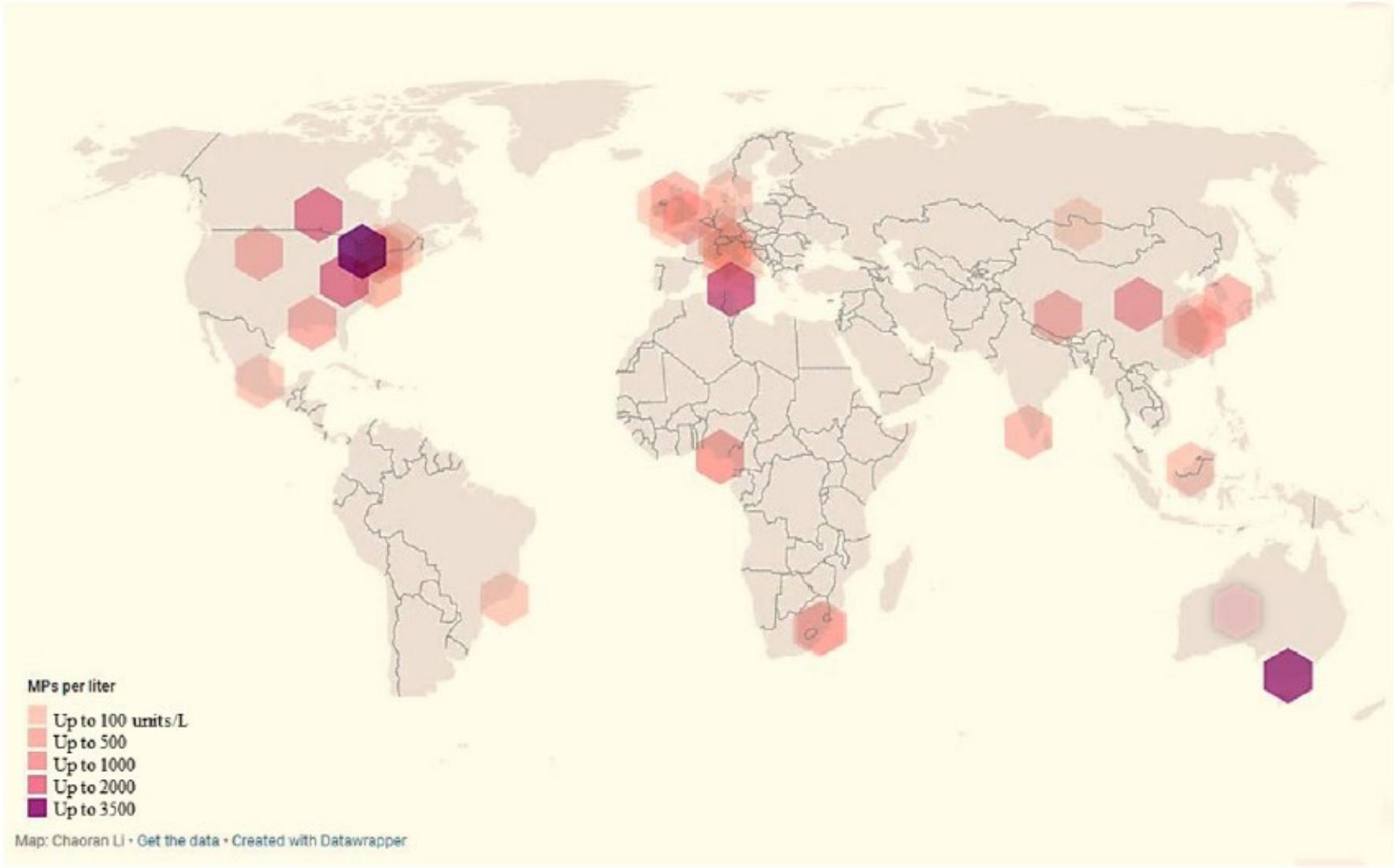


Source: Nunes et al., Environ. Pollut. 316 (2023) 120692

Microplastics in the environment

- Studies on the occurrence and distribution of **microplastics in freshwater systems** are **scarce**

Occurrence of MPs in **freshwater systems**

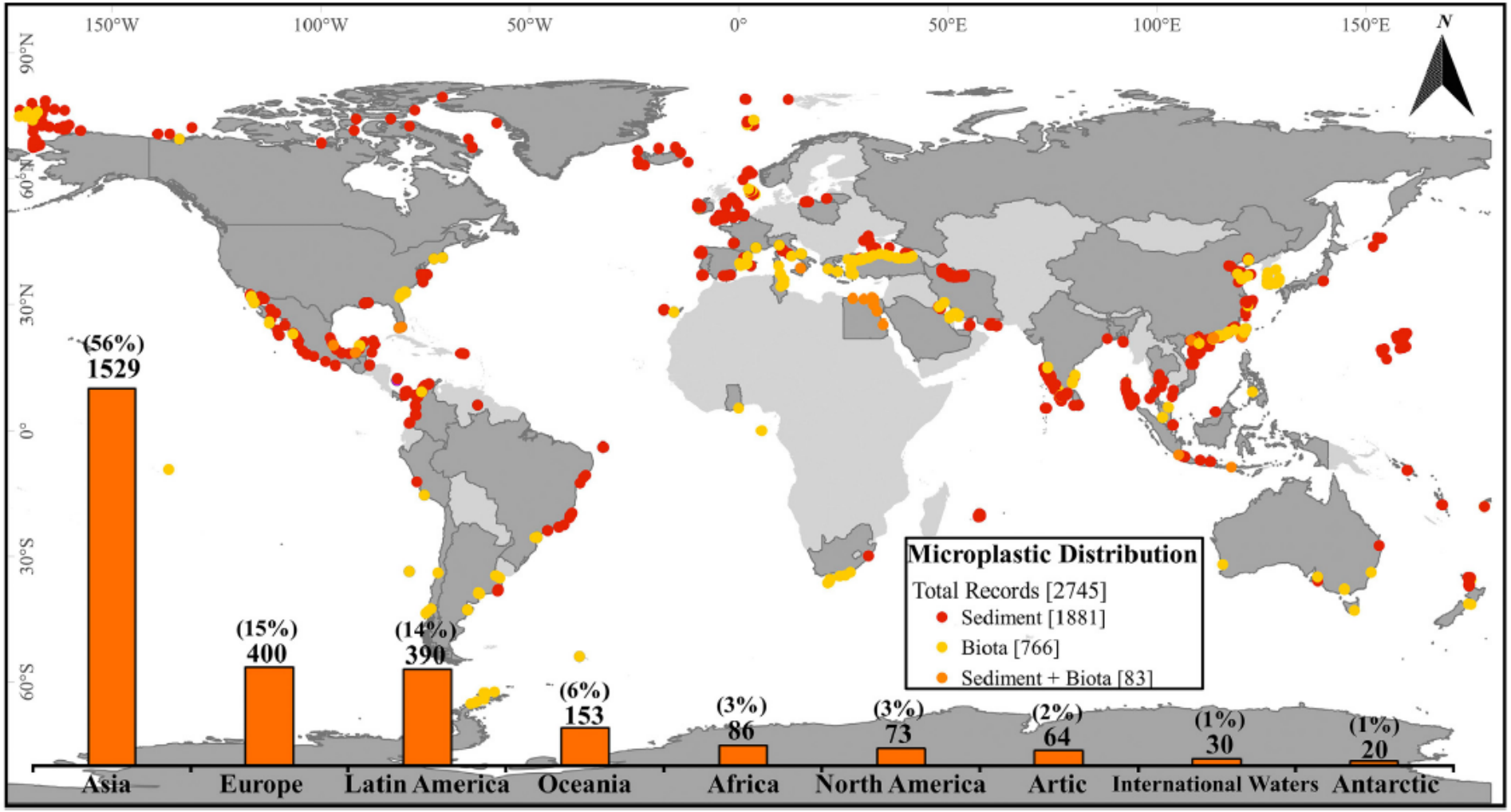


Source: Li et al., STOTEN 707 (2020) 135578

Microplastics in the environment

- **Microplastics** have been detected in **sediments and biota** worldwide
- Most results were reported in **Asia** (e.g., China, India)**, Europe** and **Latin America**

Occurrence of MPs in **sediments** and **biota**



Source: Nunes et al., STOTEN 865 (2023) 161293

Plastic litter in the environment

ARTICLES
https://doi.org/10.1038/s41893-021-00722-6
nature sustainability
Check for updates

Floating macrolitter leaked from Europe into the ocean

Daniel González-Fernández[1], Andrés Cózar[1], Georg Hanke[2], Josué Viejo[1], Carmen Morales-Caselles[1], Rigers Bakiu[3], Damià Barceló[4,5], Filipa Bessa[6], Antoine Bruge[7], María Cabrera[8], Javier Castro-Jiménez[9,26], Mel Constant[10], Roberto Crosti[11], Yuri Galletti[12], Ahmet E. Kideys[13], Nino Machitadze[14], Joana Pereira de Brito[15], Maria Pogojeva[16], Nuno Ratola[17], Júlia Rigueira[18], Elisa Rojo-Nieto[19,27], Oksana Savenko[20,21], Rosanna I. Schöneich-Argent[22,28], Grzegorz Siedlewicz[23], Giuseppe Suaria[24] and Myrto Tourgeli[25]

- Between **307 and 925 million litter items** are **released** annually **from Europe into the ocean**

- 82% observed litter is formed by **fragments** and **single-use plastics**

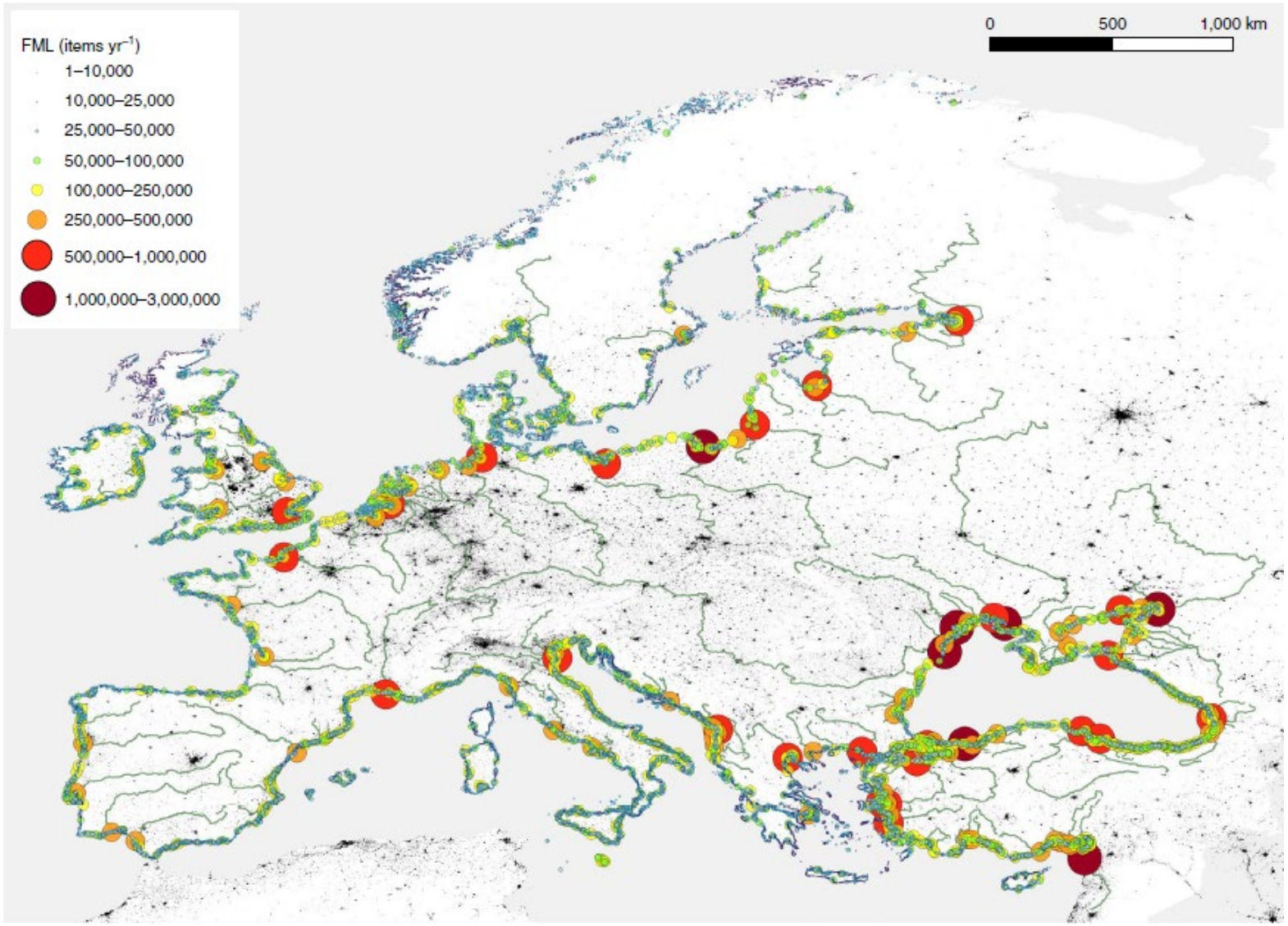


Fig. 4 | Spatial distribution of FML from Europe into the ocean. Spatial distribution of FML from Europe into the ocean based on mean-based modelled estimates. The coloured dots represent litter inputs predicted on the basis of the MW in each individual drainage basin.

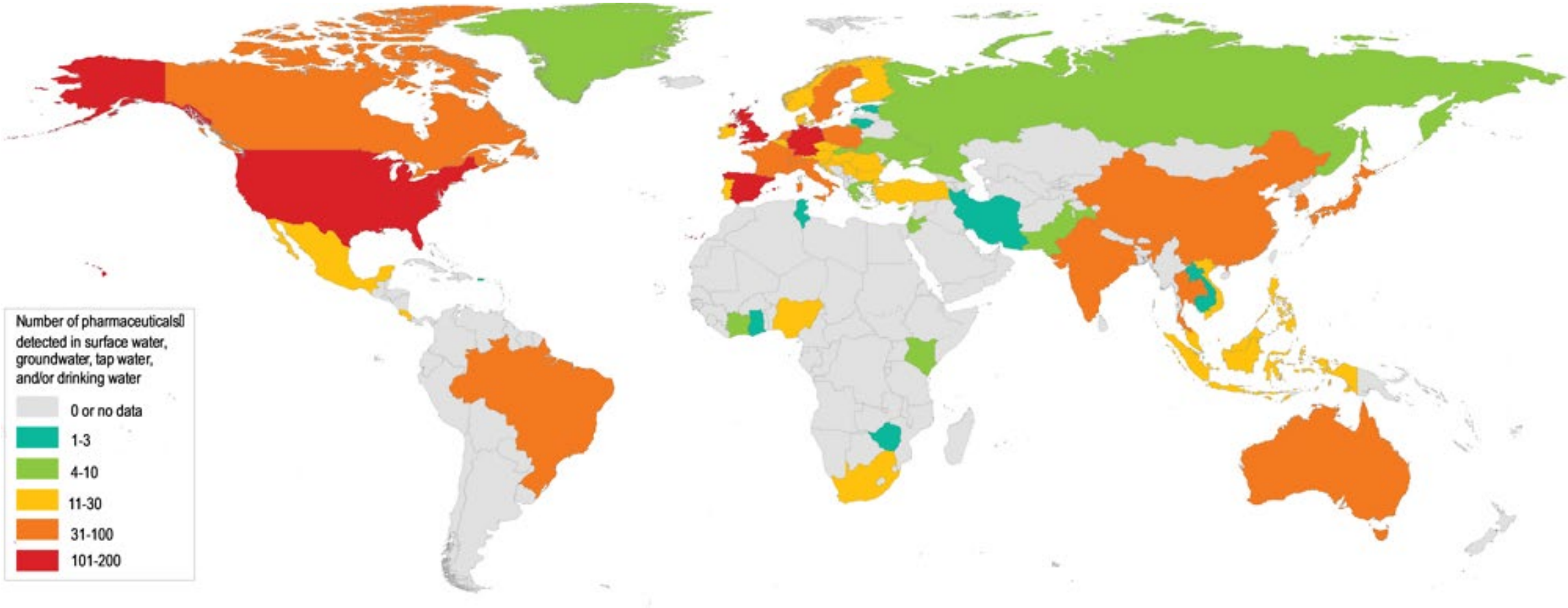
Pharmaceuticals as emerging pollutants

- ✓ Heterogeneous group
- ✓ Most of compounds are polar
- ✓ Developed to have a specific mode of action
- ✓ Resistant to biodegradation
- ✓ Do not need to persist in the environment, since they are continuously introduced → **pseudo-persistent contaminants**

+ 4000 pharmaceuticals

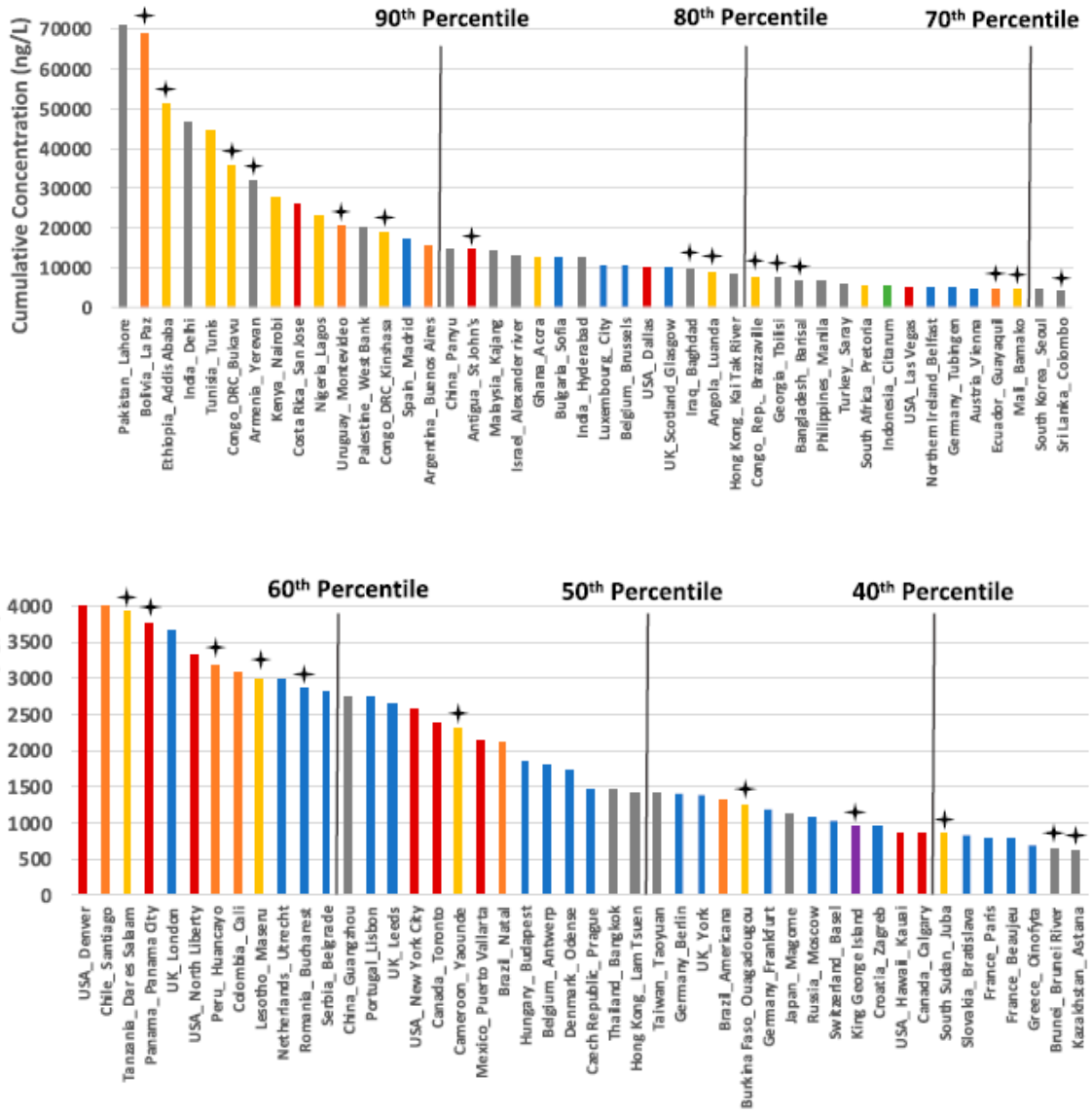
Pharmaceuticals in the environment

- **Pharmaceuticals** are **ubiquitously present** in the water bodies **worldwide**
- Nowadays there are a **few data** on the presence of pharmaceuticals **in developing countries**

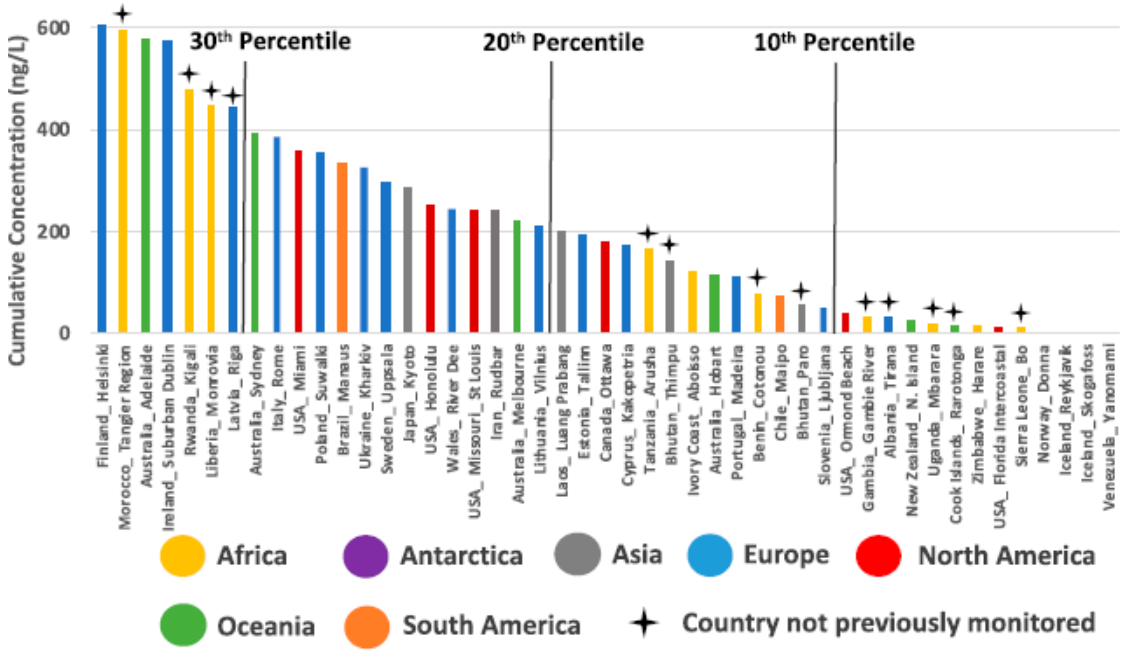


Source: aus der Beek et al., 2016 in Pharmaceutical Residues in Freshwater: Hazards and Policy Responses | OECD iLibrary (oecd-ilibrary.org)

Pharmaceuticals in the environment



- Global-scale study of the presence of **61 pharmaceuticals** in river's world covering **104 countries** across **all continents**



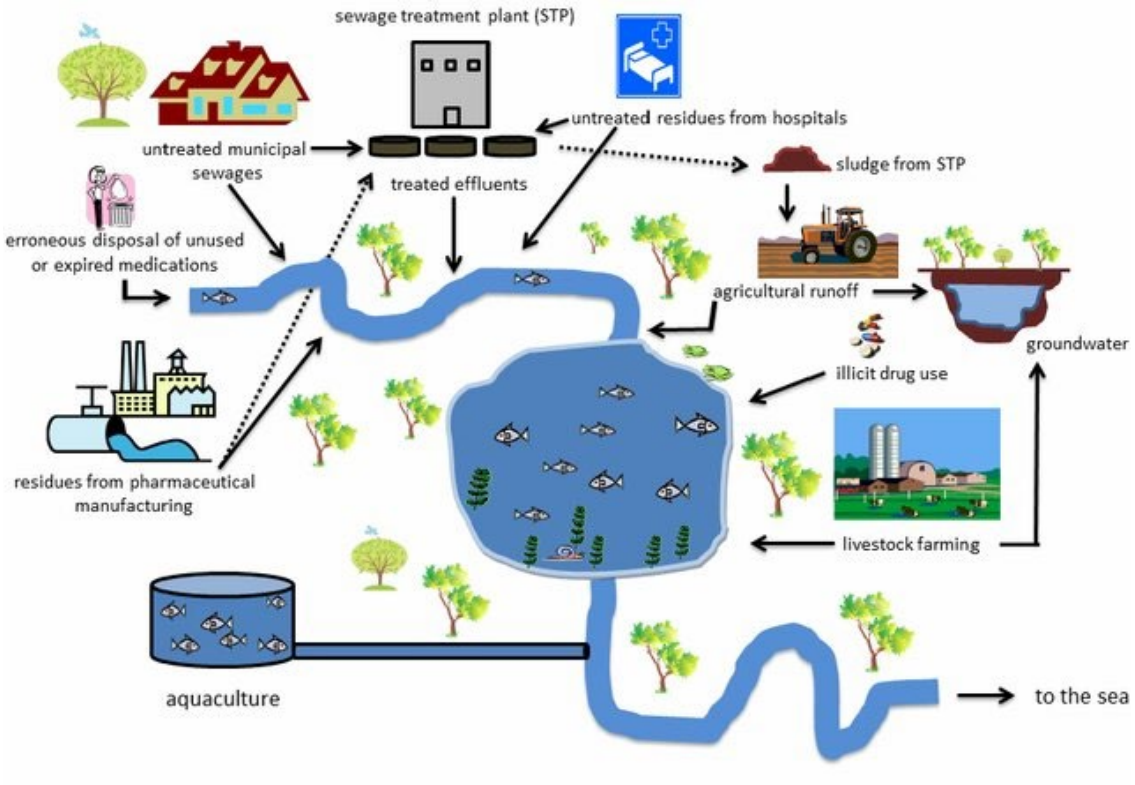
- Highest cumulative concentrations found in **Asia**, **Africa** and **South America**
- **Most contaminated sites**:

  - located in **low- to middle-income countries;**
  - associated with areas with **poor wastewater and waste management** and pharmaceutical manufacturing

Source: Wilkinson et al., PNAS 8 (2022) e2113947119

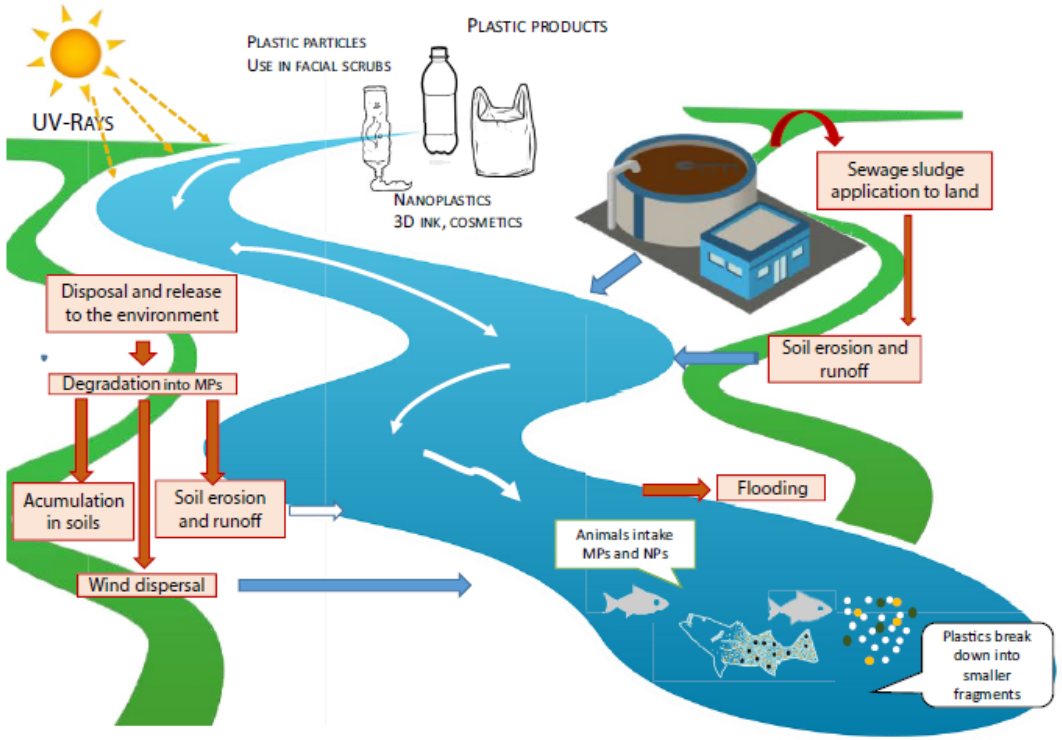
Sources and fate of contaminants in the environment

Pharmaceuticals



Source: Matozzo, ISJ 11 (2014) 163

Microplastics



Source: Picó et al., TrAC 113 (2019) 409

- **Microplastics** and **pharmaceuticals** have common sources and fate in the environment
- **Microplastics** are **ubiquitously distributed** in the environment together with other organic contaminants, such as pharmaceuticals, personal care products, pesticides, endocrine disruptor compounds, etc.

Environmental Science & Technology

pubs.acs.org/est

Critical Review

Interaction of Microplastics with Antibiotics in Aquatic Environment: Distribution, Adsorption, and Toxicity

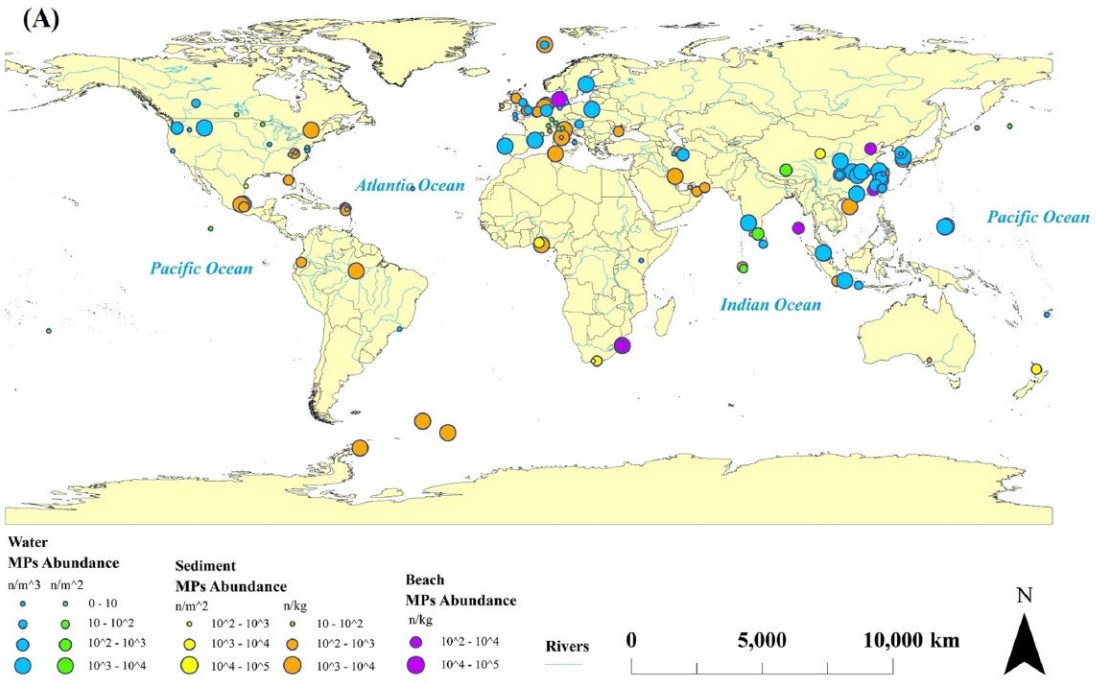
Yanhua Wang, Yanni Yang, Xia Liu, Jian Zhao,* Ruihan Liu, and Baoshan Xing*

Cite This: *Environ. Sci. Technol.* 2021, 55, 15579–15595

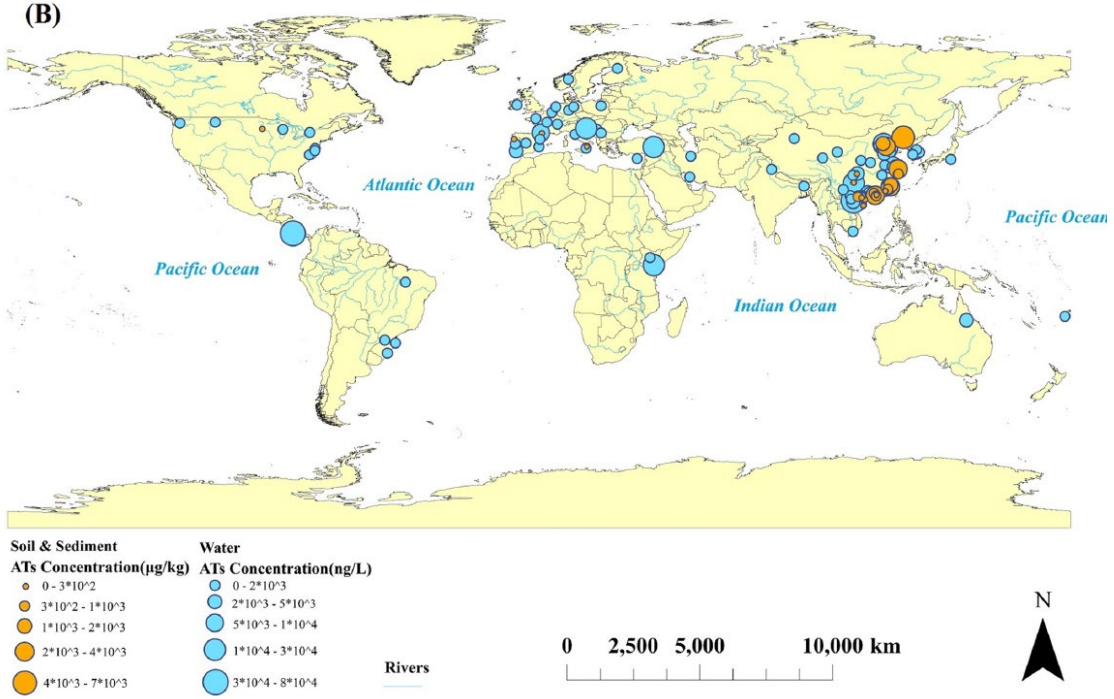
Read Online

Microplastics can **sorb organic contaminants** from the surrounding water column, acting as **vector or carrier**

Microplastics



Antibiotics



Interaction of microplastics with pharmaceuticals

- **Adsorption of pharmaceuticals on microplastics** will depend on different factors:

Environmental factors

- pH
- Dissolved organic matter
- Salinity
- Mechanical weathering
- Photodegradation

Microplastics properties

- Type of polymer
- Surface charge
- Surface area
- Degree of weathering

Pharmaceuticals properties

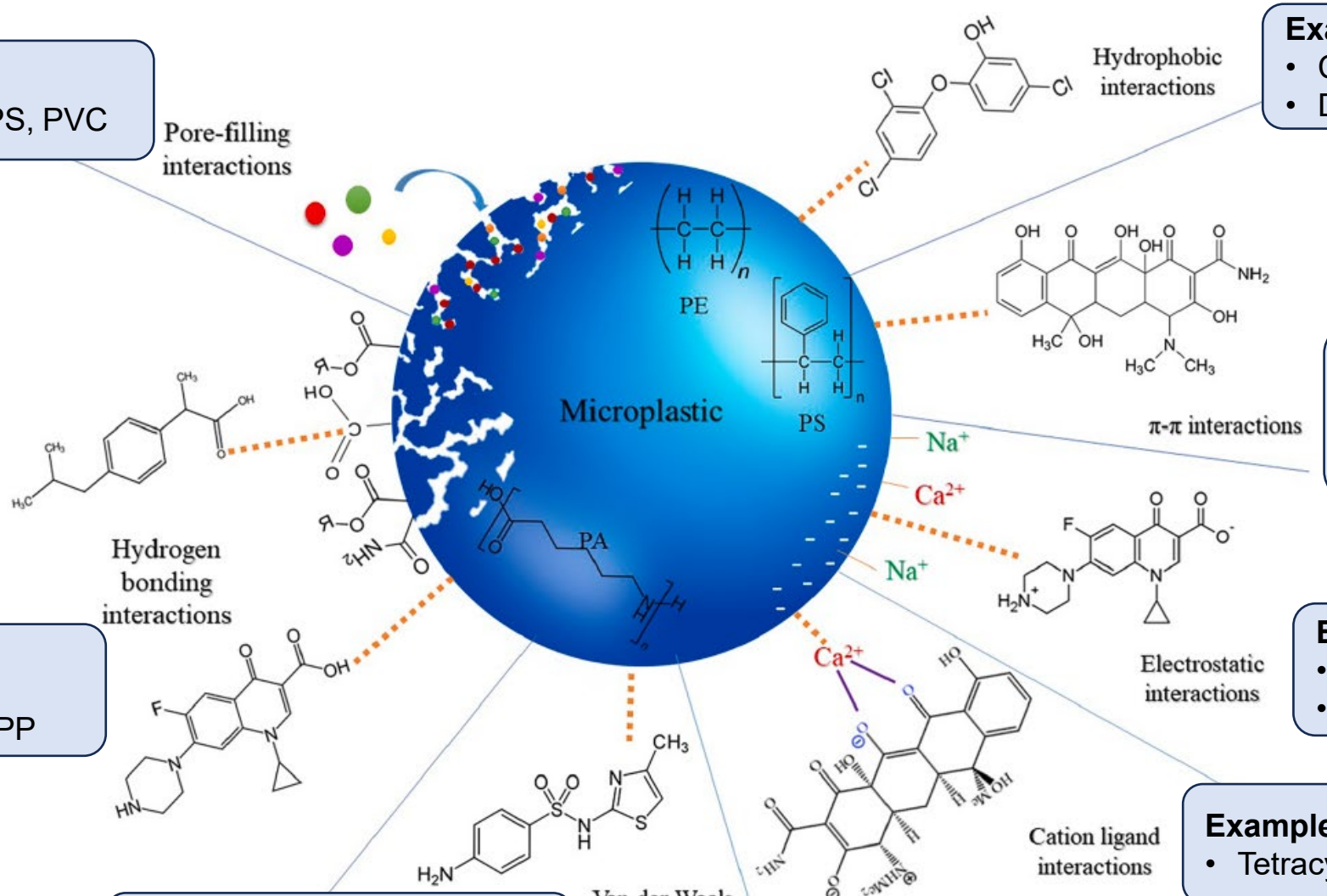
- Octanol-water partition coefficient (log K_{OW})
- p*K*a

- Microplastics and pharmaceuticals properties will be also important on the **desorption of pharmaceuticals** under **physiological conditions**, once ingested by organisms

Adapted from: Atugoda et al., Environ Int. 149 (2021) 106367; Santos et al., CSCEE 3 (2021) 100079

Interaction of microplastics with pharmaceuticals

➢ **Main mechanisms of interaction between pharmaceuticals and microplastics**



Examples:
- Ciprofloxacin/PS, PVC

Examples:
- Ciprofloxacin/PE
- Diclofenac/PS, PE, PP

Examples:
- Tetracycline/PS
- Ibuprofen, diclofenac, naproxen/PS

Examples:
- Ciprofloxacin/PA
- Diclofenac/PS, PE, PP

Examples:
- Ciprofloxacin/PE
- Sertraline/PE

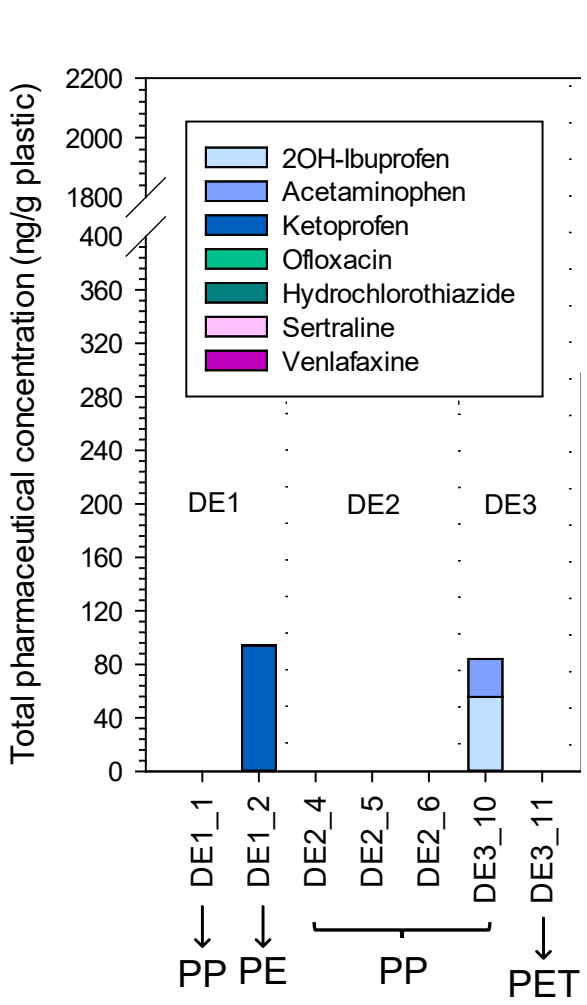
Examples:
- Tetracycline/PE, PS, PVC

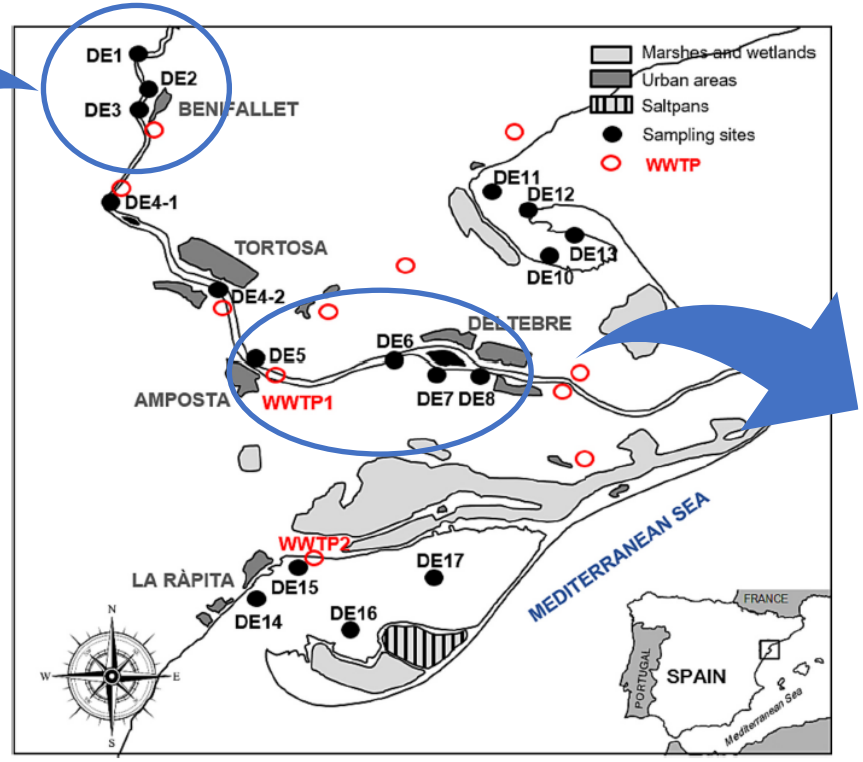
Examples:
- Sulfamethoxazole/PE

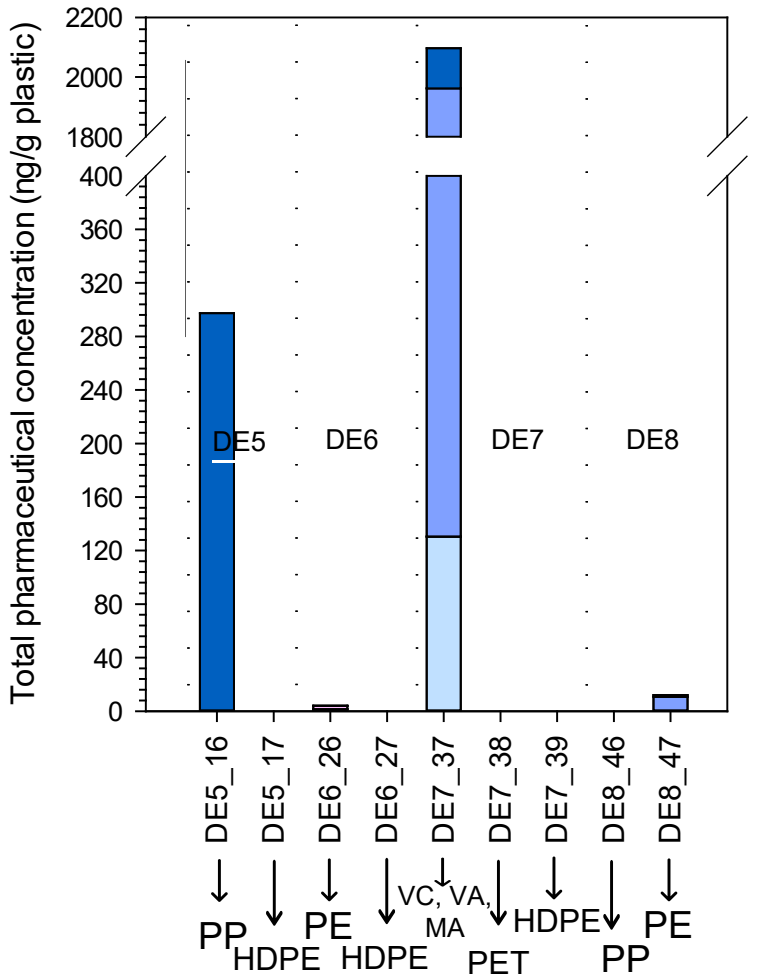
Adapted from: Atugoda et al., Environ Int. 149 (2021) 106367; Upadhyay et al., Environ. Monit. Assess 194 (2022) 803

Adsorption of pharmaceuticals in plastic litter: a case study in the Ebro River (Spain)

- **4** types of **plastic polymers** (PP, PE, PET, copolymer VC, VA, MA)
- **7 pharmaceuticals** adsorbed in plastic litter



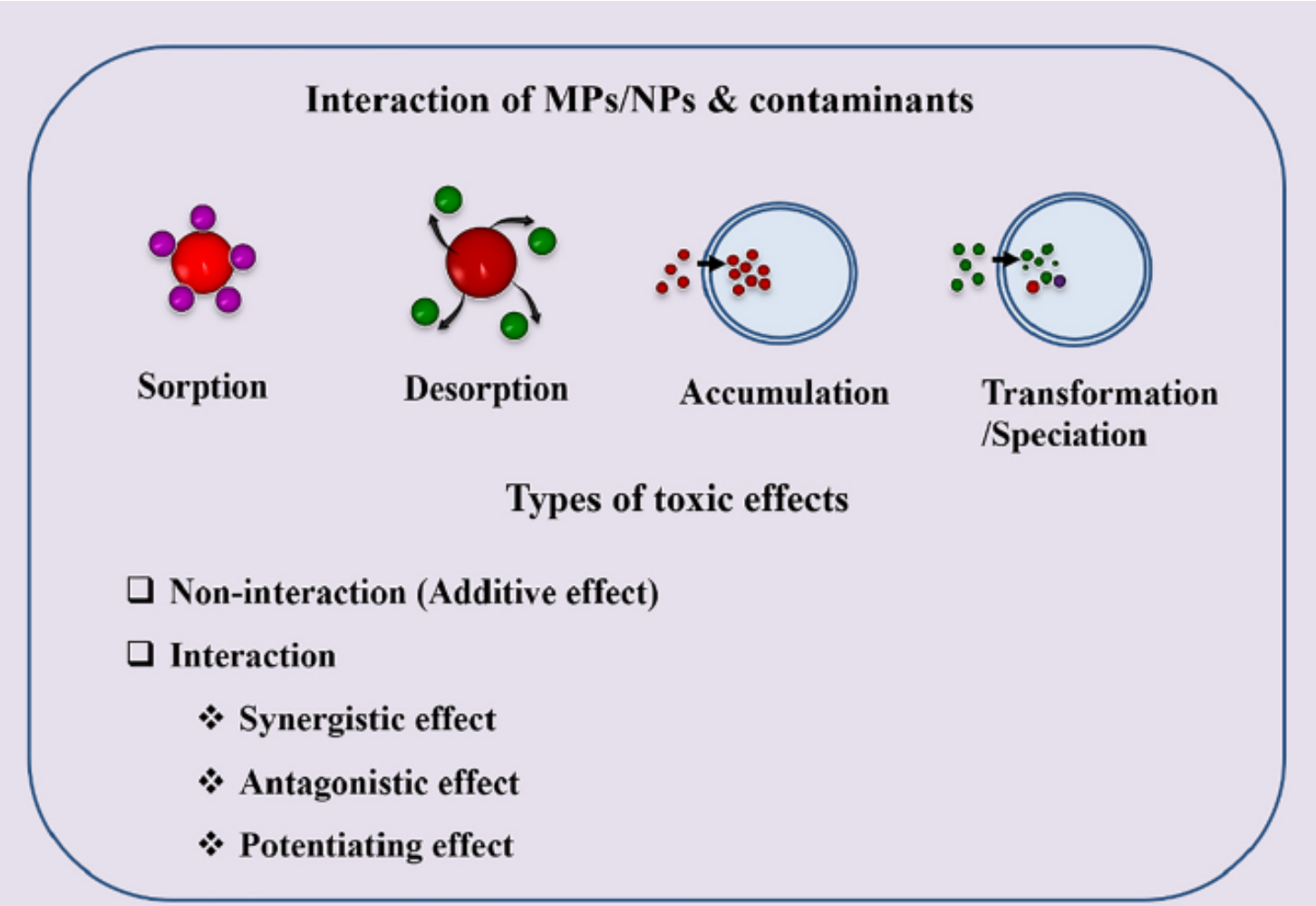




Analgesic/anti-inflammatories (e.g., ketoprofen, acetaminophen) were the most frequently detected

Adapted from: Castaño-Ortiz et al., STOTEN 906 (2024) 167467

Environmental implications of the interaction of microplastics and pharmaceuticals



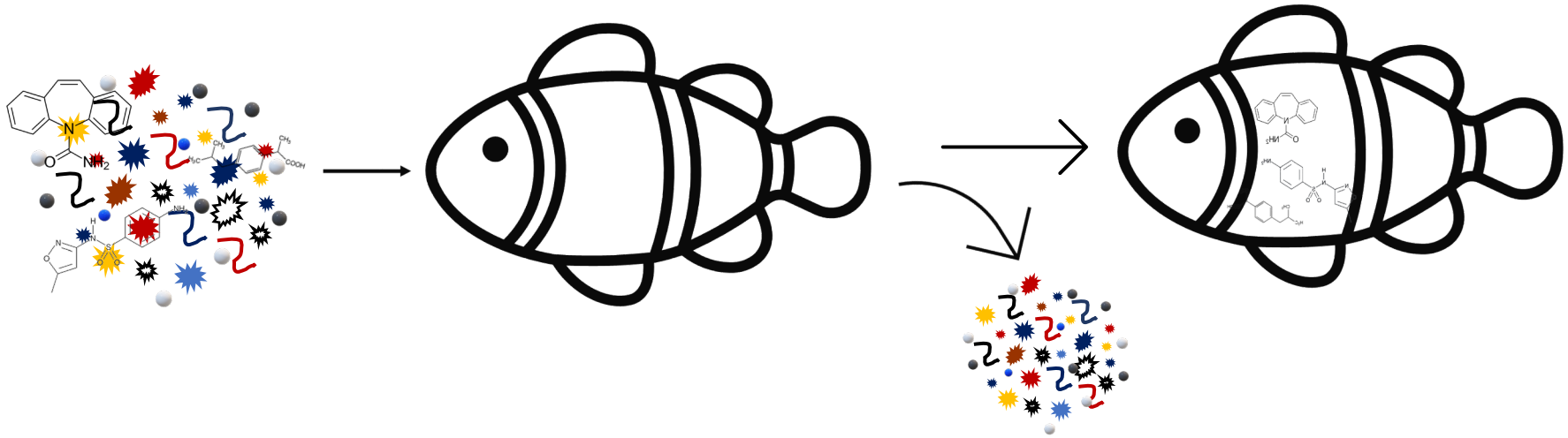
Adapted from: Bhagat et al., J. Hazard. Mat. 405 (2021) 123913

- The **interaction of pharmaceuticals and MPs** may affect their absorption, distribution, metabolism, and excretion, which may result in unpredictable ecological responses.
- The presence of **MPs/NPs can decrease or increase a negative effect of a co-contaminant** or in some cases can have a neutral effect. The generated effect is a matter of dose of each contaminant and the ratios of the concentration of the contaminants within a mixture.

Adapted from: Agathokleous et al., J. Hazard. Mat 417 (2021) 126084; Santos et al., CSCEE 3 (2021) 100079

Environmental implications of the interaction of microplastics and pharmaceuticals - Bioaccumulation

1) Microplastics potentiate bioaccumulation of pharmaceuticals

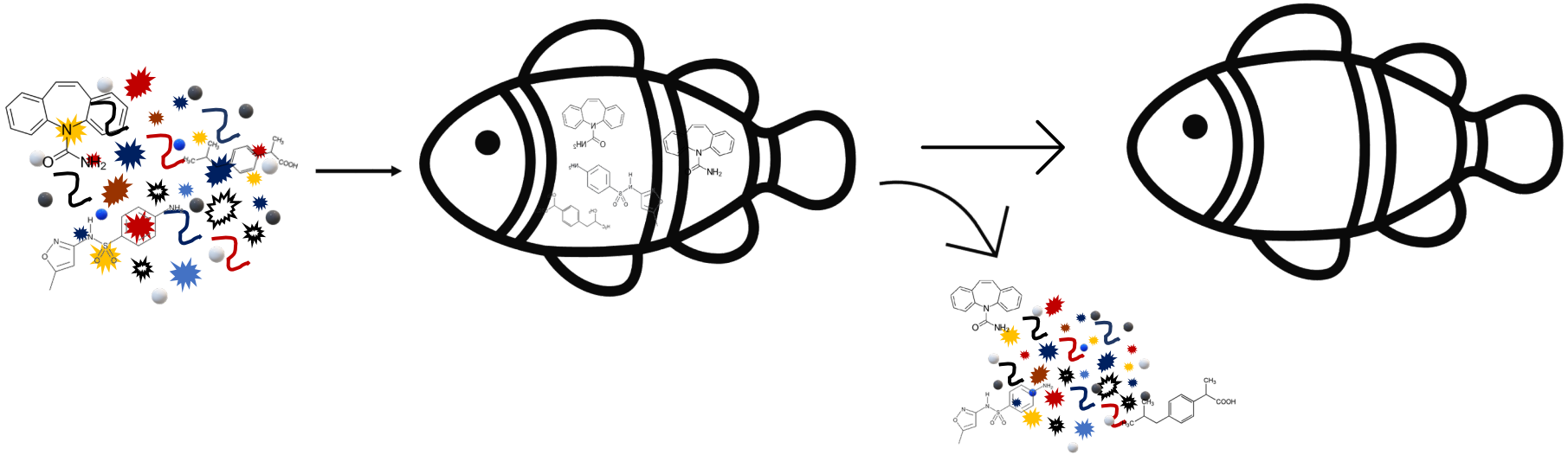


- **Enhancement** of the bioaccumulation of pharmaceuticals was found in **fish** and **bivalves**. Possible causes:
  - ✓ Desorption of pharmaceuticals from microplastics once ingested by organisms
  - ✓ Inhibition of the metabolization of pharmaceuticals by microplastics

Source: Santos et al., CSCEE 3 (2021) 100079

Environmental implications of the interaction of microplastics and pharmaceuticals - Bioaccumulation

2) Microplastics decrease bioaccumulation of pharmaceuticals

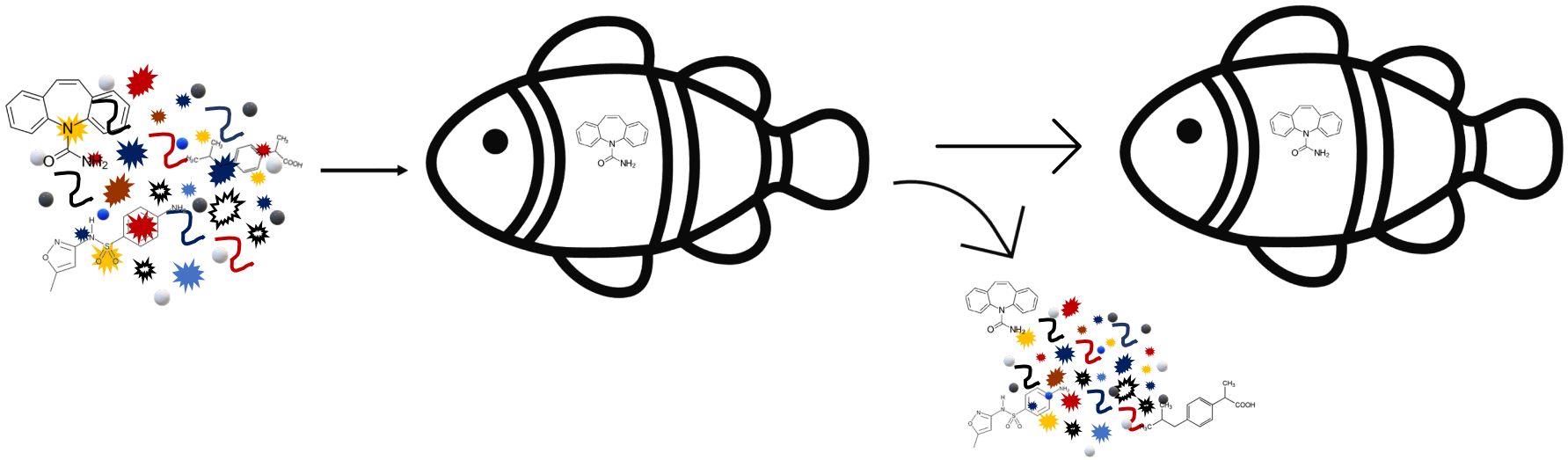


- **Decrease** of the bioaccumulation of pharmaceuticals due to:
  - ✓ Adsorption of pharmaceuticals to microplastics, removing them from water column (not bioavailable)
  - ✓ Ingested microplastics adsorb pharmaceuticals already bioaccumulated, decreasing their body burden
  - ✓ Microplastics promote degradation of pharmaceuticals

Source: Santos et al., CSCEE 3 (2021) 100079

Environmental implications of the interaction of microplastics and pharmaceuticals - Bioaccumulation

3) Microplastics do no have impact on the bioaccumulation of pharmaceuticals



- Ingested contaminated microplastics do **not have effect on the bioaccumulation** of pharmaceuticals

  ✓ Equilibrium between microplastics, pharmaceuticals and aquatic organisms was reached before the ingestion

  ✓ Fraction of pharmaceuticals accumulated from ingested microplastics can be negligible

Source: Santos et al., CSCEE 3 (2021) 100079

Environmental implications of the interaction of microplastics and pharmaceuticals - Toxicity

- **Psychiatric drugs** and **antibiotics** are among the **most studied** pharmaceuticals (33% literature each)
- Most of the ecotoxicological studies focused on **Polystyrene**

Microplastics might differently influence the toxicity of pharmaceuticals

Pharmaceutical	MPs-NPs	Organism	Toxicity	Endpoint
Ibuprofen	PS-NPs	Microalgae	↓	Growth inhibition rate
Roxithromycin	PS-MPs	Fish	↓	Neurotoxicity
Roxithromycin	PS-MPs	Fish	↓	Oxidative damage
Cefalexin	PE-MPs	Fish	↓	Predatory performance
Doxycycline	MPs	Microalgae	↑	Growth inhibition rate
Roxithromycin	PS-MPs	*Daphnia magna*	↑	SOD activity
Florfenicol	MPs	Clams	↑	Feeding activity
Venlafaxine	PVC-MPs	Fish	↑	Lipid peroxidation
Amitriptyline	PS-MPs	Fish	=	Development
Amitriptyline	PS-MPs	Fish	=	Swimming behavior
Fluoxetine	PS-NPs	Fish cell lines	=	Death

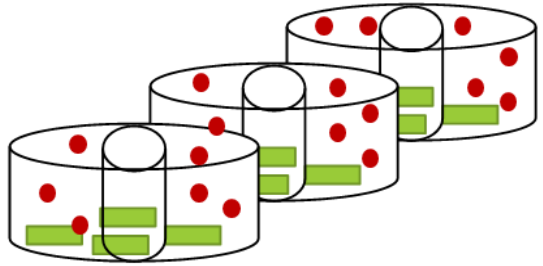
Source: Santos et al., CSCEE 3 (2021) 100079

Interaction of microplastics with pharmaceuticals – impact on aquatic organisms

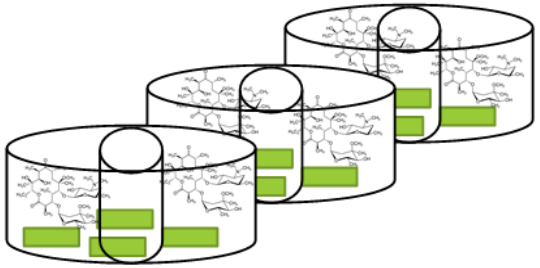
Combined exposure of river biofilms to clarithromycin and polyethylene microplastics

Exposure of river biofilm to contaminants in artificial mesocosms

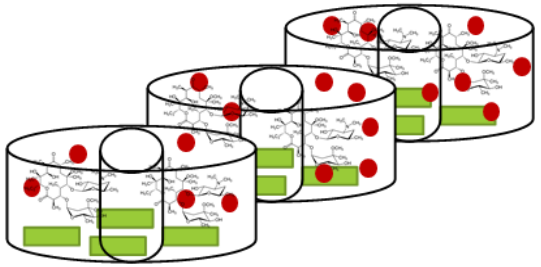
Control



Polyethylene (PE) 1 mg/L



Clarithromycin 50 µg/L

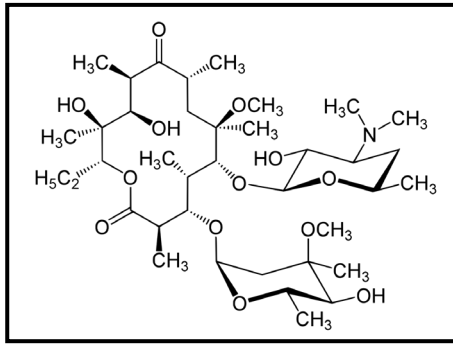


PE 1 mg/L + clarithromycin 50 µg/L

Red Fluorescent Polyethylene MPs

Size: 10-45 µm

Conc. = 1 mg/L



Clarithromycin

Conc. = 50 µg/L

EC_{50}(72h) = 46 µg/L (algae)

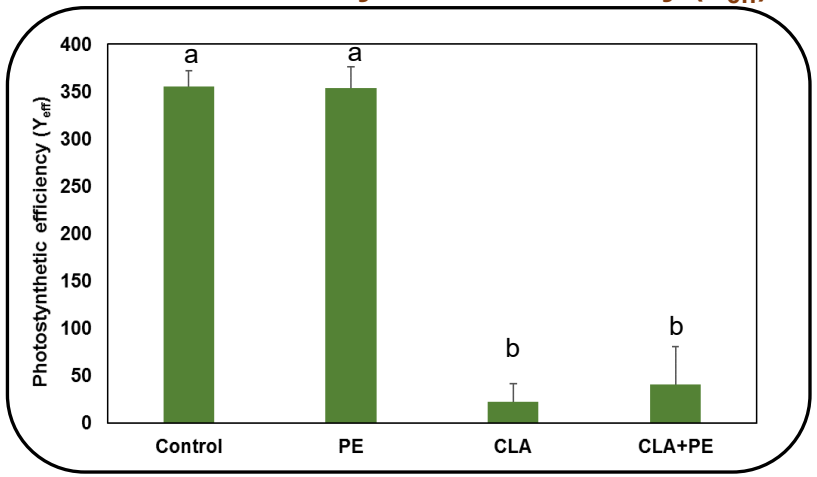
Experimental conditions:

- Biofilm colonization period → 5 weeks
- Controlled temperature (± 18 ºC)
- Constant day-night cycle (12h/12h)
- Constant agitation
- Exposure time: 72h

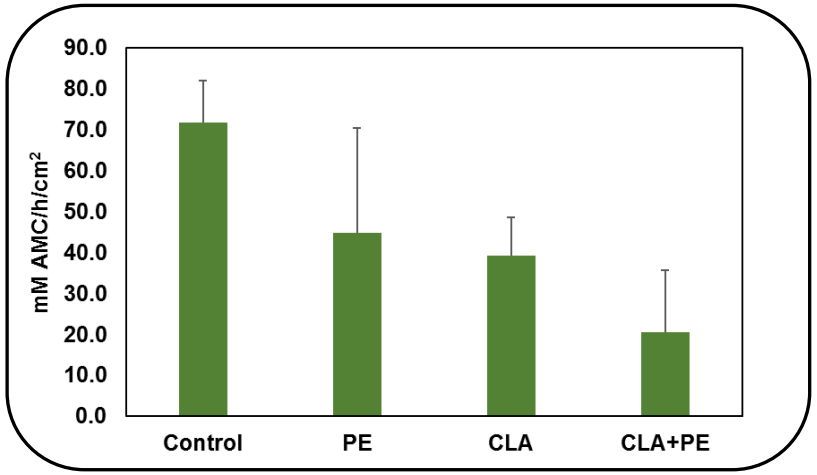
Combined exposure of river biofilms to clarithromycin and polyethylene microplastics

Structural and functional parameters of river biofilms were evaluated at the end of the experiment (72h)

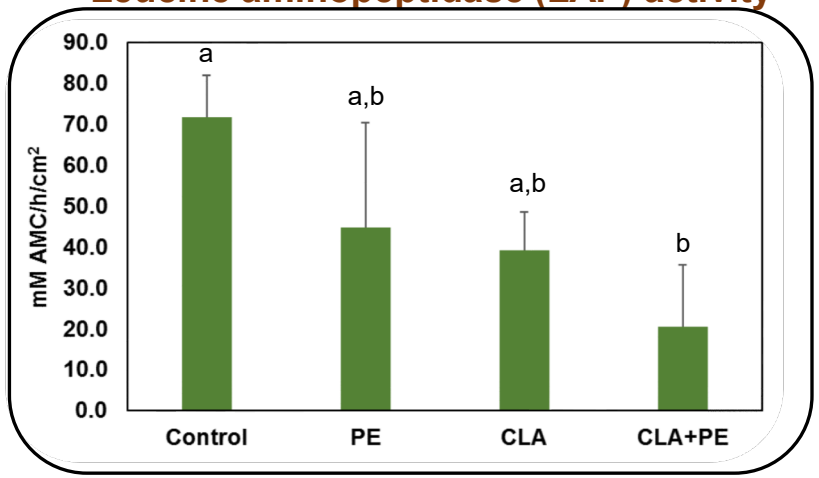
Photosynthetic efficiency (Y_{eff})



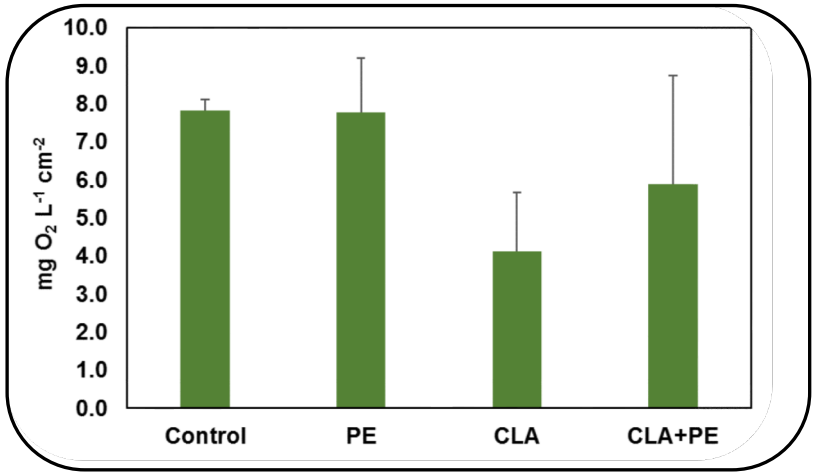
Chlorophyll-a content



Leucine aminopeptidase (LAP) activity



Net metabolism rate

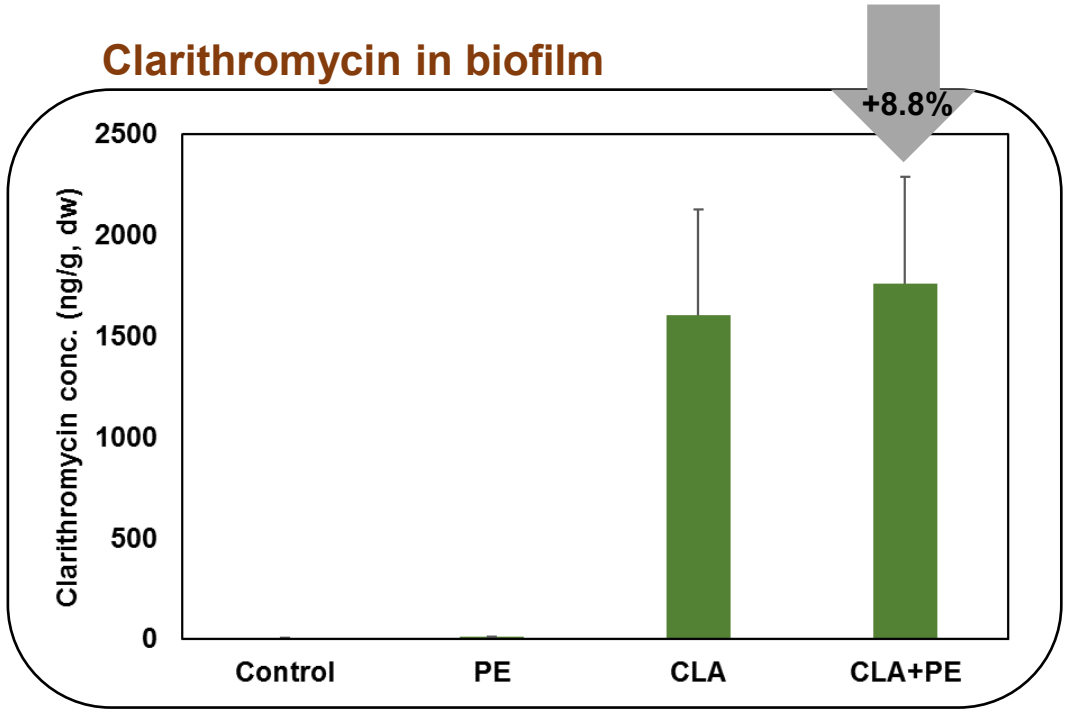


- **Clarithromycin** caused a statistically **significant decrease in the Y_{eff}** compared to control and PE
- A **co-exposure** scenario (**CLA+PE**) provoked a statistically **significant decrease in the activity of the enzyme LAP** compared to control
- **Low toxicity of PE-MPs** (1.0 mg/L) on river biofilms compared to control

Source: Santos et al., unpublished data

Combined exposure of river biofilms to clarithromycin and polyethylene microplastics

(Bio)accumulation of clarithromycin in river biofilm was evaluated at the end of the experiment (72h)



- **Clarithromycin accumulated in river biofilms**
- A small increase (8.8%) in the conc. of clarithromycin was seen in the presence of PE MPs, but it was not statistically significant.
- **River biofilms showed similar BCF, independently of the presence of PE MPs**

	BCF CLA (L/kg, dw) ± SD
CLA	30 ± 9
CLA+PE	37 ± 12

PE-MPs did not show a significant impact in the toxicity and (bio)accumulation of the antibiotic clarithromycin on river biofilms

Source: Santos et al., unpublished data

Interaction of microplastics with pharmaceuticals – impact on aquatic organisms

Combined exposure of mussels to PE-MPs and pharmaceuticals (citalopram and bezafibrate)

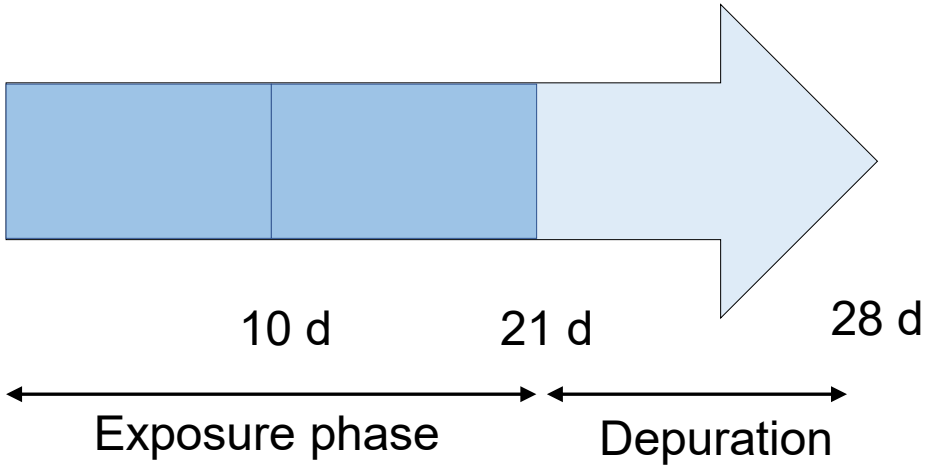
Test specie: Mediterranean mussels (*Mytilus galloprovincialis*)

Citalopram and bezafibrate exposure conc.: 0.5 µg/L

PE-MPs exposure conc.: 1.0 mg/L

PE mean particle size: 4-6 µm

Daily spike of contaminants



Journal of Hazardous Materials 458 (2023) 131904

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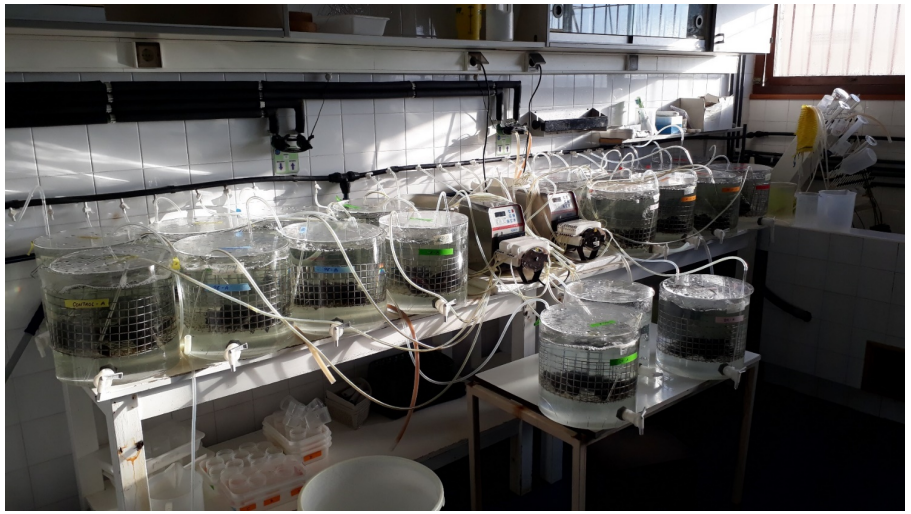
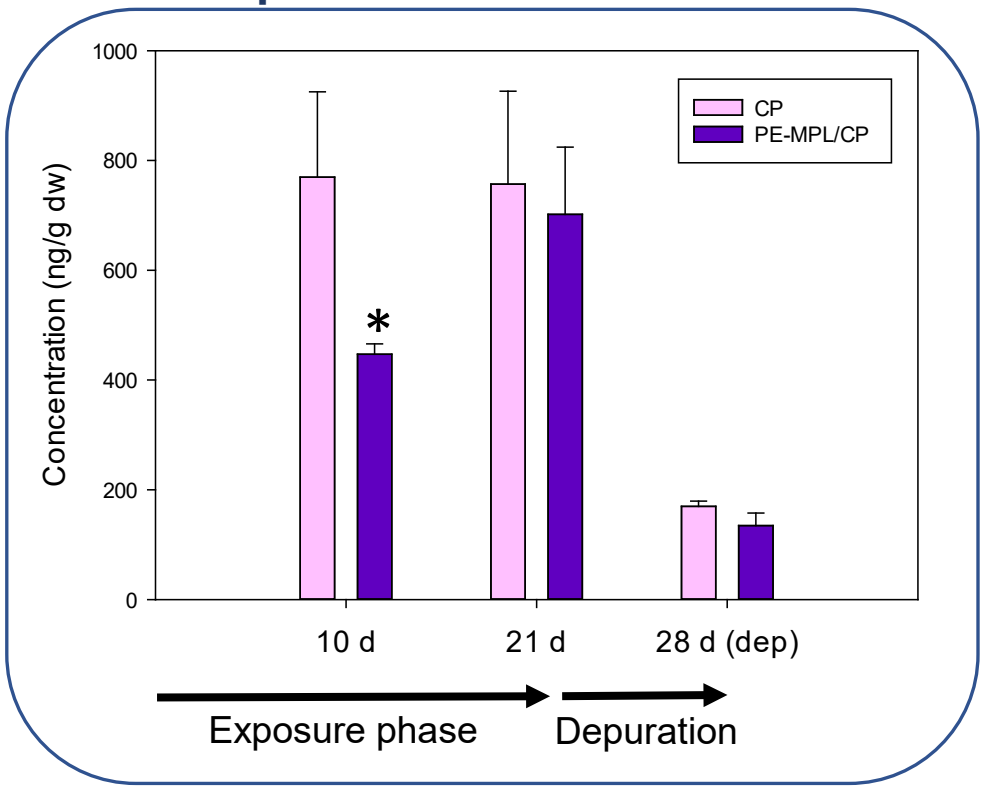
Combined exposure of the bivalve *Mytilus galloprovincialis* to polyethylene microplastics and two pharmaceuticals (citalopram and bezafibrate): Bioaccumulation and metabolomic studies

J.M. Castaño-Ortiz [a,b,*], F. Courant [c], E. Gomez [c], M.M. García-Pimentel [d], V.M. León [d], J.A. Campillo [d], L.H.M.L.M. Santos [a,b], D. Barceló [a,b,e], S. Rodríguez-Mozaz [a,b]

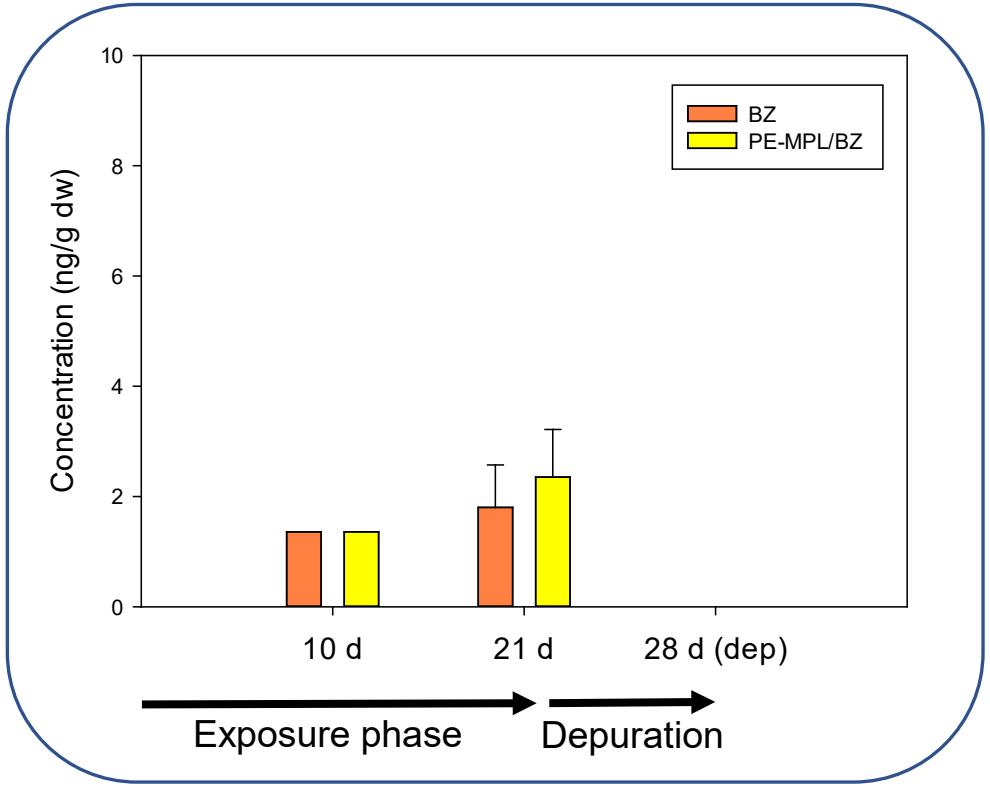


Combined exposure of mussels to PE-MPs and pharmaceuticals (citalopram and bezafibrate)

Citalopram



Bezafibrate



- **Higher bioaccumulation of citalopram** compared to bezafibrate (~ **500x** more)
- **PE-MPs delayed the bioaccumulation** of citalopram
  - ✓ PE-MPs (4-6 μm) might interfere with key surfaces for absorption of co-contaminants (e.g., gills, digestive tract)
- **After depuration,** pharmaceuticals partially (citalopram) or completely removed from mussels' tissue (bezafibrate)

Source: Castaño-Ortiz et al., J. Hazard. Mat. 458 (2023) 131904

Interaction of microplastics with pharmaceuticals – impact on terrestrial organisms

Combined exposure of wheat seeds to PE-MPs and oxytetracycline

- Exposure of wheat (*Triticum aestivum* L.) seeds to oxytetracycline (5, 50, 150 mg/L) and PE-MPs (200 µm) (800 mg/L)
- 5 days of germination

Science of the Total Environment 806 (2022) 150553

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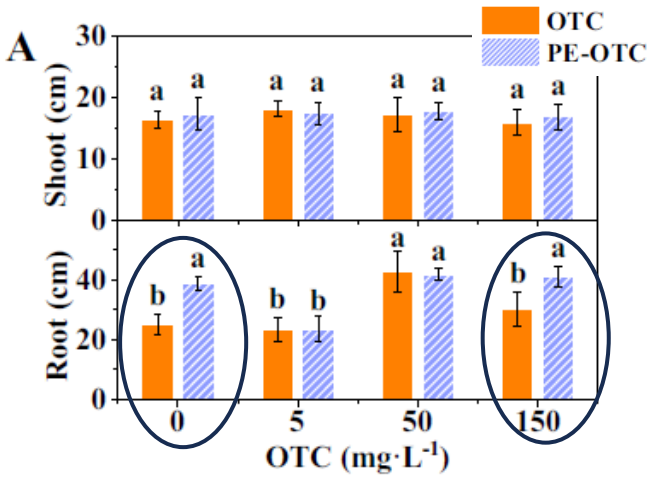
Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv

Stress response to oxytetracycline and microplastic-polyethylene in wheat (*Triticum aestivum* L.) during seed germination and seedling growth stages

Yanyu Bao [a,*], Chengrong Pan [a], Dezheng Li [a], Aiyun Guo [a], Fengbin Dai [b]

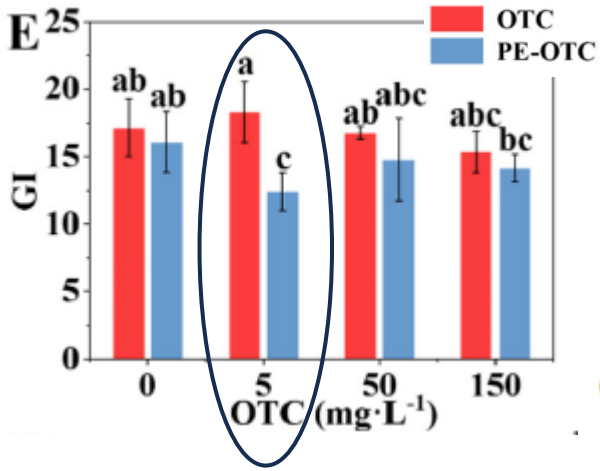
- Independently of the presence of PE-MPs, **OTC had a significant adverse effect on seeds germination**



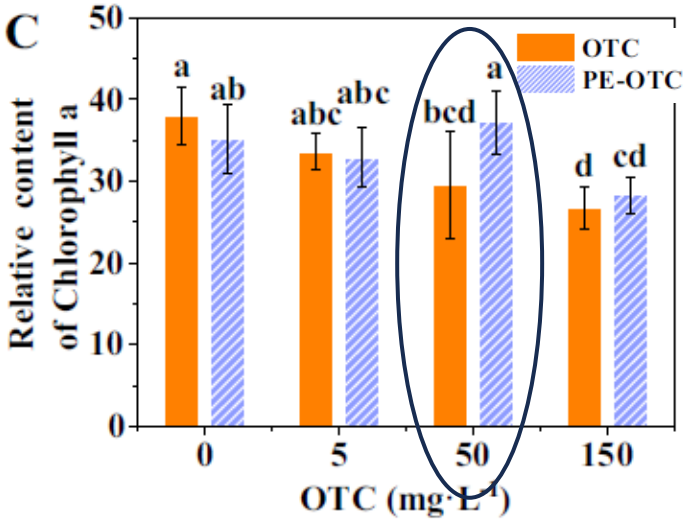
- In **PE-MPs** and **PE-MPs + OTC (150 mg/L)**, **root length significantly increased**, which could be attributed to nutrient deficiency

Interaction of microplastics with pharmaceuticals – impact on terrestrial organisms

Combined exposure of wheat seeds to PE-MPs and oxytetracycline



- The **germination index (GI) significant decreased** in the presence of **PE-MPs + OTC (5 mg/L)** compared to control and PE-MPs alone.

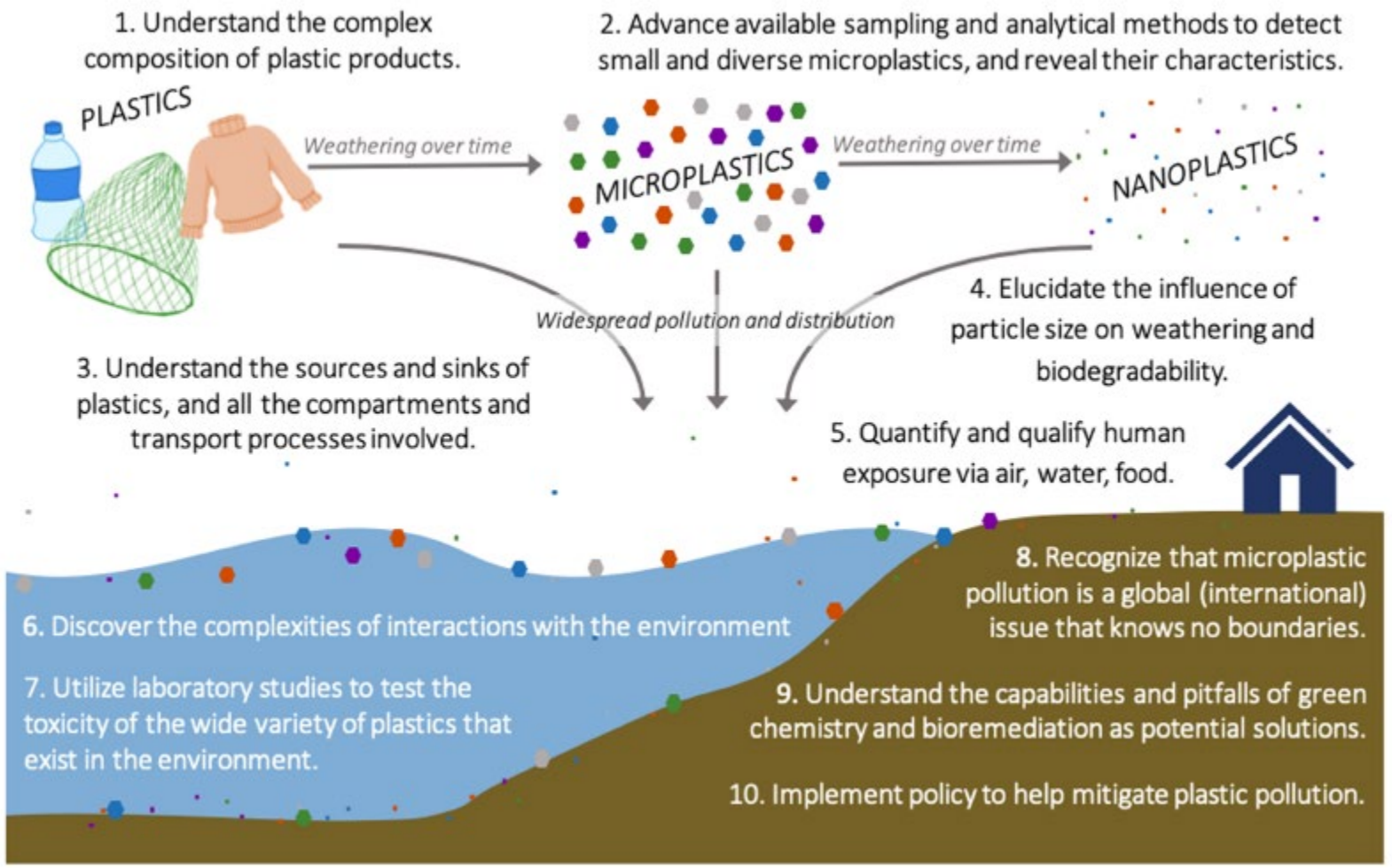


- **Chlorophyll a increased** in the presence of **PE-MPs + OTC (50 mg/L).**
- When PE-MPs were absent, chlorophyll a decreased with the increase of OTC conc.

- **Some adverse effects** (ex., root elongation, photosynthesis and photosynthetic pigments) are **dose-dependent**

Source: Bao et al., STOTEN 806 (2022) 150553

Future challenges and perspectives on microplastic pollution



Source: Hale et al., JGR Oceans 125 (2020) e2018JC014719

Take home message

- **Pharmaceuticals** and **microplastics** are ubiquitously distributed worldwide, having the potential to interact
  - **Microplastics** may sorb pharmaceuticals, acting as vector or carrier
  - **Adsorption of pharmaceuticals on microplastics** will depend on microplastics and pharmaceuticals properties and on environmental factors
  - **Interaction microplastics-pharmaceuticals** may affect the bioaccumulation and toxicity of pharmaceuticals in aquatic and terrestrial organisms
- **Aquatic organisms**, such as river biofilms and mussels, were able to **accumulate pharmaceuticals** and the presence of PE-MPs did not show a significant impact in their bioaccumulation (river biofilms) or could delay the bioaccumulation of citalopram (mussels)
- Combined exposure to pharmaceuticals and microplastics can also affect **terrestrial organisms** → impact on seed germination
- Further studies should cover different particle sizes and polymer types of microplastics as well as a wide range of pharmaceuticals. PS and PE among the most tested polymers, while antibiotics and psychiatric drugs among the most studied pharmaceuticals
- **Future laboratory studies** should be done under **environmental realistic concentrations**, using **aged microplastics** and **long-term exposure** to assess chronic effects

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PLAS-MED

(2018-2021)

Microplastics and microcontaminants in the Mediterranean coast: Toxicity and environmental and human health impacts
(FEDER-MCIU-AEI/CTM2017-89701-C3-2-R)

Reusemp³

(2021-2024)

ReUseMP3- Integrating nature-based water ReUse strategies with advanced Monitoring of the Presence and impact of MicroPollutants and MicroPlastics
(PID2020-115456RB-I00/MCIN/AEI/10.13039/501100011033)

ICRA Institut Català de Recerca de l'Aigua

CERCA Centres de Recerca de Catalunya

CSIC idaea

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AGENCIA ESTATAL DE INVESTIGACIÓN

Thank you for your attention

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