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Review

Bioaccumulation/bioconcentration of pharmaceutical active compounds in aquatic organisms: Assessment and factors database

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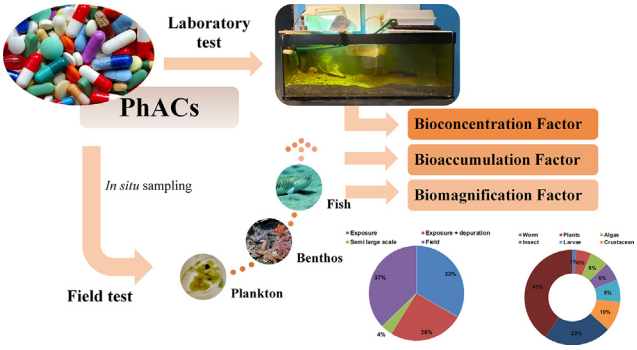
HIGHLIGHTS

- Pharmaceutical active compounds accumulation in aquatic organisms is discussed.
- Need to further standardize BCF testing for key influencing parameters.
- BAFs > BFCs denote the importance of the field study for a reliable assessment.
- BAF data seem organ-, specie- and compound-specific.
- Lower trophic positions bioaccumulate PhACs to a greater extent than higher positions.

GRAPHICAL ABSTRACT



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ABSTRACT

There is increasing evidence that the presence of certain pharmaceuticals in the environment leads to biota exposure and constitute a potential risk for ecosystems. Bioaccumulation is an essential focus of risk assessment to evaluate at what degree emerging contaminants are a hazard both to the environment and the individuals that inhabit it. The main goals of the present review are 1) to summarize and describe the research and factors that should be taken into account in the evaluation of bioaccumulation of pharmaceuticals in aquatic organisms; and 2) to provide a database and a critical review of the bioaccumulation/bioconcentration factors (BAF or BCF) of these compounds in organisms of different trophic levels.

Most studies fall into one of two categories: laboratory-scale absorption and purification tests or field studies and, to a lesser extent, large-scale, semi-natural system tests. Although in the last 5 years there has been considerable progress in this field, especially in species of fish and molluscs, research is still limited on other aquatic species like crustaceans or algae. This revision includes >230 bioconcentration factors (BCF) and >530 bioaccumulation factors (BAF), determined for 113 pharmaceuticals. The most commonly studied is the antidepressant group, followed by diclofenac and carbamazepine. There is currently no reported accumulation data on certain compounds, such as anti-cancer drugs. BCFs are highly influenced by experimental factors (notably the exposure level, time or temperature). Field BAFs are superior to laboratory BCFs, highlighting the importance of field studies for reliable assessments and in true environmental conditions. BAF data appears to be organ, species and compound-specific. The potential impact on food web transfer is also considered. Among different aquatic species, lower trophic levels and benthic organisms exhibit relatively higher uptake of these compounds.

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Contents

1. Introduction

Pharmaceutical active compounds (PhACs) are a group of substances of emerging concern in the context of environmental risk assessment (Arguello-Pérez et al., 2020; Mezzelani et al., 2018). Their continuous discharge into aquatic environments has led the European Commission to include them in a watch list of emerging water pollutants, within the Water Framework Directive (EC, 2020). This list (last updated in 2020) includes five PhACs (amoxicillin, ciprofloxacin, sulfamethoxazole, trimethoprim, and venlafaxine), as well as *o*-desmethylvenlafaxine, the main metabolite of venlafaxine. A recent water policy directive establishing a watch list of substances for Union-wide monitoring (dated July 2022) also includes ofloxacin.

The presence of PhACs in the environment can potentially influence both aquatic organisms and the ecosystem function (Chen et al., 2021; Maculewicz et al., 2022; Arguello-Pérez et al., 2020; Mezzelani et al., 2018). Organisms are exposed to PhACs through two main routes: waterborne (bioconcentration) and diet. The combined exposure is defined as bioaccumulation, the resulting discrepancy between the uptake and elimination processes (Arnot and Gobas, 2006). Bioaccumulation measurement is an essential part of risk assessment, to evaluate the scale that these emerging compounds may pose to the environment and their link with human populations (Ruan et al., 2020; Lagesson et al., 2016; Zenker et al., 2014; Nendza et al., 2018).

In a preliminary study conducted in Sweden in 2009, Wennmalm and Gunnarsson described that, of a large group of 300 PhACs, 92 % were not biodegradable, 23 % of them had bioaccumulation potential, and 61 % were classified as toxic for aquatic organisms. Bioaccumulation potential was estimated according to the PhACs' lipophilicity, following the OECD criteria (Organisation for Economic Co-operation and Development, OECD Guideline, 2005). Log K_{OW} > 3 was interpreted as "*potential to bioaccumulate in aquatic organisms*". In 2011, Howard and Muir (2011) rated 92 out of 275 PhACs commonly detected in the environment as potentially bioaccumulative, using quantitative structure property relationships (QSPR).

Nevertheless, discrepancies between predicted and measured concentrations could be significant. In fact, some authors recently stated that for ionic compounds such as PhACs, relying only on the K_{ow} may lead to a degree of underestimation (Kowalska et al., 2021). The potential of bioaccumulation of PhACs is typically determined using two factors: Bioaccumulation factor (BAF) and Bioconcentration factor (BCF), the difference between them being that BCFs are studied in laboratory conditions and exclude dietary intake.

Duarte et al. (2022) observed that lipophilicity is not a good predictor of the BCF of a group of neuroactive PhACs in fish, which in turn is highly influenced by experimental parameters (species, life stages and abiotic conditions). Bioaccumulation tests using field studies appear to best reflect environmental conditions, some of the disadvantages being time-consumption and cost.

The availability of quality information is essential to improve accuracy and reduce uncertainty in hazard and risk assessments. Until the present, no criteria have been proposed to evaluate the quality of accumulation assays and, as such, there is a lack of uniformity in the reported studies. In this paper, the accumulation potential of PhACs in aquatic organisms is reviewed and compared. First, the different performed assays to determine bioaccumulation potential, and the experimental conditions they applied, are described. A wide database on BCF/BAF values has been collected and the main variables affecting the data have been considered. Finally, on the basis of the obtained results, the potential impact on food web transfer has been contemplated.

2. Parameters

2.1. Bioconcentration factor (BCF)

Bioconcentration is the process by which a substance is absorbed by an organism from the environment via the respiratory and dermal routes. Dietary intake is not included. BCF is measured in laboratory conditions and is expressed as:

$$BCF_{SS} = \frac{C_b}{C_w}$$

C_b is the concentration of a chemical in the biota and C_w is the concentration of a chemical in the water at steady-state (SS). Note that guidelines suggest that, for a test to be valid, the concentration of the test substance in the tanks during the uptake phase is maintained within ± 20 % of the mean of the measured values. Moreover, the guidelines recommend that the whole body of the organism be used for the process. For special purposes,

when the organism is large enough (such as certain species of fish) specific tissues or organs (muscle, kidney, brain or liver) may be used.

Other parameters used to characterize bioaccumulation potential are the absorption rate constant (k_1), the depuration rate constant (k_2) and the bioconcentration kinetic factor (BCF_K):

$$\frac{dC_b}{dt} = k_1 C_w - k_2 C_b$$

$$\frac{dC_b}{dt} = -k_2 C_b$$

C_b is the concentration in biota (ng g^{-1}) ($C_{b,0}$ is the concentration when the depuration phase begins), t the time of exposure (h), k_1 the first-order uptake constant (L kg^{-1} h^{-1}), C_w the concentration in water (μg/L), and k_2 the first-order elimination rate constant (1 h^{-1}). Assuming a negligible concentration in biota samples at t_0, and considering its constant in the exposure medium, the equations can be expressed as:

$$C_b(\text{uptake}) = \frac{k_1}{k_2} C_w \left(1 - e^{-k_2 t}\right)$$

$$C_b(\text{depuration}) = C_{b,0} e^{-k_2 t})$$

$$BCF_k = \frac{k_1}{k_2}$$

2.2. Bioaccumulation factor (BAF)

Bioaccumulation is the process by which a substance is absorbed by the organism, taking into account all exposure pathways, as occurs in the natural environment (dietary and environmental sources). BAF is determined under field conditions and is calculated as:

$$BAF = \frac{C_b}{C_w}$$

C_b is the concentration in biota and C_w is the total concentration in the water phase. BAF measurements presuppose that organisms are at or near SS with the ambient water (acknowledging that natural environments are dynamic and highly variable).

Another bioaccumulation field measurement is the biota-sediment accumulation factor (*BSAF*), calculated as:

$$BSAF = \frac{C_b}{C_s}$$

C_b is the concentration in biota (ng g^{-1}) and $C_{s\ is}$ the concentration in the surrounding sediments (ng g^{-1}).

2.3. Biomagnification factor (BMF)

Biomagnification is the process by which the thermodynamic activity of the substance in the organism exceeds that of its diet. It can be determined both in the field as well as in laboratory feeding experiments, and is calculated as follows:

$$BMF = \frac{C_b}{C_d}$$

C_b is the chemical concentration in an organism and C_d is the chemical concentration in its diet at SS (when there are no significant differences in PhAC concentration in the organism over three sequential sampling periods).

Trophic Magnification Factor (*TMF*) is the diet-weighted average BMF of a chemical across food webs. TMFs are typically determined from field measurements and are calculated from the slope of a log-normal regression of chemical residues in organisms, as per their trophic levels:

$$\log\ [\text{contaminant}] = b\ (\text{Trophic position}) + a$$

$$TFM = 10^b$$

The BMF and the TMF describe changes across one or more trophic level, respectively (Burkhard et al., 2013).

3. Experimental designs

3.1. Laboratory test

3.1.1. Acclimation period

Prior to laboratory testing, the organism is acclimatized over a period of 2 to 3 weeks (OECD 305 technical guidance). Uncontaminated water from natural sources is generally used for testing, to ensure specimen survival with no abnormal appearance or behaviour. The baseline laboratory controls include water temperature, pH, dissolved oxygen, lighting type and characteristics, calcium, ammonium, nitrite, alkalinity and salinity (for marine species). The OECD establishes dissolved oxygen values of ≥60 %. Water temperature depends on the fish or organism species (for most a temperature between 20 and 25 °C is established, with some species needing lower temperatures (e.g., *Oncorhynchus mykiss* or *Rainbow trout*: 13–17 °C; *Gasterosteus aculeatus* and three-spined stickleback: 18–20 °C). Temperature variation throughout testing should be less than ±2 °C, since larger deviations can affect biological parameters relevant for uptake and depuration, as well as cause organism stress. The pH value should be within the 6.0 to 8.5 range at test initiation. According to some researchers, the use of synthetic water (demineralized water with specific added nutrients) may result more suitable to guarantee uniformity over time. For instance, the composition of fresh river water (ISO 73463) can be prepared using $CaCl_2$ (220.5 mg/L), $NaHCO_3$ (63 mg/L), KCl (5.5 mg/L) and $MgSO_4$ (60.1 mg/L) in distilled water (Molina-Fernández et al., 2021).

There are also recommended guidelines for test organism feeding (1 %–2 % body weight (bw)/day of lipid and protein content). Food remnants should be removed after feeding to avoid chemical absorption since they could reduce bioavailability and provide a secondary dietary source (OECD 305 technical guidance). Once the acclimation period has ended, the test substance is mixed into the water to begin the assay. To prepare spiked solutions agitation is the preferred method for dissolving the studied substances. The use of organic solvents (acetone, ethanol, methanol, dimethylsulfoxide or acetonitrile) is not generally recommended. However, a maximum level (0.1 mL L^{-1}) is considered acceptable in the preparation of concentrated stock solutions. The solvent concentration must be reproducible in all treatments (OECD 305 technical guidance). Some authors have used a concentration of methanol up to 0.8 mg/L (Świacka et al., 2020).

An alternative is the use of a solid-phase desorption dosing system. For example, Maulvault et al. (2018) prepared venlafaxine-enriched feed. The spiked solution was previously dissolved in ethanol and diluted with water. The organic solvent was then volatilized by a top-coating process to the pellets with a pressurized spraying container. Regarding the concentration level of the test substance, the OECD establishes concentrations of 1 % and 0.1 % of its LC_{50} value.

3.1.2. Exposure test

The studied organisms are exposed to PhACs at one or more of the selected concentration levels. A control group (without the test substance) is subjected to identical laboratory conditions. The exposure time of the specimens to contaminants runs until SS is reached. Throughout exposure, samples (of both water and biota) are periodically collected. The concentration of the test substance in the water samples should be determined both prior the addition of the organisms and during the uptake phase. Throughout the test period the water should be sampled ($N = 5$) from the test tanks

(from a central point), before feeding, and at the same time the organism is sampled. More frequent sampling after the introduction of the organisms may be useful to ensure stable concentrations. Organisms should be sampled on at least five occasions during the uptake phase. Exposure time and sampling frequency depend on the mode of action and the chemical-physical properties of the substance. For example, for different species of fish the exposure time can range from 4 days (ibuprofen in Rainbow trout (*O. mykiss*) (Brozinski et al., 2013) to 40 days (venlafaxine and its metabolite in Loach (*M. anguillicaudatus*) (Qu et al., 2019). In the case of larvae, bioconcentration experiments are developed for shorter periods, between 72 and 120 h post fecundation (Molina-Fernández et al., 2021; Pan et al., 2018). The duration of the test can be shortened or extended if necessary, if it is demonstrated as necessary as per when steady-state is reached. As for sampling, normally three replicates of the organism and at least five water samples are collected at each point in time. The medium is renewed weekly (Lopes et al., 2022), or every 24 h (Gomez et al., 2021; Maulvault et al., 2018; Lu et al., 2018), after which the substance concentration is re-established to maintain nominal values.

As mentioned earlier, aquatic organisms are exposed to chemicals via water uptake (bioconcentration), diet or both. The decision to conduct an aqueous or dietary exposure experiment should be based on water solubility and K_{ow} of the test substance. For compounds with high water solubility and log K_{ow} values between 1.5 and 6.0, as is the case for most PhACs, an aqueous exposure test should be considered first (OECD 305 technical guidance). To the best of our knowledge, only one study in the literature (Maulvault et al., 2018) uses both water and dietary exposure sources (see Table 1).

3.1.3. Up-take and depuration test

This test includes two consecutive phases: exposure (uptake) and post-exposure (depuration). During the uptake phase, the organism is exposed to a chemical compound at one or more concentration levels, under the conditions described above. To initiate the depuration phase, the remaining organisms are transferred to clean water, then the same water renewal and sampling procedures as during the exposure period are followed. The depuration phase is always necessary unless the uptake is negligible. Organisms should be sampled for the test substance on at least four occasions during this phase. This type of testing is more common in low trophic level organisms, such as molluscs.

3.1.4. Semi-natural large-scale system test

Long-term studies in a controlled aquatic system, evenly contaminated with a chemical mixture, are ideal for identifying general patterns of behaviour. Water, sediments and biota are sampled on a daily or weekly basis for a period of more than three months. This type of test is particularly successful in evaluating biomagnification along the food web, as well as bioaccumulation. However, this type of experiment is infrequent in the scientific literature.

3.2. Field studies

3.2.1. In-situ sampling collection

Currently, there are no criteria regarding field studies. Organisms are exposed throughout their lifetime, so the concentrations within them are near steady-state. Water, sediment and biota are sampled, and a range of sampling points is a key to ensure the representativeness of the data. The analytical rigor applied throughout the sampling and analysis processes is fundamental for the quality of the data. Some practices, such as the use of tags for fish labeling, has been proposed to study the changes in bioaccumulation over time under field conditions (Grabicova et al., 2017). Other authors (de Solla et al., 2016; Gillis et al., 2014) have also field-deployed organisms (i.e., caged, previously sourced locally) in the aquatic environment over the course of several weeks. Furthermore, grab sampling conducted in conjunction with passive sampling may be a more reliable and less time-intense option for assessing relative time-weighted average spatial distribution of organic contaminant concentrations (Wilkinson et al., 2018; Vystavna et al., 2012). The use of passive sampling has been recommended as a method to mimic bioconcentration uptake without the use of live organisms. In the case of polar compounds such as PhACs, the use of Polar Organic Chemical Integrative Sampler (POCIS) has been developed. Grabicova et al. (2017) concluded that integrative passive samplers with fish liver or kidney tissue can be complimentary exploratory tools and can help to distinguish between bioconcentration and bioaccumulation. The main inconvenience of this practice is the inaccessibility of the sampling rates for POCIS over long time periods.

A complex approach that includes not only water and organisms but also sediment interactions is needed to better understand the fate of PhACs in the aquatic environment. Water sediments represent a potential secondary source of PhACs when the hydrological conditions change (Wilkinson et al., 2018; Koba et al., 2018). Moreover, some organisms (e.g. benthic invertebrates) are often exposed to contaminated sediment via ingestion of sediment particles. These organisms are highly important components of the food chain in aquatic environments and contribute significantly to fish diets. Usually, the sediments are collected in the same sampling point as the water samples. A few studies were recently published on this, for example Wilkinson et al. (2018) assessed the accumulation and spatial distribution of PhACs and other emerging pollutants in aquatic sediment and five under-studied organisms (periphyton, plants (*Callitriche* sp. and *Potamogeton* sp.), as well as amphipod crustaceans (*G. pulex*) and aquatic snails (B. tentaculate) ($n = 65$ in total) from the Hogsmill, Blackwater and Bourne Rivers in Southern England. Koba et al. (2018) analysed 18 PhACs and 7 metabolites in water, sediment and fish of a treated wastewater-affected pond during a one-year experiment in the Czech Republic.

4. Analytical methods

Validated methods and quality assurance/quality control (QA/QC) protocols must be followed to ensure reliable and accurate results. A key aspect that generates uncertainty in the BAF/BCF calculation is the concentration of the compound in the water, since in many cases its value is close to the chosen method's determined detection limit. In these cases, the concentration is generally reported as “non-detected”. The statistical treatment used to address “non-detected” samples can have significant effect on the derivation of the BAF.

In order to detect PhACs in the water, matrices between 50 and 1000 mL are often required. After filtration, solid phase extraction (SPE) is the most commonly applied technique. Given the nature of biota samples, a more complex sample preparation is required prior to analysis. In the case of fish, tissues and organs are first separated for individual analyses. In the case of molluscs, cephalopods and crustaceans, they are generally removed from the shells (if present) and then pooled, without differentiating body cavities. Samples are then powdered to homogeneity and, in most cases, freeze-dried. The sample preparation involves the extraction and clean-up steps. Ultrasonic solvent extraction (USE) is still widely applied. Pressurized liquid extraction (PLE), microwave assisted extraction (MAE), matrix solid phase extraction (MSPD) and Quick, Easy, Cheap, Effective, Rugged and Safe (QuEChERS) have also emerged in last few years. For clean-up dispersive-SPE (d-SPE), C18 and PSA sorbents are frequently used. Finally, for adequate identification and quantification of compounds, and in order to define the lower bound detection limits, liquid chromatography coupled with a tandem mass spectrometry detector (LC-MS/MS) is the most suitable technique (Arenas et al., 2021; Álvarez-Ruiz and Picó, 2020; Miossec et al., 2020).

The presence of interferences that co-elute with the test substance is the main drawback of these identification and quantification methods. The evaluation of matrix effects should be included in the methods' validation processes. In practice, the use of matrix-matched calibration curves, and isotopically-labelled internal standards for quantification purposes, are commonly used to reduce matrix effects.

Table 1
Overview of accumulation studies on Pharmaceutically Active compounds (PhACs) in aquatic organisms.

Species name	PhACs	Experiment	Tanks/aquariums	Acclimataion and conditions	Spiked level (ng mL^{-1})	Organism replicates/tank	Exposure conditions	Reference
Algae								
Macroalgae *Ulva*	Oxytetracyclin	Exposure	25 L glass tanks. Flasks were pre-filled with 244 mL natural filtered seawater	2 weeks of acclimatation in deionized water at 23.2 °C. Photoperiod set to 14:10 light:dark under white fluorescent light	10 and 120	3 replicates per sampling time, each replicate containing 3 algal disks	Sampling times: 0, 0.5, 1, 2, 4, 12, 24, 48, 72, 96 h	Rosa et al., 2019
Biofilm	39 PhACs and two metabolites (Analgesics/anti-inflammatories, antibiotics, antihelmintics, antiplatelet agent, antihypertensive, β-blocking agents, histamine H1 and H2 receptor antagonists, lipid regulators, psychiatric drugs)	Field	Two lowland urban rivers in Argentine	–	–	5 sampling points/each river	Field study	Mastrángelo et al., 2022
Periphyton	Acetaminophen, diclofenac, 17alpha-ethinylestradiol	Field	Hogsmill River (Greater London), Chertsey Bourne River and the Blackwater River. Rivers received inputs from a total of five sewage treatment works effluent outfalls	–	–	4 samplimg point (N = 8): 50 m upstream from effluent outfalls, 50 m downstream of respective STW effluent outfall as well as 250 m and 1000 m downstream from the outfalls. 1 day periphyton was seeded in each stream with samples collected from a regional reference stream. They were colonized on unglazed, ceramic tiles for two weeks prior to the start of this experiment.	Field study	Wilkinson et al., 2018
Periphyton	Acetaminophen, caffeine, carbamazepine, diltiazem, diphenhydramine, fluoxetine, norfluoxetine, and sertraline	Mesocosm	BEAR Facility, with 12 outdoor mesocosms with a mixing tank (~378 L), followed by a riffle section, a run or glide section and bottom pool (~378 L), located at the Lake Waco Wetlands, Texas, USA	The flow of water originated from a large holding tank that delivered water to all 12 streams. A controlled volume of water (100 mL/min) was permanently removed from the bottom pool with an overflow drain, while the remaining water flow (~50 L/min) was recirculated to the mixing tank. Periphyton was colonized on unglazed, ceramic tiles for two weeks prior to the start of this experiment.	–		8-Day study	Burket et al., 2020
Periphyton	Acetaminophen, amitriptyline, aripiprazole, benzoylecgonine, buprenorphine, caffeine, carbamazepine, diclofenac, diltiazem, diphenhydramine, duloxetine, fluoxetine, methylphenidate, norfluoxetine, promethazine, sertraline	Field	semi-arid urban river influenced by snowmelt sited in East Canyon Creek in Park City, Utah, USA	–	–	3 sampling campaings of 3 days each, including 5 sampling point	Field study	Haddad et al., 2018
Plants								
Macrophyte (*Lemna gibba*)	39 PhACs and two metabolites (analgesics/anti-inflammatories, antibiotics, antihelmintics, antihypertensive, antiplatelet agent, β-blocking agents, histamine H1 and H2 receptor antagonists, lipid regulators, psychiatric drugs)	Field	Two lowland urban rivers in Argentine.	–	–	5 sampling points in each river	Field study	Mastrángelo et al., 2022
Acer platanoides	Sertrailine and fluoxetine	Exposure	2 constructed aquatic	10 d of acclimatation	10	One and a half grams of	7 days exposure	Boström et al.,

(continued on next page)

Table 1 (*continued*)

Species name	PhACs	Experiment	Tanks/aquariums	Acclimataion and conditions	Spiked level (ng mL^{-1})	Organism replicates/tank	Exposure conditions	Reference
			food chains of 3 trophic levels (40 L)	(12:12-h light:dark and 20 °C)		freeze-dried leaves. All trophic levels were exposed together within 1 replicate		2017
Cattail *Typha angustifolia*	Caffeine, carbamazepine, ibuprofen, fluoxetine	Field	Lorong Halus Wetland, located in north-eastern Singapore	–	–	3 sampling point	Field study	Wang et al., 2019
Callitriche sp., *Potamogeton* sp.	Acetaminophen, diclofenac, 17α-ethinylestradiol	Field	Hogsmill River (Greater London), Chertsey Bourne River and the Blackwater River. Rivers received inputs from a total of five sewage treatment works effluent outfalls	–	–	4 samplimg point (N = 7,8): 50 m upstream from effluent outfalls, 50 m downstream of respective STW effluent outfall as well as 250 m and 1000 m downstream from the outfalls. 1 day	Field study	Wilkinson et al., 2018
Larvae								
Damselfly larvae, mayfly larvae	Diphenhydramine, oxazepam, trimethoprim, diclofenac, and hydroxyzine	Semi-natural large-scale system	Semi-natural pond 400 m^2 (40 × 10 m), with a mean depth of 1.3 m	The pond (pH = 7.2) has no connection to anthropogenically surface waters. The inflow of water comes from rain and ground water	0.4	Individual numbers for each species per sampling were 10 Zygoptera, 20 Planorbidae, 30 Asellus, 30 Ephemeroptera	Sampling was carried out on a daily to weekly basis over a period of 66 days in total. Predators in the system were European perch (*Perca fluviatilis*) feeding on fish, zooplankton, and benthic macroinvertebrates, and damselfly larvae (Zygoptera: Coenagrion) preying on zooplankton and benthic macroinvertebrates	Lagesson et al., 2016
Damselfly larvae (Zygoptera)	Hydroxyzine and fexofenadine	Exposure	Aquaria (25 × 25 × 8 cm)	1.2 L aged tap water WITH coordinate grid (1 × 1 cm) drawn on the bottom	1.5 and 2.0	n = 10 for Fexofenadine and n = 12 for Hydroxyzine	7 days exposure	Jonsson et al., 2014
Dragonfly larvae (*Sympetrum* sp.)	Temazepan	Exposure	Plastic containers (8 × 8 × 8 cm) filled with 200 mL of aged tap water, at different T (10 or 20 °C) and PhAC concentration	48 h of acclimation period being fed with live zooplankton. Larvae were transferred to climate-controlled rooms and the temperature was slowly shifted towards 10 or 20 °C	0.5–5	20 per treatment (two dosis and two temperature + control)	Larvae were exposed for 8 days in an individual static exposure scenario	Cerveny et al., 2021b
Larvae	Diclofenac, ibuprofen, diphenhydramine, gemfibrozil	Exposure	15 microcosms (aquaria of 30 × 20 × 15 cm) with 3 L of water each, and equal amounts of sand (10 tablespoons), stones (3 stones >10 cm and 10 stones 2–5 cm)	20 days of acclimatation in dechlorinated tap water at 9.3 °C. Temperature was increased 0.1 °C every 15 days. Constant oxygen levels	0.5	2 tank/day	4 microcosms controls. 11 exposed to a mixture of PhACs, all randomly placed in 3 incubators, over a 65-day period. The volume of water was kept constant by adding fresh dechlorinated tap water and the concentration of each compound was kept pseudoconstant. Sampled 4 times (day 0, 21, 35,	Previšić et al., 2021

							65). Also with field studies	
Zebrafish (*Danio rerio*)	Fluoxetine, sertraline, citalopram, paroxetine, norfluoxetine, norsertraline, and desmethylcitalopram	Exposure	–	Simulated river water. Dissolved $O_2 \geq 60$ %, 27 °C and pH 7.8. Exposure medium refreshed every 24 h	80 and 300	3 by tank and day	Eleutheroembryos are obtained 72 h post fecundation and then exposed to PhACs and collected at different times (0, 24, 45, 48 h)	Molina-Fernández et al., 2021
Zebrafish (*Danio rerio*)	Fluoxetine	Exposure	6-Well plates	Fresh egg water. pH 6.8–7.2; 14:10 h light: dark cycle. 28 °C. Exposure medium refreshed every 24 h	0, 0.1, 1, 10, 100, 1000	3 by tank and day	Zebrafish embryos exposed to fluoxetine from 4 h post-fertilization until 120 hpf	Pan et al., 2018
Worm								
Aquatic worm (*Phagocata vitta*)	Diclofenac, ibuprofen, 1-OH-ibuprofen, piroxicam, propyphenazone, sulfamethoxazole, diltiazem, verapamil, norverapamil, bezafibrate, hydrochlorothiazide, gemfibrozil, parvastatin, acridone, carbamazepine, 10,11-epoxy-carbamazepine, 2-OH-carbamazepine, citalopram, fluoxetine, paroxetine, venlafaxine, azaperone, dexamethasone, metoprolol, propanolol	Field	Segre River (Ebro River basin, NE Iberian Peninsula)	–	–	125 individuals of *Ancylus fluviatilis*, 90 individuals of Hydropsyche sp., and 70 individuals of *Phagocata vitta*	Field study	Ruhí et al., 2016
Molluscs								
Molluscs (*Atrina pectinate Linnaeus*, *Meretrix lusoria*, *Trisidos kiyoni*, and *Crassostrea rivularis Gould*)	37 antibiotics: 13 sulfonamides, 5 tetracyclines, 10 fluoroquinolones, 6 macrolides and 3 ionophores	Field	Six marine aquaculture farms at the Hailing Island	–	–	14 fish, 504 shrimp, 4 crabs, 11 shellfish, 5 oyster	Field study	Chen et al., 2015
Cultured shellfish (*Ostrea gigas*, *Mimachlamys nobilis*, *Mytilus eduli*, and *Bufonaria perelegans*)	Ciprofloxacin, ofloxacin, norfloxacin, flumequine, Sulfadiazine, sulfathiazole, sulfapyridine, sulfamerazine, penicillin G, sulfamethazine, sulfamethoxazole, trimethoprim, tetracycline, cefotaxime, oxytetracycline, isochlortetracycline, spectinomycin, roxithromycin, erythromycin, clarithromycin, chloramphenicol, paracetamol, naproxen, ibuprofen, ketoprofen, diclofenac acid, carbamazepine, diltiazem, diphenhydramine, gemfibrozil	Field	Pearl River Delta (Five mariculture sites around)	–	–	$N = 459$	Field study	Xie et al., 2019
Mussel (*Mytilus trossulus*)	Diclofenac	Exposure-depuration test	Three tanks (glass aquariums) with 15 L (one as control)	3 weeks of acclimatation in artificial sea water at 8–10 °C. The water was changed and mussels were fed every 3 days	133	80 individuals in each tank with a sampling of N = 5 by tank and day	Mussels exposed to diclofenac for 5 days, following a 5-day depuration phase	Świacka et al., 2019
Mussel (*Mytilus trossulus*)	Diclofenac	Exposure-depuration test	Nine tanks (glass aquariums) with 15 L (three as control)	3 weeks of acclimatation in artificial sea water at 5–8 °C. The water was changed and mussels were fed every four days	4 and 40	73 individuals by tankwith a sampling of N = 4 by tank and day	25-Day experiment: exposure (12 d)/depuration (13 d). At the beginning of the depuration phase, the glass tanks were refilled with artificial sea water. During the exposure to diclofenac 4 individuals	Świacka et al., 2020

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Table 1 (*continued*)

Species name	PhACs	Experiment	Tanks/aquariums	Acclimataion and conditions	Spiked level (ng mL^{-1})	Organism replicates/tank	Exposure conditions	Reference
							were taken from all tanks every 4d, and at the end of depuration	
Mussel (*Mytilus trossulus*)	Diclofenac and 4OH-diclofenac	Exposure	Twelve tanks (glass aquariums) with 15 L (three as control)	2 weeks of acclimatation in artificial sea water at 10 °C, pH 8.9. Mussels were kept in the dark and fed	20 (diclofenac) and 68 (4OH diclofenac	10 per tank	7 days experiment. During experiment mussels were fed twice (day 0 and 4). On the last 7th day of the experiment, mussel were collected	Świacka et al., 2021b
Mussel (*Mytilus galloprovincialis*)	Diclofenac, Etoricoxib and caffeine	Exposure-depuration test	Three tanks (160 L): control group, the group exposed to the pollutants mixture and the group exposed to pollutants and microplastics	2 weeks of acclimatation in seawater purified using sand filters and UV (salinity 35 ppt, 18 °C, pH 8.0, O2 > 80 % and a 12 h day/night cycle)	10 and food (10 ng per specimen and day)	83 per tank	58 days of experiment separated in two stages: 1) exposure stage (days 0–28) when mussels were exposed to contaminants 2) Depuration satge (days 29–58) the tanks were emptied, rinsed and filled with clean water	Álvarez-Ruiz et al., 2021
Mussel (*Mytilus galloprovincialis*)	Carbamazepine and 10-hydroxy-10,11-Dihydro-carbamazepine	Exposure-depuration test	3 aquaria and 1 control (1.5 L)	1 week of acclimatation in filtered seawater (18 °C, 14:10 h light:dark cycle, continuously aerated and renewed daily). Mussels were fed once a day with Tetraselmis suecica	1, 10, 100	18 per tank and 6 in control	7 days of exposure	Boillot et al., 2015
Mussel (*Lasmigona costata*)	Amitriptyline, 10-HO-amitriptyline, amlodipine, amphetamine, anhydrotetracycline, azithromycin, betamethasone, cefotaxime, citalopram, clarithromycin, clotrimazole, cocaine, codeine, desmethyldiltiazem, diltiazem, 1,7-dimethylxanthine, diphenhydramine, enrofloxacin, erythromycin, fluoxetine, gemfibrozil, glyburide, hydrocortisone, iopamidol, metformin, miconazole, minocycline, naproxen, norfluoxetine, norverapamil, oxolinic acid, oxycodone, paroxetine, propranolol, sarafloxacin, sertraline, theophylline, venlafaxine, verapamil, warfarin	Field	Grand River, Ontario, receiving wastewater effluent	–	–	Two sampling point (upstream and downstream) in 1 day. Caged and wild mussels each	Field study	de Solla et al., 2016
Mussel (*Mytilus galloprovincialis*)	17 α-ethinylestradiol (EE2)	Exposure	Three tanks for each treatmern	2 weeks of acclimatation in artificial sea water: 17 °C, pH 8.0, salinity 30. 12 h light/12 h dark photoperiod with constant aeration. Frequent water renewal. Mussels fed every 2d	0.005, 0.025, 0.125 and 0.625	18 per treatment	28 days of exposure period. Mussels exposed to each concentration were maintained under two temperatures, 17 and 21 °C. Weekly, the exposure medium was renewed, after which EE2 concentration was re-established	Lopes et al., 2022
Mussel (*Mytilus galloprovincialis*)	Venlafaxine	Exposure-depuration test	Four tanks (one as control) of 1.5 L glass aquaria	7 days of acclimatation at 18 °C with a 14:10 h L/D photoperiod	10	18 per tank	7 days exposure phase followed by a 7-day depuration period. The water was almost entirely	Gomez et al., 2021

							removed every 24 h and replaced, and venlafaxine was added to reach a 10 μg/L nominal concentration. Organisms were collected at days 0, 1, 3, 7, 8, 10, and 13	
Mussel (*Mytilus galloprovincialis*)	Sotalol, sulfamethoxazole, venlafaxine, carbamazepine and citalopram	Exposure and depuration test	Ten tanks	1 week of acclimatation period in sea water at 18 °C, pH 8.00, dissolved oxygen >5 mg/L, salinity = 35 ‰ and photoperiod of 12 h light and 12 h dark (12 L:12D). Mussels were fed three times per day and 25 % of water was renewed	Up to 15.7	1 control and 4 treatmenst: two temperature and two pH (50 animals per tank)	20 days of exposure and 20 days of depuration. Sampling at days, 0, 2, 10, 20 (exposure) 22, 30 and 40 (depuration).	Serra-Compte et al., 2018
Clam (*Ruditapes philippinarum*)	17α-ethinylestradiol	Exposure test	Ten tanks (3 L) (at different concentration) and two temperature (17 and 21 °C)	10 days of acclimatation in artificial seawater (salinity 30), under continuous aeration, 17 C and a photoperiod of 12:12 h (light/dark). Clams were fed every 2–3 days. Seawater was renewed every 2–3 days	0, 0.005, 0.025, 0.125 and 0.625	6 individuals per container and three containers per treatment (a total of eighteen individuals/treatment)	28 d of exposure period. The water was renewed once a week after which EE2 concentrations were re-established.	Silva et al., 2022
Clam (*Corbicula fluminea*)	acetaminophen, caffeine, carbamazepine, diltiazem, diphenhydramine, fluoxetine, norfluoxetine, and sertraline	Mesocosm study	BEAR Facility, with 12 outdoor mesocosms with a mixing tank (~378 L), followed by a riffle section, a run or glide section and bottom pool (~378 L), located at the Lake Waco Wetlands, Texas, USA	The flow of water originated from a large holding tank that delivered water to all 12 streams. A controlled volume of water (100 mL/min) was permanently removed from the bottom pool with an overflow drain, while the remaining water flow (~50 L/min) was recirculated to the mixing tank. Clam trays were placed at the beginning of the run section in each stream	–	3 randomly selected clams were collected from trays in each stream (N = 12)	8-Day study. Sampling on days 0, 1, 3 and 8.	Burket et al., 2020
Clam pen shell	Hydrochlorothiazide	Field	Mar Menor lagoon	–	–	9 sampling points	Field study	Moreno-González et al., 2016
Clam (*Crassostrea gigas*, *Patinopecten yessoensis* and *Chlamys farreri*)	Antibiotics (14 sulfonamides, two chloramphenicols and four tetracyclines)	Field	Coastal environment of Dalian (China)	–	–	A total of 20 seawater, 20 sediment and 13 biota samples	Field study	Na et al., 2013
Clam (*Ancylus fluviatilis*)	Diclofenac, ibuprofen, 1-OH-ibuprofen, piroxicam, propyphenazone, sulfamethoxazole, diltiazem, norverapamil, hydrochlorothiazide, verapamil, bezafibrate, gemfibrozil, parvastatin, carbamazepine, acridone, 10,11-epoxy-carbamazepine, 2-OH-carbamazepine, citalopram, fluoxetine, paroxetine, venlafaxine, azaperone, dexamethasone, metoprolol, propanolol	Field	Segre River (Ebro River basin, NE Iberian Peninsula)	–	–	125 individuals of *Ancylus fluviatilis*, 90 individuals of Hydropsyche sp., and 70 individuals of *Phagocata vitta*	Field study	Ruhí et al., 2016

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Table 1 (*continued*)

Species name	PhACs	Experiment	Tanks/aquariums	Acclimataion and conditions	Spiked level (ng mL^{-1})	Organism replicates/tank	Exposure conditions	Reference
Ramshorn snail	Diphenhydramine, oxazepam, trimethoprim, diclofenac, and hydroxyzine	Semi-natural large-scale system	Semi-natural pond 400 m^2 (40 × 10 m), with a mean depth of 1.3 m	The pond (pH = 7.2) has no connection to anthropogenically surface waters. The inflow of water comes from rain and ground water	0.4	Individual numbers for each species per sampling were 10 Zygoptera, 20 Planorbidae, 30 Asellus, and 30 Ephemeroptera	Sampling daily to weekly. Period: 66 days in total. Predators in the system were European perch (*Perca fluviatilis*) feeding on fish, zooplankton, and benthic macroinvertebrates, and damselfly larvae (Zygoptera: Coenagrion) preying on zooplankton and benthic macroinvertebrates	Lagesson et al., 2016
Snails (*Lymnaeidea* & *Physidae*)	Acetaminophen, amitriptyline, aripiprazole, benzoylecgonine, buprenorphine, caffeine, carbamazepine, diclofenac, diltiazem, diphenhydramine, duloxetine, fluoxetine, methylphenidate, norfluoxetine, promethazine, sertraline	Field	Semi-arid urban river influenced by snowmelt sited in East Canyon Creek in Park City, Utah, USA	–	–	3ampling campaings of 3 days each and including five sampling point	Field study	Haddad et al., 2018
Crustaceans								
Crabs (*Calappa philargius*)	37 antibiotics: 13 sulfonamides, 5 tetracyclines, 10 fluoroquinolones, 6 macrolides and 3 ionophores	Field	Marine aquaculture farms	–	–	14 fish, 504 shrimp, 4 crabs, 11 shellfish, 5 oyster	Field study	Chen et al., 2015
Waterlouse	Diphenhydramine, oxazepam, trimethoprim, diclofenac, and hydroxyzine	Semi-natural large-scale system	Semi-natural pond 400 m^2 (40 × 10 m), with a mean depth of 1.3 m	The pond (pH = 7.2) has no connection to anthropogenically surface waters. The inflow of water comes from rain and ground water	0.4	Individual numbers for each species per sampling were 10 Zygoptera, 20 Planorbidae, 30 Asellus, and 30 Ephemeroptera	Sampling: daily to weekly. Period: 66 days in total. Predators in the system were European perch (*Perca fluviatilis*) feeding on fish, zooplankton, and benthic macroinvertebrates, and damselfly larvae (Zygoptera: Coenagrion) preying on zooplankton and benthic macroinvertebrates	Lagesson et al., 2016
Waterlouse (*Asellus aquaticus*)	Sertrailine and fluoxetine	Exposure	2 constructed aquatic food chains of 3 trophic levels (40 L)	10 d of acclimatation (12:12-h light:dark and 20 °C)	10	N = 270 *A. aquaticus*. All trophic levels were exposed together within 1 replicate	7 days exposure	Boström et al., 2017
D. magna	Roxithromycin and propranolol	Exposure and depuration	500 mL glass beakers in dark	Artificial freshwater. The culture medium (at 22 °C with a light/dark cycle of 16 h/8 h) was renewed three times each week, and the daphnia was fed daily	5 and 100	Approximately 100 adult daphnids (21–28 days old) were placed in each beaker	24 h uptake phase followed by a 24 h depuration phase. Time points of 0, 3, 6, 12 and 24 h. Then, the remaining daphnia were transferred into clean water for the depuration test	Ding et al., 2016
Shrimps (*Gammarus pulex*)	Acetaminophen, diclofenac, 17alpha-ethinylestradiol	Field	Hogsmill River (Greater London), Chertsey Bourne River and the Blackwater River. Rivers received inputs from a total of five sewage treatment	–	–	4 samplimg point (N = 10): 50 m upstream from effluent outfalls, 50 m downstream of respective STW effluent outfall as well as 250 m and 1000 m downstream from the	Field study	Wilkinson et al., 2018

			works effluent outfalls			outfalls. 1 day		
Shrimps (*Gammarus pulex*)	Moclobemide, 5-fluoruracil, carbamazepine, diazepam, carvedilol, fluoxetine	Exposure and depuration	5 L tank	Water collected from Bishop Wilton Beck. All species were kept at c. 20 °C under a natural light regime and were fed	0.8, 0.4, 0.2, 0.4, 0.3 and 0.4 mmol/L	Three replicates of 12 animals	48 h exposure phase followed by a 48 h depuration phase (extended to 72 h fluoxetine and carvedilol). Sampling 0, 3, 6, 12, 24 and 48 h. In depuration stage the organisms were transferred into clean water. The same time points were used in the depuration phase.	Meredith-Williams et al., 2012
Planorbarius corneus	Moclobemide, 5-fluoruracil, carbamazepine, diazepam, carvedilol, fluoxetine	Exposure and depuration	15 L tank	Artificial pond water. All species were kept at c. 20 °C under a natural light regime and were fed	0.8, 0.4, 0.2, 0.4, 0.3 and 0.4 mmol/L	three replicates of 12 animals	Studies consisted of a 48 h exposure phase followed by a 48 h depuration phase (extended to 72 h fluoxetine and carvedilol). Sampling 0, 3, 6, 12, 24 and 48 h. In depuration stage the organisms were transferred into clean water. The same time points were used in the depuration phase.	Meredith-Williams et al., 2012
Shrimps (*Fenneropenaeus penicillatus*)	37 antibiotics: 13 sulfonamides, 5 tetracyclines, 10 fluoroquinolones, 6 macrolides and 3 ionophores	Field	Marine aquaculture farms	–	–	14 fish, 504 shrimp, 4 crabs, 11 shellfish, 5 oyster	Field study	Chen et al., 2015
Insects								
Hydropsyche sp.	Diclofenac, ibuprofen, 1-OH-ibuprofen, piroxicam, propyphenazone, sulfamethoxazole, diltiazem, verapamil, norverapamil, bezafibrate, hydrochlorothiazide, gemfibrozil, parvastatin, carbamazepine, acridone, 10,11-epoxy-carbamazepine, 2-OH-carbamazepine, citalopram, fluoxetine, paroxetine, venlafaxine, azaperone, dexamethasone, metoprolol, propanolol	Field	Segre River (Ebro River basin, NE Iberian Peninsula)	–	–	125 individuals *Ancylus fluviatilis*, 90 Hydropsyche sp., 70 individuals *Phagocata vitta*	Field study	Ruhí et al., 2016
Aquatic snails (*Bithynia tentaculata*)	Acetaminophen, diclofenac, 17alpha-ethinylestradiol	Field	Hogsmill River (Greater London), Chertsey Bourne River and the Blackwater River. Rivers received inputs from a total of five sewage treatment works effluent outfalls	–	–	4 samplimg point (N = 9): 50 m upstream from effluent outfalls, 50 m downstream of respective STW effluent outfall as well as 250 m and 1000 m downstream from the outfalls. 1 day	Field study	Wilkinson et al., 2018
Water boatman (*Notonecta glauca*)	Moclobemide, 5-fluoruracil, carbamazepine, diazepam, carvedilol, fluoxetine	Exposure and depuration	1.5 L aquarium in water	Artificial pond water. All species were kept at c. 20 °C under a natural light regime and were fed	0.8, 0.4, 0.2, 0.4, 0.3 and 0.4 mmol/L	three replicates of 12 animals	48 h exposure phase followed by a 48 h depuration phase (extended to 72 h fluoxetine and carvedilol. Sampling 0, 3, 6, 12, 24 and 48 h. In depuration	Meredith-Williams et al., 2012

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Table 1 (*continued*)

Species name	PhACs	Experiment	Tanks/aquariums	Acclimataion and conditions	Spiked level (ng mL^{-1})	Organism replicates/tank	Exposure conditions	Reference
							stage the organisms were transferred into clean water. The same time points were used in the depuration phase.	
Notonecta glauca	Sertrailine and fluoxetine	Exposure	2 constructed aquatic food chains of 3 trophic levels (40 L)	10 d of acclimatation (12:12-h light:dark and 20 °C)	10	N = 4 *N. glauca*. All trophic levels were exposed together within 1 replicate	7 days exposure	Boström et al., 2017
Mayflies (*Ephemerella* sp.), crane fly (*Tipula* sp.), snails (Lymnaeidea & Physidae), and caddis fly (*Trichopterans*: *Helicopsyche* sp., *Hydropsyche* sp.)	Acetaminophen, amitriptyline, aripiprazole, benzoylecgonine, buprenorphine, caffeine, carbamazepine, diclofenac, diltiazem, diphenhydramine, duloxetine, fluoxetine, methylphenidate, norfluoxetine, promethazine, sertraline	Field	Semi-arid urban river influenced by snowmelt sited in East Canyon Creek in Park City, Utah, USA	–	–	3 sampling campaings of 3 days each and including 5 sampling point	Field study	Haddad et al., 2018
Fish								
14 fish species	NSAIDs (diclofenac, ibuprofen, ketorolac and naproxen)	Field	Coastal Lagoons (Central Mexican Pacific)	–	–	4 specimens per species	Field study	Arguello-Pérez et al., 2020
European perch (*Perca fluviatilis*)	Temazepan and oxazepan	Exposure	Aquaria of 50 L were filled with 10 L of aged tap water, with each also being enriched with 1 L of water from the lake of larvae origin. Organic debris from the lakes was also added to provide shelter for individual larvae.	40-day acclimation period (14 °C, oxygen saturation: >100 %, pH: 7.8–8.2, light:dark regime of 12:12 h). Fish were fed with frozen chironomid larvae daily, and with live zooplankton collected from a fishless local pond	0.2–2	14 exposure treatments with 15 individuals each under two separate temperature regimes (10 or 20 °C) and different concentration levels	Larvae were exposed for 8 days in an individual static exposure scenario	Cerveny et al., 2021b
Pimephales notatus and *Ictalurus punctatus*	Carbamazepine	Exposure and depuration	Tanks of 20 L	Fish were kept in 16:8 light/dark cycle at 25–21 °C, pH 8.0 and O_2 7.8 mg/L. Fish were fed	300	Control tank and five exposure tanks. Minnows (n = 60) were randomly distributed	Minnows were exposed for 28 d and then moved into clean tanks containing only dilution water for a 14 d depuration period. In the 14 d CBZ BCF study, juvenile catfish were placed into four 80 L aquaria and exposed to a continuous 83 μg/L carbamazepine solution. Catfish were exposed to CBZ for 7 d and then moved into clean aquaria for a 7 d depuration phase	Garcia et al., 2012
Oreochromis niloticus	Carbamazepine	Field	Pecan Creek Wastewater Reclamation Plant (PCWRP) in Denton, Texas	–	–	1 sampling date	–	Garcia et al., 2012
Common carp (*Cyprinus carpio*) and pikeperch	66 PhACs (alfuzosin, amitriptyline, atenolol, atorvastatin, azithromycin,	Field	Wastewater stabilization ponds	–	–	12 specimens from each fish species	After six-month exposure to reclaimed wastewater,	Grabicová et al., 2020

(*Sander lucioperca*), Stone moroko (*Pseudorasbora parva*)	bezafibrate, biperiden, bisoprolol, carbamazepine (þits metabolites 10,11-trans-dihydrocarbamazepine, 10,11-dihydrocarbamazepine), cetirizine, cilazapril, citalopram (þN-desmethylcitalopram), clemastine, clindamycin (þclindamycin sulfoxide), clonazepam, dicycloverine, diltiazem, donepezil, diphenhydramine, disopyramide, erythro-mycin, fenofibrate, fexofenadine, glibenclamide, halo-peridol, glimepiride, irbesartan, loperamide, maprotiline, meclozine, memantine, methamphetamine, metoprolol, mianserin, miconazole, mirtazapine, orphenadrine, oseltamivir carboxylate, oxazepam, oxcarbazepine, pizotifen, propranolol, ropinirole, roxithromycin, sertraline, sotalol, sulfaclozine, sulfamethazine, sulfamethizole, sulfamethoxazole (þN1-acetylsulfamethoxazole), telmisartan, terbinafine, terbutaline, tramadol, triamterene, trimethoprim, valsartan, venlafaxine (þO-desme-thylvenlafaxine) and verapamil)		(Czech Republic)				fish were caught.	
Stoneroller minnows (*Campostoma anomalum*)	Acetaminophen, caffeine, carbamazepine, diltiazem, diphenhydramine, fluoxetine, norfluoxetine, and sertraline	Mesocosm study	BEAR Facility, with 12 outdoor mesocosms with a mixing tank (~378 L), followed by a riffle section, a run or glide section and bottom pool (~378 L), located at the Lake Waco Wetlands, Texas, USA	The flow of water originated from a large holding tank that delivered water to all 12 streams. A controlled volume of water (100 mL/min) was permanently removed from the bottom pool with an overflow drain, while the remaining water flow (~50 L/min) was recirculated to the mixing tank. Stoneroller minnows were acclimated for 24 h in outdoor storage tanks at the BEAR facility and transplanted to cages in the experimental streams. Fish cages were also placed in the run section of each stream	–	One fish sampled per stream ($N = 12$) on each sampling day	8-Day study. Sampling on days 3 and 8.	Burket et al., 2020
Brown trout (*Salmo trutta* m. fario)	Citalopram, clomipramine, haloperidol, hydroxyzine, levomepromazine, mianserin, mirtazapine, paroxetine, sertraline, tramadol and venlafaxine	Field	Zivny Stream (tributary of the Blanice River, the Czech Republic), which is a small stream highly affected by effluent from a sewage treatment plant	–	–	Trouts (N from 11 to 44) were sampled at 1, 3, 6 months in two sampling points. One point was also sampled at 18 months (N = 2)	Field study	Grabicova et al., 2017
Rainbow trout (*Oncorhynchus mykiss*)	Carbamazepine, diphenhydramine, diltiazem, and fluoxetine	Field	Effluent-dominated river influenced by	–	–	In situ upstream and at incremental distances	Fish were acclimated for 24 h before deployment	Sims et al., 2020

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Table 1 (*continued*)

Species name	PhACs	Experiment	Tanks/aquariums	Acclimataion and conditions	Spiked level (ng mL^{-1})	Organism replicates/tank	Exposure conditions	Reference
			snowmelt in East Canyon Creek in Park City, Utah, USA			downstream (0.1, 1.4, 13 miles) with two 7-day studies in the Summer and Fall seasons	and were not fed before or during the field campaign. Trout were caged in 25.4 cm PVC tubing with a diameter of 10.2 cm and mesh fiberglass. Mesh pore size allowed small aquatic invertebrates to enter cages. On study day 0, cages were deployed at each site with one fish per cage. At each site, triplicate samples were collected days 1, 3, and 7 ($n = 3$)	
Common carps (*Cyprinus carpio* L.)	Diclofenac, tramadol, atenolol, irbesartan, metoprolol, cetirizine, fexofenadine, meclozine, clarytromycin, clindamycin, erythromicyn, sulfamethoxazole, carbamazepine, oxcarbamazepine, citalopram, methamphetamine, sertraline, and venlafaxine and their metabolites/transformation products metoprolol/atenolol acid, clindamycin sulfoxide, N4-acetyl sulfamethoxazole, 10,11-epoxycarbamazepine, trans-10,11-dihydro-10,11-dihydroxy carbamazepine, N-desmethylcitalopram, and *O*-desmethylvenlafaxine	Field	Cezarka pond (2.6 ha) designed to treat effluent from the Vodnany WWTP, in Czech Republic	–	–	Samplings were performed during 1 year (N = 60)	One-thousand tagged carps were stocked in the pond. Twelve fish were caught during each sampling campaign	Koba et al., 2018
(*Pungitius pungitius*)	Sertrailine and fluoxetine	Exposure	2 constructed aquatic food chains of 3 trophic levels (40 L)	10 d of acclimatation (12:12-h light:dark and 20 °C)	10	N = 1 *P. pungitius*. All trophic levels were exposed together within 1 replicate	7 days exposure	Boström et al., 2017
Caged goldfish (*Carassius auratus*), Wild carp (*Cyprinus carpio*)	Amitriptyline, benztropine, caffeine, citalopram, diazepam, diphenhydramine, erythromycin, flumequine, ofluoxetine, gemfibrozil, oibuprofen, iopamidol, sertraline, sulfamethazine, valsartan, venlafaxine	Field	Cootes Paradise Marsh, an urban wetland that receives tertiary treated municipal waste waters as well as urban storm runoff	–	–	The goldfish was caged for 21 days in 3 locations and also collected 1 day. Wild carp was collected in two days	Fish (13/cage) were fed during the visits (20 g/cage)	Muir et al., 2017
Fathead minnow and channel catfish	Verapamil and clozapine	Exposure and depuration	20-L and 60-L tanks for fathead minnow and catfish tests, respectively	Acclimatation for 1 week under a 18:6-h light:dark photoperiod at 20 °C in glass aquaria with continuously aerated, carbon-!ltered, dechlorinated tap water under flow-through conditions	500 and 40	For verapamil test, 50 fish (25 each in 2 exposure tanks). For clozapine BCF test, 60 fish (30 each in 2 exposure tanks)	28 days exposure and 14 days of depuration period. Sampling at 1, 3, 7, 14, and 28 days. After up take phase the fish were transferred to clean. Sampling at 35 and 42 days	Nallani et al., 2016
Bluegill sunfish (*Lepomis macrochirus*)	Diclofenac, methocarbamol, rosuvastatin, sulfamethoxazole, and temazepam	Exposure and depuration	Flow-through system. Three exposure experiments	1 week of acclimatation. Fish were fed with commercial pellets at a rate of 1–2 % bodyweight per day.	1–4		Kinetics of uptake (0–14 d) and elimination (14–28 d). Fish were fed every other day for the duration of the uptake exposure. Sampling days	Zhao et al., 2017

							0, 1, 2, 3, 5, 8, 13, 14 for uptake, and days 14, 15, 16, 17, 20, 22, 28 for elimination	
Hemiculter leucisculus, *Carassius auratus*	Oxithromycin, erythromycin and ketoconazole, ibuprofen and diclofenac, propranolol, carbamazepine, 17α-ethinylestradiol	Field	Downstream rivers of sewage treatment plants in Nanjing, China (four Rivers)	–	–	3 sampling point for water and 4 for fishes in 1 day and each River	Field study	Liu et al., 2015
Gambusia affinis	Carbamazepine and atenolol	Field	5 L of aquarium water	Acclimatation 1 month in 100 L aerated glass aquaria, fed twice a day. One week before starting the bioassay, fish were acclimatized to 12:12 h light:dark, 21 °C. Twenty-four hours before the test fish were randomly separated in 5 L aquaria and stopped feeding	10, 100, 1000	Each aquarium contained five individuals and two replicates were made for each of the five treatments	Exposure for 96 h. Test solutions were half renewed every day	Valdés et al., 2014
Rainbow trout (*Oncorhynchus mykiss*)	NSAID (Ibuprofen)	Exposure	Four tanks (500 L)	Fish were acclimatized changing non-chlorinated artesian well water (pH 7.6, temperature 9.9–11.6) for 1 week. The 0.5-year old fish were fed twice a day and 1-year old fish every other day. Feeding was stopped 3d before experiments	0.17, 1.9, 13 and 145	At each level, 9 troutsused	Exposure via intraperitoneal and water for 4 d. A periodic water replacement system was used, where 20 % of the water was changed daily. Analysis of ibuprofen and their metabolites in bile	Brozinski et al., 2013
Juvenile meagre (*Argyrosomus regius*)	Venlafaxine	Exposure	27 tanks (50 L)	Tanks had independent functioning, being equipped with protein skimmer, UV disinfection, biological filtration and chemical filtration to maintain seawater quality. Furthermore, each tank had independent temperature and pH control	20 (for exposure via water) and 160 μg/kg dw for feed exposure (~4 times the values commonly found in species inhabiting contaminated coastal areas)	3 replicates × 9 treatments = 27 tanks; treatments randomly assigned to each tank/replicate.10 animals analysed for each treatment	Water and dietary exposure sources. Daily spike seawater during the 28 days of exposure. Study of the effcet of temperature ($\Delta T^{\circ}C = +5$ °C) and high CO2 levels ($\Delta pCO2 \sim 1000$ μatm; equivalent to $\Delta pH = -0.4$ units). By the end of exposure, behavioural tests were conducted in ten animals randomly selected out of the three replicate tanks composing each treatment.	Maulvault et al., 2018
Crucian carp (*Carassius auratus*)	Diclofenac	Exposure	Three water tanks	2 weeks of acclimatation in dechlorinated municipal water (20 °C; pH, 7.2; dissolved O_2, 6.7 mg/L; and total hardness, 119.7 mg/L $CaCO_3$). The photoperiod was a 12:12 h light:dark regime. The fish were fed every day	4, 20 and 100	3 tanks of three fish each were used for every exposure concentration and control group	Fish were exposed to increasing concentrations of diclofenax. The semistatic exposures were renewed every 24 h with 50 % of water changes. Sampling at 7, 14, and 21 days	Lu et al., 2018
European perch (*Perca uviatilis*)	Benzodiazepine (temazepam)	Exposure-depuration test	Ten water aquariums (30 L)	2 weeks of acclimatation in aerated flow-through tank of non-chlorinated	2	Seven individuals in each of 10 exposure tanks	Fish were exposed to 2 μg/L for 10 days. 50 % of the water was renewed	Cerveny et al., 2021a

(continued on next page)

Table 1 (*continued*)

Species name	PhACs	Experiment	Tanks/aquariums	Acclimataion and conditions	Spiked level (ng mL^{-1})	Organism replicates/tank	Exposure conditions	Reference
				tap water (pH, 8.2; ammonium < 0.004 mg/L; nitrite < 0.003 mg/L; oxygen saturation, >100 %). The light/dark regime was set to 12/12 h. Fish were fed on a daily basis.			every 2nd day. 4 to 5 individuals sampled from different tanks at 6, 12, 24, 48, 96, 144, 192, and 240 h after the commencement of exposure. After 10 days of exposure, the remaining fish were transferred to clean water and the depuration period started with exactly the same design as the exposure period. Water samples were taken from 4 randomly selected tanks at 13 sampling points. Fish were fed on a daily basis during both periods	
Largemouth bass, White sucker, Yellow perch, Smallmouth bass	Carbamazepime, Hydrochlorothiazide	Field	164 urban rivers in the U.S.	–	–	Fish samples were collected at 542 randomly selected river locations in 48 states	Field study	Huerta et al., 2018
European perch	Diphenhydramine, oxazepam, trimethoprim, diclofenac, and hydroxyzine	Semi-natural large-scale system	Semi-natural pond 400 m^2 (40 × 10 m), with a mean depth of 1.3 m	The pond (pH = 7.2) has no connection to anthropogenically surface waters. The inflow of water comes from rain and ground water	0.4	10 species per sampling. Zygoptera, 20 Planorbidae, 30 Asellus, 30 Ephemeroptera	Sampling was carried out on a daily to weekly basis over a period of 66 days in total. Predators in the system were European perch (*Perca fluviatilis*) feeding on fish, zooplankton, and benthic macroinvertebrates, and damselfly larvae (Zygoptera: Coenagrion) preying on zooplankton and benthic macroinvertebrates	Lagesson et al., 2016
Sea trout (*Salmo trutta*)	Temazepam and irbesartan	Exposure	Three 400 L flow-through tanks	Tanks supplied with river water from the Ume River and equipped with two airstones at 7–11 °C, pH 4.5. Fish were fed daily until satiation	temazepam (0.08 and 1.5), irbesartan (0.2 and 20)	16 fish by tank	Exposure over 7 days. Sampling (N = 4) after 8 h, 16 h, 1 d, 2 d, 3 d, 4 d, 5 d, 6 d, and 7 d of exposure	McCallum et al., 2019
Golden grey mullet	Hydrochlorothiazide	Field	Mar Menor lagoon	–	–	8 sampling points	Field study	Moreno-González et al., 2016
Crucian cap (*Carassius auratus*)	Fluoxetine	Exposure or exposure + depuration	10 L glass tanks	Fresh egg water. pH 6.8–7.2; 14:10-h light: dark cycle at 28C. Exposure medium was refreshed every 24 h	0.1, 1, 10, 100, 1000	3 tank and day	Long term: 30-day exposure. The test solutions were replaced every 24 h. Short term: 6 days exposure. Fish exposed for 6 days at 0.1 mg/L, followed by a 6-day recovery period (clean water), for a total of 12 days. The test solution and water were	Pan et al., 2018

							replaced every 24 h. Sampling on days 0, 3, 6, 9, and 12	
Loach (*Misgurnus anguillicaudatus*)	Venlafaxine and its metabolite	Exposure	30-L glass tanks	4 weeks of acclimatation in deionized water at 25 °C. The water was renewed and the tanks were cleaned once a day. Each tank was equipped with an aeration stone.	500	–	Exposure experiments: 1) Loaches were exposed to rac-venlafaxine. 2) Loaches were exposed to rac-venlafaxine with microplastic. 3) Loaches exposed to only microplastic. Sampling on days 0, 0.5, 1, 3, 6, 10, 16, 25 and 40	Qu et al., 2019
Epinephelus awoara, *Ephippus orbis*, *Culter alburnus*. *Shellfish*: *Ostrea gigas*, *Mimachlamys nobilis*, *Mytilus edulis*, *Bufonaria perelegans*	Sulfadiazine, sulfamerazine, sulfamethazine, sulfamethoxazole, trimethoprim, sulfathiazole, sulfapyridine, ciprofloxacin, norfloxacin, ofloxacin, flumequine, tetracycline, oxytetracycline, isochlortetracycline, penicillin G sodium, cefotaxime sodium, spectinomycin, roxithromycin, erythromycin-H_2O, clarithromycin, chloramphenicol, paracetamol, naproxen, ibuprofen, ketoprofen, diclofenac acid, carbamazepine, diltiazem, diphenhydramine, gemfibrozil	Field	Pearl River Delta (Five mariculture sites around)	–	–	$N = 30$	Field study	Xie et al., 2019
Crucian carp (*Carassius auratus*)	Diclofenac	Exposure	Three tanks per treatment	2 weeks acclimatation in dechlorinated tap water at 20 °C; 12 h:12 h light-dark cycle. pH, 6.9; dissolved O_2 6.8 mg/L; total hardness, 121.6 mg/L$CaCO_3$	1, 10, 100 and 1000	Each treatment was applied in triplicate glass tanks with 6 fish per tank.	Fish were exposed to Cu and diclofenac alone or in combination for 7 days. The fish were not fed throughout the experimental period. The exposure solutions were refreshed every 24 h.	Xie et al., 2020
Lutjanus russelli, *Lutjanus erythopterus* and *Trachinotus ovatus*	37 antibiotics: 13 sulfonamides, 5 tetracyclines, 10 fluoroquinolones, 6 macrolides and 3 ionophores	Field	Marine aquaculture farms	–	–	14 fish, 504 shrimp, 4 crabs, 11 shellfish, 5 oyster	Field study	Chen et al., 2015
Smallmouth bass (*Micropterus dolomieu*), largemouth bass (*Micropterus salmoides*), the exotic common rudd (*Scardinius erythrophthalmus*), rock bass (*Ambloplites rupestris*), white bass (*Morone chrysops*), white perch (*Morone americana*), walleye (*Sander vitreus*), bowfin (*Amia calva*), steelhead trout (*Oncorhynchus mykiss*), and yellow perch (*Perca flavescens*).	Antidepressants	Field	Niagara River (North American Great lakes)	–	–	Locations of the two WWTPs relative to the Niagara River	Field study	Arnnok et al., 2017
Cnesterodom decemmaculatus Jennyns and *Cyphocharax voga* Hensel	39 PhACs and two metabolites (Analgesics/anti-inflammatories, Antibiotics, Antihelmintics, Antihypertensive, Antiplatelet agent, B-blocking agents, Histamine H1 and H2	Field	Two lowland urban rivers in Argentine.	–	–	Five sampling points in each river	Field study	Mastrángelo et al., 2022

(continued on next page)

Table 1 (*continued*)

Species name	PhACs	Experiment	Tanks/aquariums	Acclimatation and conditions	Spiked level (ng mL^{-1})	Organism replicates/tank	Exposure conditions	Reference
	receptor antagonists, Lipid regulators, Psychiatric drugs)							
Brown trout (*Salmo trutta*) and mottled sculpin (*Cottus bairdii*).	Acetaminophen, amitriptyline, aripiprazole, benzoylecgonine, buprenorphine, caffeine, carbamazepine, diclofenac, diltiazem, diphenhydramine, duloxetine, fluoxetine, methylphenidate, norfluoxetine, promethazine, sertraline	Field	Semi-arid urban river influenced by snowmelt sited in East Canyon Creek in Park City, Utah, USA	–	–	3 sampling campaings of three days each and including five sampling point	Field study	Haddad et al., 2018
Marine medaka (*Oryzias melastigma*)	Sulfamethazine	Exposure	35 L glass vessel	2 weeks of acclimatation in artificial seawater with dissolved O_2 6.0 0.2 mg/L and at 28 °C in a 14 h/10 h light/dark photoperiod cycle	40 and 200	Each treatment was applied in triplicate with four fish per tank.	Fish were exposed to sulfamethazine for 24 h and samples were collected at each time point (0, 1, 2, 7, 12 and 24 h). Fish was not fed during the exposure period	Zhao et al., 2016

5. Results and discussion

Table 1 summarizes the research found in the scientific literature dedicated to the evaluation of the bioaccumulation potential of PhACs in aquatic organisms.

This data has been obtained from over 100 scientific sources published between 2010 and 2022, with over 95 % of the data generated in last 5 years. Information concerning the species, PhACs, concentration levels, acclimation period and experimental designs are included in the table.

Fish are the most commonly used organisms in bioaccumulation studies (n = 32), followed by molluscs (n = 18), crustaceans (n = 8) and, finally, minor invertebrates (larvae) (n = 6) (Fig. 1). Fish play a key role in the environment, regulating the biological structure of habitats as well as being an important food source for many other aquatic organisms. The most frequently studied species are the crucian carp (*Carassius auratus*), common carp (*Cyprinus carpio*), rainbow trout (*Oncorhynchus mykiss*) and European perch (*Perca fluviatilis*). The preferred tissues or organs for BCF/BAF measurements were the muscle (35 %), brain (18 %), liver (15 %), whole individual (9 %), and other organs (20 %) which include gills, gonad, kidney or bile. Molluscs, especially bivalves, are given particular attention in bioaccumulation studies, their sessile lifestyles and either filtering or deposit feeding making them of particular interest (Świacka et al., 2021a). In these cases the whole organism is commonly analysed.

Laboratory experiments were conducted by water exposure (33 %) or by water uptake and purification phase (25 %). Only one of them (Maulvault et al., 2018) used both exposure sources (water and diet). The remaining 37 % of the reviewed articles were field studies; the majority of them in freshwater. To the best of our knowledge, only two studies were semi-natural large-scale system tests (Lagesson et al., 2016; Burket et al., 2020). Lagesson et al. (2016) selected a semi-natural pond of 400 m^2 to assess the extent at which PhACs are taken up by a vertebrate top consumer and four invertebrate species of an aquatic food web. Burket et al. (2020) used a municipal wastewater effluent as the source water in an outdoor stream mesocosm to simulate effluent-dependent lotic systems to examine the bioaccumulation of several widely-used PhACs.

Table 2 collects a total of >230 BCF and >530 BAF values for 113 PhACs in a range of aquatic species. BAF/BCFs are expressed in wet weight (w.w.) or dry weight (d.w.) bases and the units are L kg^{-1}.

Some PhACs have a considerable number of reported BCF/BFA values. Specifically, there are >35 observations for the antihistamine diphenhydramine (n = 52), followed by carbamazepine (n = 48), diclofenac (n = 41), and the antidepressant therapeutic group (venlafaxine (n = 42), citalopram (n = 40) and sertraline (n = 40) and their metabolite norsertraline (n = 22). There are only one or two BCF/BAF values for 52 % of the PhACs and there are five or fewer reported BCF/BAF values for 62 % of the PhACs. To the best of our knowledge, there are no observations for the anticancer drug group, with the exception of 5-fluorouracile.

Figs. 1 and 2 show the general trend of the bibliographic data in this field of research. It can be observed that the distribution for individual PhACs is not uniform.

One of the main explanations for the lack of data uniformity is the disparate factors used in the design of the surveys (water temperature, exposure time, exposure route, dissolved organic matter, feeding and growth rates, or selected tissue or organ). BCF values are highly influenced by experimental and biotic factors (Duarte et al., 2022). Some authors have pointed to temperature and exposure time as the variables higher weight in BCF data. Maulvault et al. (2018) assessed the effect of increased temperature ($\Delta T°C$ = 5 °C) and high CO_2 levels (equivalent to $\Delta pH = -0.4$ units). Their data suggest an increase of BCF with the combination of warming and acidification. Recently, Cerveny et al. (2021b) assessed how temperature affects temazepam biotransformation and the subsequent accumulation of its metabolite (oxazepam) in two organisms of the food chain ecosystem (the European perch (*Perca fluviatilis*) and the dragonfly larvae (*Sympetrum* sp.). Their results showed that exposure to PhACs may change across temperature gradients in the environment. While the bioconcentration of temazepam in perch was reduced at higher

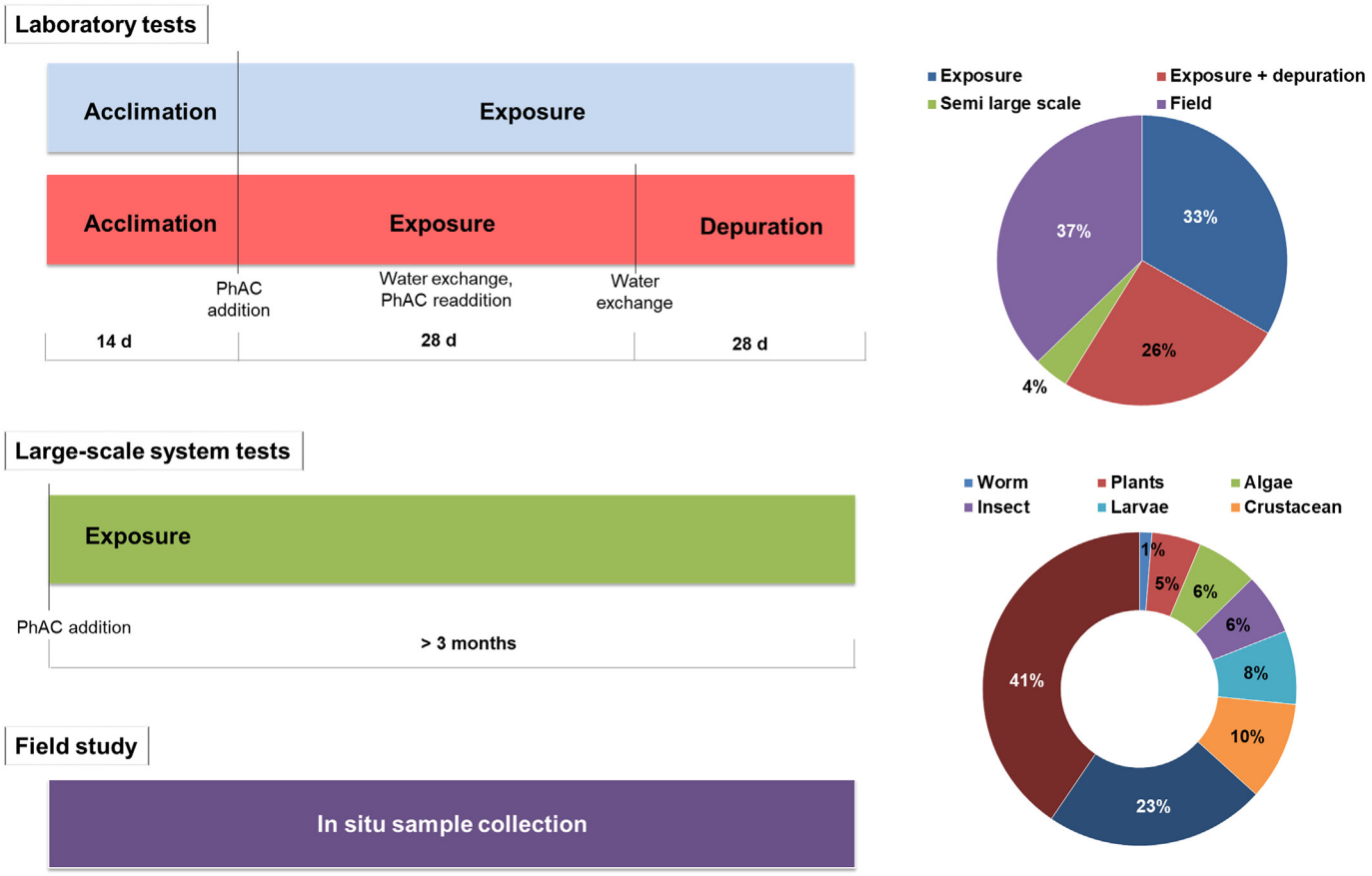

Fig. 1. Schematic representation of the possible scenarios to assess bioconcentration/bioaccumulation potential.

temperatures as a consequence of the biotransformation and accumulation of its main metabolite in the fish (two-fold higher at 20 °C compared to 10 °C), no temperature influence was found for larvae. Temperature may affect metabolic activity and, as a consequence, the bioconcentration pattern (Buckman et al., 2004). In a previous study, Opperhuizen et al. (1998) observed an increase in BCF values for chlorinated benzenes with increasing water temperature. In other research, Lu et al. (2018) reported that in the presence of higher dissolved organic matter content (DOM), the potential bioconcentration of diclofenac in fish decreased significantly. Feeding and the hydrodynamic experiment also led to lower bioaccumulation of diclofenac in fish tissues.

Taking into account the route of exposure, in the case pf PhACs exposure through water may be more important for uptake and bioaccumulation rates than dietary exposure (Du et al., 2014). For example, Maulvault et al. (2018) observed plasma concentration levels of venlafaxine 50 times higher in fish exposed via water (46 μg/L day) compared to fish exposed via diet (0.5 μg/L day). Nunes et al. (2020) suggested that direct (waterborne) and trophic (via contaminated feed) exposures to diclofenac caused significantly different physiological modifications in aquatic organisms. Variability of results is reduced if standard protocols are met and with better knowledge of the key experimental parameters. Heynen et al. (2016) compare uptake of oxazepam from water (bioconcentration) and via a contaminated diet (trophic transfer) in Eurasian perch *(Perca fluviatilis)* and dragonfly larvae (*Aeshna grandis*). Bioconcentration and trophic transfer of oxazepam were found in both predator species. However, higher bioconcentrations were observed for perch (BCF 3.7) than for dragonfly larvae (BCF 0.5). The relative contribution via prey consumption was 14 % and 42 % for perch and dragonflies, respectively.

Though theoretically BCF should not be affected by the concentration to which the organism is exposed since it is a result of the difference between the absorption and elimination processes, different levels were regularly tested in the reviewed literature. In some cases, a different bioconcentration pattern has been observed, suggesting that this factor must be taken into consideration (Lopes et al., 2022; Świacka et al., 2020; Lu et al., 2018; McCallum et al., 2019; Pan et al., 2018; Molina-Fernández et al., 2021; Xie et al., 2020; Brozinski et al., 2013). Pan et al. (2018) reported that the BCF of fluoxetine in red crucian carp was inversely proportional to the exposure concentrations. Similarly, Zhao et al. (2016) observed that the BCF of sulfamethazine at a concentration of 40 ng mL^{-1} was higher than at 200 ng mL^{-1}. Rosa et al. (2019) observed that the oxytetracycline levels in the macroalgae *Ulva* decreased significantly slower at 40 ng mL^{-1} (48 h) than at 120 ng mL^{-1} (24 h).

On the other hand, for organic substances there is a clear correlation between the lipid content of biota and BCF values (Miller et al., 2019; Gobas et al., 1999). Hydrophobic substances (log K_{ow} > 3) reach equilibrium in the lipid fraction and the bioaccumulation potential is theoretically indicated by log Kow. Arnot and Gobas (2006) reported that doubling the lipid content approximately doubles the BCF. Thus it is important to normalize lipids to reduce variability and allow better comparison of results. However, bioaccumulation is also empirically demonstrated by organism concentrations exceeding the surrounding water concentration (Meredith-Williams et al., 2012; Grabicova et al., 2015). Variations of the pH in the exposure system may significantly change the ionization states of PhACs and consequently influence their bioaccumulation. A number of studies on aquatic organisms and on a range of PhACs (sertraline, fluoxetine, sulfathiazole, ciprofloxacin, lincomycin, enrofloxacin and chlortetracycline, ibuprofen or acetaminophen) have demonstrated that uptake and toxicity of ionizable PhACs can also be very sensitive to changes in pH of the environment (Meredith-Williams et al., 2012; Rendal et al., 2011; Valenti et al., 2009). For example, Ding et al. (2016) examined the bioconcentration profiles of roxithromycin and propranolol in *D. magna* after 24 h of exposure under different pH levels (7–9). Their results showed that daphnia body

Table 2
BAF/BCF observations for PhACs in aquatic organisms belonging to different throphic levels.

Pharmaceutical	Organism	Tissue; dry weight (dw) or wet weight (ww)	BAF	BCF	Reference
1-Hydroxy-ibuprofen	Limpet (*Ancylus fluviatilis*)	Whole organism (dw)	7.28–10.8		Ruhí et al., 2016
	Caddisfly (*Hydropsyche* sp.)	Whole organism (dw)	7.28–10.8		Ruhí et al., 2016
	Flatworm (*Phagocata vitta*)	Whole organism (dw)	7.28–10.8		Ruhí et al., 2016
	Predicted	–	0.29		Ruhí et al., 2016
5-Fluorouracil	Shrimps (*Gammarus pulex*)	Whole organism (dw)		4.37–9.17	Meredith-Williams et al., 2012
	Water boatman (*Notonecta glauca*)	Whole organism (dw)		0.07–0.21	Meredith-Williams et al., 2012
10,11-Epoxycarbamazepine	Macrophyte (*Lemna gibba*)		308		Mastrángelo et al., 2022
10-Hydroxy-10,11-dihydro-carbamazepine	Mussel (*M. galloprovincialis*)	Whole organism (dw)		4.5	Boillot et al., 2015
10-Hydroxy-amitriptyline	Mussel (*Lasmigona costata*)	Tisseus (gill, digestive gland (excluding stomach and its contents), and gonadal tissues (ww))	74–134		de Solla et al., 2016
17α-Ethynylestradiol	Mussel (*Mytilus galloprovincialis*)	Whole organism (ww)		30–39	Lopes et al., 2022
	Fish (*Hemiculter leucisculus*)	Liver (ww)	**20,392**		Liu et al., 2015
	Fish (*Hemiculter leucisculus*)	Brain (ww)	**8357**		Liu et al., 2015
	Fish (*Hemiculter leucisculus*)	Muscle (ww)	857		Liu et al., 2015
	Fish (*Hemiculter leucisculus*)	Gill (ww)	**4071**		Liu et al., 2015
	Fish (*Carassius auratus*)	Liver (ww)	**16,642**		Liu et al., 2015
	Fish (*Carassius auratus*)	Brain (ww)	**7214**		Liu et al., 2015
	Fish (*Carassius auratus*)	Gill (ww)	**5714**		Liu et al., 2015
	Clam (*Ruditapes philippinarum*)	Whole organism (ww)		0.024–0.031	Silva et al., 2022
2-Hydroxycarbamazepine	Bifilm		125		Mastrángelo et al., 2022
	Macrophyte (*Lemna gibba*)		250		Mastrángelo et al., 2022
4-Hydroxy-diclofenac	Mussel (*Mytilus trossulus*)	Whole organism (dw)		69.7	Świacka et al., 2021b
	Biofilm	(dw)		49.8	Świacka et al., 2021b
Amitriptyline	*Cottus bairdii*	Whole organism (ww)	161–**2279**		Haddad et al., 2018
	Lymnaeidea & Physidae	Whole organism (ww)	917		Haddad et al., 2018
	Periphyton	Whole organism (ww)	833–**17,209**		Haddad et al., 2018
	Salmo trutta	Whole organism (ww)	119–1605		Haddad et al., 2018
	Trichoptera	Whole organism (ww)	161–1083		Haddad et al., 2018
	Mussel (*Lasmigona costata*)	Tisseus (gill, digestive gland (excluding stomach and its contents), and gonadal tissues (ww))	**4384–8341**		de Solla et al., 2016
Amlodipine	Mussel (*Lasmigona costata*)	Tisseus (gill, digestive gland (excluding stomach and its contents), and gonadal tissues (ww))	**4077–7578**		de Solla et al., 2016
Amphetamine	Mussel (*Lasmigona costata*)	Tisseus (gill, digestive gland (excluding stomach and its contents), and gonadal tissues (ww))	109–284		de Solla et al., 2016
Atenolol	A. Common carp (*Cyprinus carpio*)	Liver (ww)	31		Grabicová et al., 2020
	Fish (*Gambusia affinis*)	Whole organism (ww)		0.08–0.13	Valdés et al., 2014
Atorvastatin	Fish Predicted (BCFBAF v3.10)	–		56.23	Reis et al., 2021
Azithromycin	A. Common carp (*Cyprinus carpio*)	Liver (ww)	1200		Grabicová et al., 2020
	B. Pikeperch (*Sander lucioperca*)	Liver (ww)	770		Grabicová et al., 2020
	A. Common carp (*Cyprinus carpio*)	Kidney (ww)	1500		Grabicová et al., 2020
	B. Pikeperch (*Sander lucioperca*)	Kidney (ww)	690		Grabicová et al., 2020
	B. Pikeperch (*Sander lucioperca*)	Brain (ww)	160		Grabicová et al., 2020
	Plankton	(ww)	**4800**		Grabicová et al., 2020
	Mussel (*Lasmigona costata*)	Tisseus (gill, digestive gland (excluding stomach and its contents), and gonadal tissues (ww))	98–346		de Solla et al., 2016
Benztropine	Caged goldfish (*Carassius auratus*)	Plasma	49–165		Muir et al., 2017
	Wild carp (*Cyprinus carpio*)	Plasma	153–1158		Muir et al., 2017
Betamethasone	Fish Predicted (BCFBAF v3.10)	–		8.85	Reis et al., 2021
Bezafibrate	Limpet (*Ancylus fluviatilis*)	Whole organism (dw)	4.86–7.78		Ruhí et al., 2016
	Caddisfly (*Hydropsyche* sp.)	Whole organism (dw)	4.86–7.78		Ruhí et al., 2016
	Flatworm (*Phagocata vitta*)	Whole organism (dw)	4.86–7.78		Ruhí et al., 2016
	Predicted	–	3.47		Ruhí et al., 2016
Bisoprolol	Stone moroko (*Pseudorasbora parva*)	(ww)	1.6		Grabicová et al., 2020
	Plankton	(ww)	48		Grabicová et al., 2020
Bupropion	Fish (smallmouth bass)	Brain (dw)	3–8		Arnnok et al., 2017

Table 2 (*continued*)

Pharmaceutical	Organism	Tissue; dry weight (dw) or wet weight (ww)	BAF	BCF	Reference
	Fish (smallmouth bass)	Gonad (dw)	1–9		Arnnok et al., 2017
	Fish (smallmouth bass)	Liver (dw)	1–4		Arnnok et al., 2017
	Fish (largemouth bass)	Brain (dw)	6		Arnnok et al., 2017
	Fish (largemouth bass)	Gonad (dw)	3		Arnnok et al., 2017
	Fish (largemouth bass)	Liver (dw)	2–5		Arnnok et al., 2017
	Fish (white bass)	Gonad (dw)	1–26		Arnnok et al., 2017
	Fish (white perch)	Gonad (dw)	62		Arnnok et al., 2017
	Fish (walleye)	Gonad (dw)	46		Arnnok et al., 2017
	Fish (yellow perch)	Gonad (dw)	30		Arnnok et al., 2017
Caffeine	Fish stoneroller minnows (*C. anomalum*)	Fish tissues (ww)	100		Burket et al., 2020
	Cattail (*Typha angustifolia*)	ww		110.68	Wang et al., 2019
	Fish Predicted (BCFBAF v3.10)	–		3.16	Reis et al., 2021
	Baetidae	Whole organism (ww)	299–451		Haddad et al., 2018
	Cottus bairdii	Whole organism (ww)	15–169		Haddad et al., 2018
	Lymnaeidea & Physidae	Whole organism (ww)	20		Haddad et al., 2018
	Periphyton	Whole organism (ww)	21–642		Haddad et al., 2018
	Salmo trutta	Whole organism (ww)	19–169		Haddad et al., 2018
	Trichoptera	Whole organism (ww)	20–1056		Haddad et al., 2018
	Caged goldfish (*Carassius auratus*)	Plasma	15–16		Muir et al., 2017
	Wild carp (*Cyprinus carpio*)	Plasma	16–51		Muir et al., 2017
	Haemolymph	Whole organism (ww)		1.2	Álvarez-Ruiz et al., 2021
Carbamazepine	Limpet (*Ancylus fluviatilis*)	Whole organism (dw)	1.27–2.00		Ruhí et al., 2016
	Caddisfly (*Hydropsyche* sp.)	Whole organism (dw)	1.27–2.00		Ruhí et al., 2016
	Flatworm (*Phagocata vitta*)	Whole organism (dw)	1.27–2.00		Ruhí et al., 2016
	Predicted	–	229		Ruhí et al., 2016
	A. Common carp (*Cyprinus carpio*)	Liver (ww)	1.2		Grabicová et al., 2020
	B. Pikeperch (*Sander lucioperca*)	Liver (ww)	2.9		Grabicová et al., 2020
	B. Pikeperch (*Sander lucioperca*)	Kidney (ww)	2.4		Grabicová et al., 2020
	B. Pikeperch (*Sander lucioperca*)	Brain (ww)	3.9		Grabicová et al., 2020
	B. Pikeperch (*Sander lucioperca*)	Muscle (ww)	1.5		Grabicová et al., 2020
	Stone moroko (*Pseudorasbora parva*)	(ww)	0.47		Grabicová et al., 2020
	Plankton	(ww)	3.6		Grabicová et al., 2020
	Cattail (*Typha angustifolia*)	ww		1289.29	Wang et al., 2019
	Mussel (*M. galloprovincialis*)	Whole organism (dw)		3.9	Boillot et al., 2015
	Shrimps (*Gammarus pulex*)	Whole organism (dw)		5.47–8.93	Meredith-Williams et al., 2012
	Water boatman (*Notonecta glauca*)	Whole organism (dw)		0.17–0.33	Meredith-Williams et al., 2012
	Fish (*Largemouth bass*)	Ventral muscle and skin (dw)		4.3	Huerta et al., 2018
	Fish (*White sucker*)	Ventral muscle and skin (dw)		5.1	Huerta et al., 2018
	Fish (*Yellow perch*)	Ventral muscle and skin (dw)		11.3	Huerta et al., 2018
	Fish (*Smallmouth bass*)	Ventral muscle and skin (dw)		90.9	Huerta et al., 2018
	Fish (predicted)	–		318	Huerta et al., 2018
	Mussel (*M. galloprovincialis*)	Whole organism (dw)		25.8–35.3	Serra-Compte et al., 2018
	Clam (*Corbicula fluminea*)	Whole organism (ww)	70		Burket et al., 2020
	Fish stoneroller minnows (*C. anomalum*)	Fish tissues (ww)	4		Burket et al., 2020
	Common carp (*Cyprinus carpio* L.)	Liver (ww)	0.8–2.2		Sims et al., 2020
	Fish (*Oreochromis niloticus*)	Liver (ww)	0.7		Garcia et al., 2012
	Fish (*Oreochromis niloticus*)	Muscle (ww)	0.9		Garcia et al., 2012
	Fish (*Oreochromis niloticus*)	Blood	2.5		Garcia et al., 2012
	Fish (*Pimephales notatus*)	Muscle (ww)		1.9	Garcia et al., 2012
	Fish (*Pimephales notatus*)	Liver (ww)		4.6	Garcia et al., 2012
	Fish (*Ictalurus punctatus*)	Muscle (ww)		1.8	Garcia et al., 2012
	Fish (*Ictalurus punctatus*)	Liver (ww)		1.5	Garcia et al., 2012
	Fish (*Ictalurus punctatus*)	Brain (ww)		1.6	Garcia et al., 2012
	Fish (*Ictalurus punctatus*)	Plasma (ww)		7.1	Garcia et al., 2012
	Fish (*Hemiculter leucisculus*)	Liver (ww)	615–**2750**		Liu et al., 2015
	Fish (*Hemiculter leucisculus*)	Brain (ww)	385–1000		Liu et al., 2015
	Fish (*Hemiculter leucisculus*)	Muscle (ww)	77–250		Liu et al., 2015
	Fish (*Hemiculter leucisculus*)	Gill (ww)	269–500		Liu et al., 2015
	Fish (*Carassius auratus*)	Liver (ww)	235–1200		Liu et al., 2015
	Fish (*Carassius auratus*)	Brain (ww)	29–400		Liu et al., 2015

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Table 2 (*continued*)

Pharmaceutical	Organism	Tissue; dry weight (dw) or wet weight (ww)	BAF	BCF	Reference
	Fish (*Carassius auratus*)	Muscle (ww)	8.8–200		Liu et al., 2015
	Fish (*Carassius auratus*)	Gill (ww)	200		Liu et al., 2015
	Fish (*Gambusia affinis*)	Whole organism (ww)		0.7–0.9	Valdés et al., 2014
	Bifilm		10		Mastrángelo et al., 2022
	Macrophyte (*Lemna gibba*)		141		Mastrángelo et al., 2022
	Cottus bairdii	Whole organism (ww)	3–6.5		Haddad et al., 2018
	Lymnaeidea & Physidae	Whole organism (ww)	15		Haddad et al., 2018
	Periphyton	Whole organism (ww)	3		Haddad et al., 2018
	Trichoptera	Whole organism (ww)	10.0–21.0		Haddad et al., 2018
Carbediol	Shrimps (*Gammarus pulex*)	Whole organism (dw)		240–303	Meredith-Williams et al., 2012
	Water boatman (*Notonecta glauca*)	Whole organism (dw)		1.14–2.18	Meredith-Williams et al., 2012
	Planorbarius corneus	Whole organism (dw)		50.4–71.2	Meredith-Williams et al., 2012
Cefotaxime	Fish (*Epinephelus awoara*)	Muscle (dw)		**3981**	Xie et al., 2019
	Fish (*Ephippus orbis*)	Muscle (dw)		1585	Xie et al., 2019
	Fish (*Culter alburnus*)	Muscle (dw)		1585	Xie et al., 2019
	Shellfish (Ostrea gigas)	Whole organism (dw)		1259	Xie et al., 2019
	Shellfish (*Mimachlamys nobilis*)	Whole organism (dw)		1585	Xie et al., 2019
	Shellfish (*Mytilus edulis*)	Whole organism (dw)		1778	Xie et al., 2019
	Shellfish (*Bufonaria perelegans*)	Whole organism (dw)		794	Xie et al., 2019
Cetirizine	Common carp (*Cyprinus carpio* L.)	Liver (ww)	0.38–1.4		Sims et al., 2020
	Plankton	(ww)	47		Grabicová et al., 2020
Chloramphenicol	Clams (*Crassostrea gigas*, *Patinopecten yessoensis*, *Chlamys farreri*)	Whole organism (ww)	**5376**		Na et al., 2013
Chlortetracycline	Clams (*Crassostrea gigas*, *Patinopecten yessoensis*, *Chlamys farreri*)	Whole organism (ww)	0		Na et al., 2013
Ciprofloxacin	Shrimp (Young *Fenneropenaeus penicillatus*)	Whole organism (ww)		23	Chen et al., 2015
	Bifilm		717		Mastrángelo et al., 2022
	Macrophyte (*Lemna gibba*)		481		Mastrángelo et al., 2022
Citalopram	Zebrafish (*Danio rerio*)	Whole organism (ww)		1.6–3.75	Molina-Fernández et al., 2021
	Zebrafish (*Danio rerio*)	Whole organism (ww)		1.45–3.66	Molina-Fernández et al., 2021
	A. Common carp (*Cyprinus carpio*)	Liver (ww)	140		Grabicová et al., 2020
	B. Pikeperch (*Sander lucioperca*)	Liver (ww)	10		Grabicová et al., 2020
	A. Common carp (*Cyprinus carpio*)	Kidney (ww)	140		Grabicová et al., 2020
	B. Pikeperch (*Sander lucioperca*)	Kidney (ww)	31		Grabicová et al., 2020
	A. Common carp (*Cyprinus carpio*)	Brain (ww)	81		Grabicová et al., 2020
	A. Common carp (*Cyprinus carpio*)	Muscle (ww)	43		Grabicová et al., 2020
	B. Pikeperch (*Sander lucioperca*)	Muscle (ww)	1.4		Grabicová et al., 2020
	Stone moroko (*Pseudorasbora parva*)	(ww)	64		Grabicová et al., 2020
	Plankton	(ww)	**3000**		Grabicová et al., 2020
	Mussel (*M. galloprovincialis*)	Whole organism (dw)		959–**2606**	Serra-Compte et al., 2018
	Brown trout (*Salmo trutta*)	Liver (ww)	260–590		Grabicova et al., 2017
	Brown trout (*Salmo trutta*)	Kidney (ww)	70–**3100**		Grabicova et al., 2017
	Brown trout (*Salmo trutta*)	Brain (ww)			Grabicova et al., 2017
	Brown trout (*Salmo trutta*)	Muscle (ww)			Grabicova et al., 2017
	Common carp (*Cyprinus carpio* L.)	Liver (ww)	140–870		Sims et al., 2020
	Caged goldfish (*Carassius auratus*)	Plasma	15–58		Muir et al., 2017
	Fish (smallmouth bass)	Muscle (dw)	2		Arnnok et al., 2017
	Fish (largemouth bass)	Brain (dw)	8		Arnnok et al., 2017
	Fish (largemouth bass)	Gonad (dw)	4–5		Arnnok et al., 2017
	Fish (largemouth bass)	Liver (dw)	5		Arnnok et al., 2017
	Fish (rudd)	Brain (dw)	4		Arnnok et al., 2017
	Fish (rudd)	Gonad (dw)	2–4		Arnnok et al., 2017
	Fish (rudd)	Liver (dw)	20		Arnnok et al., 2017

Table 2 (*continued*)

Pharmaceutical	Organism	Tissue; dry weight (dw) or wet weight (ww)	BAF	BCF	Reference
	Fish (rudd)	Muscle (dw)	1		Arnnok et al., 2017
	Fish (rock bass)	Brain (dw)	18		Arnnok et al., 2017
	Fish (rock bass)	Gonad (dw)	2–3		Arnnok et al., 2017
	Fish (rock bass)	Liver (dw)	9		Arnnok et al., 2017
	Fish (white bass)	Brain (dw)	6		Arnnok et al., 2017
	Fish (white bass)	Gonad (dw)	9		Arnnok et al., 2017
	Fish (white bass)	Liver (dw)	1–19		Arnnok et al., 2017
	Fish (white bass)	Muscle (dw)	2		Arnnok et al., 2017
	Fish (white perch)	Gonad (dw)	8		Arnnok et al., 2017
	Fish (walleye)	Gonad (dw)	5		Arnnok et al., 2017
	Fish (walleye)	Liver (dw)	3		Arnnok et al., 2017
	Fish (bowfin)	Liver (dw)	1		Arnnok et al., 2017
	Fish (steelhead)	Liver (dw)	17		Arnnok et al., 2017
	Fish (yellow perch)	Brain (dw)	4		Arnnok et al., 2017
	Fish (yellow perch)	Gonad (dw)	1–4		Arnnok et al., 2017
Clarithromycin	Fish Predicted (BCFBAF v3.10)	–		56.49	Reis et al., 2021
	Bifilm		178		Mastrángelo et al., 2022
	Macrophyte (*Lemna gibba*)		94		Mastrángelo et al., 2022
	Mussel (*Lasmigona costata*)	Tisseus (gill, digestive gland (excluding stomach and its contents), and gonadal tissues (ww))	6.8–61		De Solla et al., 2016
Clindamycin	Common carp (*Cyprinus carpio* L.)	Liver (ww)	2.0–4.9		Sims et al., 2020
	Plankton	(ww)	17		Grabicová et al., 2020
Clindamycin-sulfoxide	Plankton	(ww)	9.1		Grabicová et al., 2020
Clozapine	Fish, channel catfish	Plasma		30.5	Nallani et al., 2016
	Fish, channel catfish	Brain (ww)		392	Nallani et al., 2016
	Fish, channel catfish	Muscle (ww)		81	Nallani et al., 2016
	Fish, channel catfish	Gill (ww)		501	Nallani et al., 2016
	Fish, channel catfish	Kidney (ww)		958	Nallani et al., 2016
	Fish, channel catfish	Liver (ww)		1048	Nallani et al., 2016
	Fish, fathead minnow	Brain (ww)		375–538	Nallani et al., 2016
	Fish, fathead minnow	Muscle (ww)		71–92.8	Nallani et al., 2016
	Fish, fathead minnow	Gill (ww)		475–830	Nallani et al., 2016
	Fish, fathead minnow	Kidney (ww)		520–556	Nallani et al., 2016
	Fish, fathead minnow	Liver (ww)		605–939	Nallani et al., 2016
Cocaine	Mussel (*Lasmigona costata*)	Tisseus (gill, digestive gland (excluding stomach and its contents), and gonadal tissues (ww))	249–433		De Solla et al., 2016
Codeine	Mussel (*Lasmigona costata*)	Tisseus (gill, digestive gland (excluding stomach and its contents), and gonadal tissues (ww))	31–62		De Solla et al., 2016
Danofloxacin	Fish Predicted (BCFBAF v3.10)	–		3.16	Reis et al., 2021
Diazepam	Shrimps (*Gammarus pulex*)	Whole organism (dw)		26.5–50.2	Meredith-Williams et al., 2012
	Water boatman (*Notonecta glauca*)	Whole organism (dw)		0.70–1.36	Meredith-Williams et al., 2012
	Caged goldfish (*Carassius auratus*)	Plasma	38–124		Muir et al., 2017
	Wild carp (*Cyprinus carpio*)	Plasma	109–**3120**		Muir et al., 2017
Diclofenac	Limpet (*Ancylus fluviatilis*)	Whole organism (dw)	8.77–12.8		Ruhí et al., 2016
	Caddisfly (*Hydropsyche* sp.)	Whole organism (dw)	231–484		Ruhí et al., 2016
	Flatworm (*Phagocata vitta*)	Whole organism (dw)	8.77–12.8		Ruhí et al., 2016
	Predicted	–	6.12		Ruhí et al., 2016
	Fish predicted	–	13		Lagesson et al., 2016
	Invertebrate predicted	–	2		Lagesson et al., 2016
	Mussel (*Mytilus trossulus*)	Whole organism (dw)		57	Świacka et al., 2019
	Mussel (*Mytilus trossulus*)	Whole organism (ww)		10–180	Ericson et al., 2010
	Mussel (*M. galloprovincialis*)	Visceral mass (ww)		13	Álvarez-Ruiz et al., 2021
	Mussel (*M. galloprovincialis*)	Visceral mass (ww)		9.8	Álvarez-Ruiz et al., 2021
	Bluegill sunfish (*Lepomis macrochirus*)	Muscle (ww)		0–0.67	Zhao et al., 2017
	Bluegill sunfish (*Lepomis macrochirus*)	Gill (ww)		2.80–3.66	Zhao et al., 2017
	Plant (*Potamogeton* sp.)	Whole organism (dw)	3.92		Wilkinson et al., 2018
	Plant (*Callitriche* sp.)	Whole organism (dw)	8.69		Wilkinson et al., 2018
	Periphyton	Whole organism (dw)	213		Wilkinson et al., 2018
	Aquatic snails (*Bithynia tentaculate*)	Whole organism (dw)	13.2		Wilkinson et al., 2018
	Crustaceans (*Gammarus pulex*)	Whole organism (dw)	12.9		Wilkinson et al., 2018
	Fish (*Hemiculter leucisculus*)	Liver (ww)	34–959		Liu et al., 2015

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Table 2 (*continued*)

Pharmaceutical	Organism	Tissue; dry weight (dw) or wet weight (ww)	BAF	BCF	Reference
	Fish (*Hemiculter leucisculus*)	Brain (ww)	14–608		Liu et al., 2015
	Fish (*Hemiculter leucisculus*)	Muscle (ww)	5–174		Liu et al., 2015
	Fish (*Hemiculter leucisculus*)	Gill (ww)	6–565		Liu et al., 2015
	Fish (*Carassius auratus*)	Liver (ww)	121–836		Liu et al., 2015
	Fish (*Carassius auratus*)	Brain (ww)	14–291		Liu et al., 2015
	Fish (*Carassius auratus*)	Muscle (ww)	6–36		Liu et al., 2015
	Fish (*Carassius auratus*)	Gill (ww)	18–44		Liu et al., 2015
	Mussel (*M. galloprovincialis*)	Whole organism (dw)		11.3–16.5	Bonnefille et al., 2017
	Mussel (*Dreissena polymorpha*)	–		4.0–13	Daniele et al., 2016
	Trout (*O. mykiss*)	Whole organism (ww)		0.3–**2732**	Schwaiger et al., 2004
	Trout (*O. mykiss*)	Whole organism (ww)		3.0–5.0	Memmert et al., 2013
	Duckweed (*L. minor*)	Whole organism (dw)		3.4–12.1	Kummerová et al., 2016
	Trout (*O. mykiss*)	Whole organism (ww)		320–950	Kallio et al., 2010
	Mussel (*Mytilus trossulus*)	Whole organism (dw)		118.5	Świacka et al., 2021b
	Biofilm	(dw)		119	Świacka et al., 2021b
	Crucian carp (*Carassius auratus*)	Liver (ww)		121	Lu et al., 2018
	Crucian carp (*Carassius auratus*)	Gill (ww)		52.3	Lu et al., 2018
	Crucian carp (*Carassius auratus*)	Muscle (ww)		46.8	Lu et al., 2018
	Crucian carp (*Carassius auratus*)	Muscle (dw)		0.56–8.55	Xie et al., 2020
	Crucian carp (*Carassius auratus*)	Brain (dw)		2.73–22.1	Xie et al., 2020
	Crucian carp (*Carassius auratus*)	Gill (dw)		2.61–28.7	Xie et al., 2020
	Crucian carp (*Carassius auratus*)	Kidney (dw)		3.41–61.7	Xie et al., 2020
	Crucian carp (*Carassius auratus*)	Liver (dw)		3.09–56	Xie et al., 2020
Diltiazem	Stone moroko (*Pseudorasbora parva*)	(ww)	290		Grabicová et al., 2020
	Baetidae	Whole organism (ww)	38–233		Haddad et al., 2018
	Cottus bairdii	Whole organism (ww)	25–267		Haddad et al., 2018
	Lymnaeidea & Physidae	Whole organism (ww)	53		Haddad et al., 2018
	Periphyton	Whole organism (ww)	48–**8667**		Haddad et al., 2018
	Salmo trutta	Whole organism (ww)	11–167		Haddad et al., 2018
	Trichoptera	Whole organism (ww)	13–280		Haddad et al., 2018
	Rainbow trout (*Oncorhynchus mykiss*)	Whole body (minus liver) (ww)	10.1–72.5		Sims et al., 2020
	Clam (*Corbicula fluminea*)	Whole organism (ww)	350		Burket et al., 2020
	Fish stoneroller minnows (*C. anomalum*)	Fish tissues (ww)	300		Burket et al., 2020
	Mussel (*Lasmigona costata*)	Tisseus (gill, digestive gland (excluding stomach and its contents), and gonadal tissues (ww))	26–50		De Solla et al., 2016
	Plankton	(ww)	76		Grabicová et al., 2020
Diphenhydramine	Fish predicted	–	285		Lagesson et al., 2016
	Invertebrate predicted	–	36		Lagesson et al., 2016
	Amshorn snail (*Planorbidae*)	Whole organism (ww)	1250		Lagesson et al., 2016
	Waterlouse (*Asellus aquaticus*)	Whole organism (ww)	600		Lagesson et al., 2016
	Mayfly larvae (*Ephemeropteras*)	Whole organism (ww)	125		Lagesson et al., 2016
	Damselfly larvae (*Zygoptera*)	Whole organism (ww)	250		Lagesson et al., 2016
	European perch (*Perca fluviatilis*)	Muscle (ww)	100		Lagesson et al., 2016
	Plankton	(ww)	1300		Grabicová et al., 2020
	Fish (smallmouth bass)	Brain (dw)	4–6		Arnnok et al., 2017
	Fish (smallmouth bass)	Gonad (dw)	1–5		Arnnok et al., 2017
	Fish (smallmouth bass)	Liver (dw)	2–4		Arnnok et al., 2017
	Fish (smallmouth bass)	Muscle (dw)	1		Arnnok et al., 2017
	Fish (largemouth bass)	Brain (dw)	5–15		Arnnok et al., 2017
	Fish (largemouth bass)	Gonad (dw)	1–2		Arnnok et al., 2017
	Fish (largemouth bass)	Liver (dw)	1–4		Arnnok et al., 2017
	Fish (largemouth bass)	Muscle (dw)	1		Arnnok et al., 2017
	Fish (rudd)	Brain (dw)	4–18		Arnnok et al., 2017
	Fish (rudd)	Gonad (dw)	1–2		Arnnok et al., 2017
	Fish (rudd)	Liver (dw)	3–21		Arnnok et al., 2017
	Fish (rudd)	Muscle (dw)	1		Arnnok et al., 2017
	Fish (rock bass)	Brain (dw)	5–29		Arnnok et al., 2017
	Fish (rock bass)	Gonad (dw)	1–9		Arnnok et al., 2017

Table 2 (*continued*)

Pharmaceutical	Organism	Tissue; dry weight (dw) or wet weight (ww)	BAF	BCF	Reference
	Fish (rock bass)	Liver (dw)	1–7		Arnnok et al., 2017
	Fish (rock bass)	Muscle (dw)	1		Arnnok et al., 2017
	Fish (white bass)	Brain (dw)	8–9		Arnnok et al., 2017
	Fish (white bass)	Gonad (dw)	1–2		Arnnok et al., 2017
	Fish (white bass)	Liver (dw)	1–15		Arnnok et al., 2017
	Fish (white bass)	Muscle (dw)	1–2		Arnnok et al., 2017
	Fish (white perch)	Brain (dw)	4		Arnnok et al., 2017
	Fish (white perch)	Gonad (dw)	8		Arnnok et al., 2017
	Fish (white perch)	Liver (dw)	1		Arnnok et al., 2017
	Fish (white perch)	Muscle (dw)	1		Arnnok et al., 2017
	Fish (walleye)	Brain (dw)	5–11		Arnnok et al., 2017
	Fish (walleye)	Gonad (dw)	1–2		Arnnok et al., 2017
	Fish (walleye)	Liver (dw)	2–4		Arnnok et al., 2017
	Fish (walleye)	Muscle (dw)	1		Arnnok et al., 2017
	Fish (steelhead)	Gonad (dw)	1		Arnnok et al., 2017
	Fish (yellow perch)	Gonad (dw)	1–2		Arnnok et al., 2017
	Fish (yellow perch)	Liver (dw)	1		Arnnok et al., 2017
	Fish (yellow perch)	Muscle (dw)	0.2		Arnnok et al., 2017
	Periphyton	Whole organism (ww)	300		Burket et al., 2020
	Clam (*Corbicula fluminea*)	Whole organism (ww)	1600		Burket et al., 2020
	Fish stoneroller minnows (*C. anomalum*)	Fish tissues (ww)	250		Burket et al., 2020
	Rainbow trout (*Oncorhynchus mykiss*)	Whole body (minus liver) (ww)	32–88		Sims et al., 2020
	Mussel (*Lasmigona costata*)	Tisseus (gill, digestive gland (excluding stomach and its contents), and gonadal tissues (ww))	712–1331		De Solla et al., 2016
	Caged goldfish (*Carassius auratus*)	plasma	45–193		Muir et al., 2017
	Baetidae	Whole organism (ww)	145–168		Haddad et al., 2018
	Cottus bairdii	Whole organism (ww)	48–522		Haddad et al., 2018
	Lymnaeidea & Physidae	Whole organism (ww)	220		Haddad et al., 2018
	Periphyton	Whole organism (ww)	239–**5581**		Haddad et al., 2018
	Salmo trutta	Whole organism (ww)	23–105		Haddad et al., 2018
	Trichoptera	Whole organism (ww)	81–1279		Haddad et al., 2018
Donepezil	A. Common carp (*Cyprinus carpio*)	Liver (ww)	470		Grabicová et al., 2020
	B. Pikeperch (*Sander lucioperca*)	Liver (ww)	320		Grabicová et al., 2020
	B. Pikeperch (*Sander lucioperca*)	Kidney (ww)	280		Grabicová et al., 2020
	B. Pikeperch (*Sander lucioperca*)	Brain (ww)	310		Grabicová et al., 2020
	Stone moroko (*Pseudorasbora parva*)	(ww)	190		Grabicová et al., 2020
	Plankton	(ww)	390		Grabicová et al., 2020
Doxycycline	Clams (*Crassostrea gigas*, *Patinopecten yessoensis*, *Chlamys farreri*)	Whole organism (ww)	**4456**		Na et al., 2013
Enoxacin	Fish Predicted (BCFBAF v3.10)	–		3.16	Reis et al., 2021
Enrofloxacin	Fish Predicted (BCFBAF v3.10)	–		3.16	Reis et al., 2021
	Shrimp (Young *Fenneropenaeus penicillatus*)	Whole organism (ww)		650	Chen et al., 2015
	Fish (Adult *Trachinotus ovatus*)	Muscle (ww)		861	Chen et al., 2015
Erythromycin	Fish (*Hemiculter leucisculus*)	Liver (ww)	**7559–7900**		Liu et al., 2015
	Fish (*Hemiculter leucisculus*)	Brain (ww)	1088–**2900**		Liu et al., 2015
	Fish (*Hemiculter leucisculus*)	Muscle (ww)	700–971		Liu et al., 2015
	Fish (*Hemiculter leucisculus*)	Gill (ww)	1200–1412		Liu et al., 2015
	Fish (*Carassius auratus*)	Liver (ww)	31–120		Liu et al., 2015
	Fish (*Carassius auratus*)	Brain (ww)	160–226		Liu et al., 2015
	Fish (*Carassius auratus*)	Muscle (ww)	528–760		Liu et al., 2015
	Fish (*Carassius auratus*)	Gill (ww)	1480–1616		Liu et al., 2015
	Caged goldfish (*Carassius auratus*)	Plasma	34–101		Muir et al., 2017
	Wild carp (*Cyprinus carpio*)	Plasma	53–121		Muir et al., 2017
Estrone	Flatworm (*Phagocata vitta*)	Whole organism (dw)	**4207**		Ruhí et al., 2016
	Predicted	–	**81,846**		Ruhí et al., 2016
Etoricoxib	Mussel (*M. galloprovincialis*)	Visceral mass (ww)		6.4	Álvarez-Ruiz et al., 2021
	Mussel (*M. galloprovincialis*)	Visceral mass (ww)		6.7	Álvarez-Ruiz et al., 2021

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Table 2 (*continued*)

Pharmaceutical	Organism	Tissue; dry weight (dw) or wet weight (ww)	BAF	BCF	Reference
	Haemolymph	Whole organism (ww)		0.90	Álvarez-Ruiz et al., 2021
Fenofibrate	Fish Predicted (BCFBAF v3.10)	–		322.2	Reis et al., 2021
Fexofenadine	Plankton	(ww)	68		Grabicová et al., 2020
	Damselfly larvae	Whole organism (dw)		120	Jonsson et al., 2014
Florophenicol	Clams (*Crassostrea gigas*, *Patinopecten yessoensis*, *Chlamys farreri*)	Whole organism (ww)	266		Na et al., 2013
Fluconazole	Fish Predicted (BCFBAF v3.10)	–		3.16	Reis et al., 2021
Flumequine	Caged goldfish (*Carassius auratus*)	Plasma	68–626		Muir et al., 2017
	Wild carp (*Cyprinus carpio*)	Plasma	72–562		Muir et al., 2017
Fluoxetine	Zebrafish (*Danio rerio*)	Whole organism (ww)		8–8.1	Molina-Fernández et al., 2021
	Zebrafish (*Danio rerio*)	Whole organism (ww)		7.27–7.3	Molina-Fernández et al., 2021
	Cattail (*Typha angustifolia*)	ww		658.56	Wang et al., 2019
	Shrimps (*Gammarus pulex*)	Whole organism (dw)		**161,800–209,500**	Meredith-Williams et al., 2012
	Water boatman (*Notonecta glauca*)	Whole organism (dw)		1.08–1.75	Meredith-Williams et al., 2012
	Zebrafish (*Danio rerio*)	Whole organism (ww)		0.019–0.22	Pan et al., 2018
	Zebrafish (*Danio rerio*)	Whole organism (ww)		1.73–6.88	Pan et al., 2018
	Red crucian cap (*Carassius auratus*)	Brain (ww)		12.4–110	Pan et al., 2018
	Red crucian cap (*Carassius auratus*)	Liver (ww)		11.1–1.37	Pan et al., 2018
	Red crucian cap (*Carassius auratus*)	Muscle (ww)		12.1–166	Pan et al., 2018
	Caged goldfish (*Carassius auratus*)	Plasma	310–1480		Muir et al., 2017
	Wild carp (*Cyprinus carpio*)	Plasma	176–334		Muir et al., 2017
	Rainbow trout (*Oncorhynchus mykiss*)	Whole body (minus liver) (ww)	251–426		Sims et al., 2020
	Plant (*A. platanoides*)	Pooled samples (dw)	1300		Boström et al., 2017
	Crustacean (*A. aquaticus*)	Whole organism (ww)	110		Boström et al., 2017
	Insect (*N. glauca*)	Whole organism (ww)	11		Boström et al., 2017
	Fish (*P. pungitus*)	–	41		Boström et al., 2017
	Clam (*Corbicula fluminea*)	Whole organism (ww)	200		Burket et al., 2020
	Baetidae	Whole organism (ww)	356		Haddad et al., 2018
	Cottus bairdii	Whole organism (ww)	38–**2929**		Haddad et al., 2018
	Lymnaeidea & Physidae	Whole organism (ww)	**3431**		Haddad et al., 2018
	Periphyton	Whole organism (ww)	118–**6192**		Haddad et al., 2018
	Salmo trutta	Whole organism (ww)	19–**2134**		Haddad et al., 2018
	Trichoptera	Whole organism (ww)	47–**4352**		Haddad et al., 2018
Gemfibrozil	Limpet (*Ancylus fluviatilis*)	Whole organism (dw)	0.26–0.48		Ruhí et al., 2016
	Caddisfly (*Hydropsyche* sp.)	Whole organism (dw)	0.26–0.49		Ruhí et al., 2016
	Flatworm (*Phagocata vitta*)	Whole organism (dw)	0.33–153		Ruhí et al., 2016
	Predicted	–	10.59		Ruhí et al., 2016
	Fish Predicted (BCFBAF v3.10)	–		3.16	Reis et al., 2021
Haloperidol	B. Pikeperch (*Sander lucioperca*)	Liver (ww)	170		Grabicová et al., 2020
	Caged goldfish (*Carassius auratus*)	Plasma	190–1110		Muir et al., 2017
	Wild carp (*Cyprinus carpio*)	Plasma	208–1088		Muir et al., 2017
	Mussel (*Lasmigona costata*)	Tisseus (gill, digestive gland (excluding stomach and its contents), and gonadal tissues (ww))	0–62		De Solla et al., 2016
	B. Pikeperch (*Sander lucioperca*)	Kidney (ww)	280		Grabicová et al., 2020
Hydrochlorothiazide	Limpet (*Ancylus fluviatilis*)	Whole organism (dw)	0.16–0.22		Ruhí et al., 2016
	Caddisfly (*Hydropsyche* sp.)	Whole organism (dw)	0.16–0.23		Ruhí et al., 2016
	Flatworm (*Phagocata vitta*)	Whole organism (dw)	0.16–0.24		Ruhí et al., 2016
	Predicted	–	2.43		Ruhí et al., 2016
	Fish (*Largemouth bass*)	Ventral muscle and skin (dw)		0.4	Huerta et al., 2018
	Fish (*White sucker*)	Ventral muscle and skin (dw)		4.5	Huerta et al., 2018
	Fish (*Yellow perch*)	Ventral muscle and skin (dw)		9.7	Huerta et al., 2018
	Fish (*Smallmouth bass*)	Ventral muscle and skin (dw)		12.5	Huerta et al., 2018
	Fish (predicted)	–		16.7	Huerta et al., 2018
	Cockle (*Cerastodema glaucum*)	Whole organism (dw)	321–590		Moreno-González et al., 2016
	Noble pen shell (*Pinna nobilis*)	Whole organism (dw)	109.7		Moreno-González et al., 2016

Table 2 (*continued*)

Pharmaceutical	Organism	Tissue; dry weight (dw) or wet weight (ww)	BAF	BCF	Reference
	Golden grey mullet (*Liza aurata*)	Whole organism (dw)	182.5		Moreno-González et al., 2016
	Bifilm		34		Mastrángelo et al., 2022
	Macrophyte (*Lemna gibba*)		70		Mastrángelo et al., 2022
Hydroxyzine	Fish predicted	–	40		Lagesson et al., 2016
	Invertebrate predicted	–	6		Lagesson et al., 2016
	Damselfly larvae	Whole organism (dw)		**2000**	Jonsson et al., 2014
	Amshorn snail (*Planorbidae*)	Whole organism (ww)	**97,000**		Lagesson et al., 2016
	Waterlouse (*Asellus aquaticus*)	Whole organism (ww)	**7000**		Lagesson et al., 2016
	Mayfly larvae (*Ephemeropteras*)	Whole organism (ww)	**5000**		Lagesson et al., 2016
	Damselfly larvae (*Zygoptera*)	Whole organism (ww)	**18,000**		Lagesson et al., 2016
	European perch (*Perca fluviatilis*)	Muscle (ww)	1000		Lagesson et al., 2016
Ibuprofen	Limpet (*Ancylus fluviatilis*)	Whole organism (dw)	1.66–2.75		Ruhí et al., 2016
	Caddisfly (*Hydropsyche* sp.)	Whole organism (dw)	1.66–954		Ruhí et al., 2016
	Flatworm (*Phagocata vitta*)	Whole organism (dw)	1.70–160		Ruhí et al., 2016
	Predicted	–	6.12		Ruhí et al., 2016
	Cattail (*Typha angustifolia*)	ww		157.57	Wang et al., 2019
	Wild carp (*Cyprinus carpio*)	Plasma	115		Muir et al., 2017
	Rainbow trout (*Oncorhynchus mykiss*)	Bile		**14,000–49,000**	Brozinski et al., 2013
	Fish Predicted (BCFBAF v3.10)	–		3.16	Reis et al., 2021
	Biofilm	–	13		Mastrángelo et al., 2022
Iopamidol	Caged goldfish (*Carassius auratus*)	Plasma	37–40		Muir et al., 2017
Irbesartan	Plankton	(ww)	2.5		Grabicová et al., 2020
Ketoprofen	Fish (*Epinephelus awoara*)	Muscle (dw)		**39,811**	Xie et al., 2019
	Fish (*Culter alburnus*)	Muscle (dw)		1995	Xie et al., 2019
	Shellfish (*Ostrea gigas*)	Whole organism (dw)		**70,795**	Xie et al., 2019
	Shellfish (*Mimachlamys nobilis*)	Whole organism (dw)		**70,795**	Xie et al., 2019
	Shellfish (*Mytilus edulis*)	Whole organism (dw)		**39,811**	Xie et al., 2019
	Fish Predicted (BCFBAF v3.10)	–		3.16	Reis et al., 2021
Loratadine	Fish Predicted (BCFBAF v3.10)	–		1253	Reis et al., 2021
Metformin	Fish Predicted (BCFBAF v3.10)	–		3.16	Reis et al., 2021
	Mussel (*Lasmigona costata*)	Tisseus (gill, digestive gland (excluding stomach and its contents), and gonadal tissues (ww))	0.15–1.29		De Solla et al., 2016
Methocarbamol	Bluegill sunfish (*Lepomis macrochirus*)	Muscle (ww)		0.13–0.35	Zhao et al., 2017
	Bluegill sunfish (*Lepomis macrochirus*)	Liver (ww)		0.19–0.58	Zhao et al., 2017
	Bluegill sunfish (*Lepomis macrochirus*)	Brain (ww)		0.23–0.53	Zhao et al., 2017
	Bluegill sunfish (*Lepomis macrochirus*)	Bile (ww)		5.90–48.6	Zhao et al., 2017
	Bluegill sunfish (*Lepomis macrochirus*)	Plasma		0.13–0.24	Zhao et al., 2017
	Bluegill sunfish (*Lepomis macrochirus*)	Gut (ww)		0.34–0.75	Zhao et al., 2017
	Bluegill sunfish (*Lepomis macrochirus*)	Gill (ww)		0.14–0.21	Zhao et al., 2017
Methylphenidate	*Cottus bairdii*	Whole organism (ww)	15–21		Haddad et al., 2018
	Lymnaeidea & Physidae	Whole organism (ww)	29		Haddad et al., 2018
	Periphyton	Whole organism (ww)	50–155		Haddad et al., 2018
	Salmo trutta	Whole organism (ww)	**3190–21,429**		Haddad et al., 2018
	Trichoptera	Whole organism (ww)	29		Haddad et al., 2018
Metoprolol	Common carp (*Cyprinus carpio* L.)	Liver (ww)	1.4–11		Sims et al., 2020
	Stone moroko (*Pseudorasbora parva*)	(ww)	6.3		Grabicová et al., 2020
	Plankton	(ww)	81		Grabicová et al., 2020
	A. Common carp (*Cyprinus carpio*)	Liver (ww)	11		Grabicová et al., 2020
	A. Common carp (*Cyprinus carpio*)	Kidney (ww)	21		Grabicová et al., 2020

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Table 2 (*continued*)

Pharmaceutical	Organism	Tissue; dry weight (dw) or wet weight (ww)	BAF	BCF	Reference
	Plankton	(ww)	3.8		Grabicová et al., 2020
Metoprolol acid	Common carp (*Cyprinus carpio* L.)	Liver (ww)	7.3–16		Sims et al., 2020
Mianserin	Plankton	(ww)	520		Grabicová et al., 2020
	Brown trout (*Salmo trutta*)	Kidney (ww)	630–670		Grabicova et al., 2017
Miconazole	Plankton	(ww)	1000		Grabicová et al., 2020
Mirtazapine	Stone moroko (*Pseudorasbora parva*)	(ww)	140		Grabicová et al., 2020
	Plankton	(ww)	440		Grabicová et al., 2020
	Brown trout (*Salmo trutta*)	Liver (ww)	110–300		Grabicova et al., 2017
	Brown trout (*Salmo trutta*)	Kidney (ww)	**2100–6000**		Grabicova et al., 2017
	Brown trout (*Salmo trutta*)	Brain (ww)	4.0–6.0		Grabicova et al., 2017
Moclobemide	Shrimps (*Gammarus pulex*)	Whole organism (dw)		3.18–6.32	Meredith-Williams et al., 2012
	Water boatman (*Notonecta glauca*)	Whole organism (dw)		0.19–0.52	Meredith-Williams et al., 2012
N-Desmethylcitalopram	Common carp (*Cyprinus carpio* L.)	Liver (ww)	250–1700		Sims et al., 2020
	A. Common carp (*Cyprinus carpio*)	Liver (ww)	370		Grabicová et al., 2020
	A. Common carp (*Cyprinus carpio*)	Kidney (ww)	1400		Grabicová et al., 2020
	B. Pikeperch (*Sander lucioperca*)	Kidney (ww)	71		Grabicová et al., 2020
	A. Common carp (*Cyprinus carpio*)	Muscle (ww)	22		Grabicová et al., 2020
	Stone moroko (*Pseudorasbora parva*)	(ww)	100		Grabicová et al., 2020
	Plankton	(ww)	**2600**		Grabicová et al., 2020
	Zebrafish (*Danio rerio*)	Whole organism (ww)		0.35–0.7	Molina-Fernández et al., 2021
	Zebrafish (*Danio rerio*)	Whole organism (ww)		0.21–0.69	Molina-Fernández et al., 2021
N-Desmethydiltiazem	Mussel (*Lasmigona costata*)	Tisseus (gill, digestive gland (excluding stomach and its contents), and gonadal tissues (ww))	33–66		De Solla et al., 2016
Naproxen	Mussel (*Lasmigona costata*)	Tisseus (gill, digestive gland (excluding stomach and its contents), and gonadal tissues (ww))	0–9.2		De Solla et al., 2016
Norfloxacin	Fish (*Epinephelus awoara*)	Muscle (dw)		**3981**	Xie et al., 2019
	Fish (*Culter alburnus*)	Muscle (dw)		1000	Xie et al., 2019
	Shellfish (Ostrea gigas)	Whole organism (dw)		200	Xie et al., 2019
	Shellfish (*Mimachlamys nobilis*)	Whole organism (dw)		8	Xie et al., 2019
	Shellfish (*Mytilus edulis*)	Whole organism (dw)		16	Xie et al., 2019
	Fish Predicted (BCFBAF v3.10)	–		3.16	Reis et al., 2021
Norfluoxetine	Zebrafish (*Danio rerio*)	Whole organism (ww)		12.0–20.0	Molina-Fernández et al., 2021
	Zebrafish (*Danio rerio*)	Whole organism (ww)		7.6–8.4	Molina-Fernández et al., 2021
	Fish (smallmouth bass)	Brain (dw)	15–49		Arnnok et al., 2017
	Fish (smallmouth bass)	Gonad (dw)	5–39		Arnnok et al., 2017
	Fish (smallmouth bass)	Muscle (dw)	1–7		Arnnok et al., 2017
	Fish (largemouth bass)	Brain (dw)	15–97		Arnnok et al., 2017
	Fish (largemouth bass)	Gonad (dw)	8		Arnnok et al., 2017
	Fish (largemouth bass)	Muscle (dw)	1–3		Arnnok et al., 2017
	Fish (rudd)	Brain (dw)	21–24		Arnnok et al., 2017
	Fish (rudd)	Gonad (dw)	5–9		Arnnok et al., 2017
	Fish (rock bass)	Brain (dw)	15–130		Arnnok et al., 2017
	Fish (rock bass)	Gonad (dw)	49		Arnnok et al., 2017
	Fish (white bass)	Brain (dw)	18–66		Arnnok et al., 2017
	Fish (white bass)	Muscle (dw)	3–6		Arnnok et al., 2017
	Fish (white perch)	Gonad (dw)	1		Arnnok et al., 2017
	Fish (walleye)	Muscle (dw)	1		Arnnok et al., 2017
	Clam (*Corbicula fluminea*)	Whole organism (ww)	700		Burket et al., 2020
	Cottus bairdii	Whole organism (ww)	68–**6328**		Haddad et al., 2018
	Lymnaeidea & Physidae	Whole organism (ww)	**2034**		Haddad et al., 2018
	Periphyton	Whole organism (ww)	46–**8249**		Haddad et al., 2018
	Salmo trutta	Whole organism (ww)	31–**2712**		Haddad et al., 2018
	Trichoptera	Whole organism (ww)	1808–**4351**		Haddad et al., 2018
Norsertraline	Zebrafish (*Danio rerio*)	Whole organism (ww)		38	Molina-Fernández et al., 2021
	Zebrafish (*Danio rerio*)	Whole organism (ww)		26.5	Molina-Fernández et al., 2021

Table 2 (*continued*)

Pharmaceutical	Organism	Tissue; dry weight (dw) or wet weight (ww)	BAF	BCF	Reference
	Fish (smallmouth bass)	Brain (dw)	470–910		Arnnok et al., 2017
	Fish (smallmouth bass)	Gonad (dw)	150		Arnnok et al., 2017
	Fish (smallmouth bass)	Liver (dw)	240–320		Arnnok et al., 2017
	Fish (smallmouth bass)	Muscle (dw)	84–170		Arnnok et al., 2017
	Fish (largemouth bass)	Brain (dw)	590–1200		Arnnok et al., 2017
	Fish (largemouth bass)	Gonad (dw)	130–160		Arnnok et al., 2017
	Fish (largemouth bass)	Liver (dw)	310–470		Arnnok et al., 2017
	Fish (largemouth bass)	Muscle (dw)	140–160		Arnnok et al., 2017
	Fish (rudd)	Brain (dw)	420–680		Arnnok et al., 2017
	Fish (rudd)	Gonad (dw)	150		Arnnok et al., 2017
	Fish (rudd)	Liver (dw)	300–**3000**		Arnnok et al., 2017
	Fish (rudd)	Muscle (dw)	110–310		Arnnok et al., 2017
	Fish (rock bass)	Brain (dw)	500–1800		Arnnok et al., 2017
	Fish (rock bass)	Gonad (dw)	130–200		Arnnok et al., 2017
	Fish (rock bass)	Liver (dw)	770–1600		Arnnok et al., 2017
	Fish (rock bass)	Muscle (dw)	94–150		Arnnok et al., 2017
	Fish (white bass)	Brain (dw)	510–920		Arnnok et al., 2017
	Fish (white bass)	Liver (dw)	150–520		Arnnok et al., 2017
	Fish (white bass)	Muscle (dw)	140–190		Arnnok et al., 2017
	Fish (white perch)	Brain (dw)	840		Arnnok et al., 2017
	Fish (white perch)	Liver (dw)	1100		Arnnok et al., 2017
	Fish (white perch)	Muscle (dw)	150		Arnnok et al., 2017
	Fish (walleye)	Brain (dw)	350–670		Arnnok et al., 2017
	Fish (walleye)	Gonad (dw)	200		Arnnok et al., 2017
	Fish (walleye)	Liver (dw)	290		Arnnok et al., 2017
	Fish (walleye)	Muscle (dw)	96–330		Arnnok et al., 2017
	Fish (bowfin)	Brain (dw)	1500		Arnnok et al., 2017
	Fish (bowfin)	Liver (dw)	260		Arnnok et al., 2017
	Fish (bowfin)	Muscle (dw)	150		Arnnok et al., 2017
	Fish (steelhead)	Brain (dw)	160–600		Arnnok et al., 2017
	Fish (steelhead)	Liver (dw)	270–630		Arnnok et al., 2017
	Fish (steelhead)	Muscle (dw)	140–160		Arnnok et al., 2017
	Fish (yellow perch)	Brain (dw)	250		Arnnok et al., 2017
O-Desmethylvenlafaxine	Common carp (*Cyprinus carpio* L.)	Liver (ww)	1.3–5.6		Sims et al., 2020
	A. Common carp (*Cyprinus carpio*)	Liver (ww)	6		Grabicová et al., 2020
	A. Common carp (*Cyprinus carpio*)	Kidney (ww)	4.9		Grabicová et al., 2020
	Plankton	(ww)	100		Grabicová et al., 2020
	Loach (*Misgurnus anguillicaudatus*)	Liver (ww)		0.15–0.97	Qu et al., 2019
	Loach (*Misgurnus anguillicaudatus*)	Liver (ww)		4.31–22.81	Qu et al., 2019
Ofloxacin	Fish (Adult *Trachinotus ovatus*)	Muscle (ww)		1164	Chen et al., 2015
	Macrophyte (*Lemna gibba*)		429		Mastrángelo et al., 2022
Oxazepam	European perch (*Perca fluviatilis*)	Muscle (ww)		13–19	Cerveny et al., 2021b
	European perch (*Perca fluviatilis*)	Brain (ww)		56–70	Cerveny et al., 2021b
	Fish predicted	–	25		Lagesson et al., 2016
	Invertebrate predicted	–	4		Lagesson et al., 2016
	Amshorn snail (*Planorbidae*)	Whole organism (ww)	37.5		Lagesson et al., 2016
	Waterlouse (*Asellus aquaticus*)	Whole organism (ww)	45		Lagesson et al., 2016
	Mayfly larvae (*Ephemeropteras*)	Whole organism (ww)	20		Lagesson et al., 2016
	Damselfly larvae (*Zygoptera*)	Whole organism (ww)	10		Lagesson et al., 2016
	European perch (*Perca fluviatilis*)	Muscle (ww)	18		Lagesson et al., 2016
Oxycodone	Mussel (*Lasmigona costata*)	Tisseus (gill, digestive gland (excluding stomach and its contents), and gonadal tissues (ww))	0–23.6		De Solla et al., 2016
Oxytetracycline	Shrimp (Young *Fenneropenaeus penicillatus*)	Whole organism (ww)		2	Chen et al., 2015
	Clams (*Crassostrea gigas*, *Patinopecten yessoensis*, *Chlamys farreri*)	Whole organism (ww)	509		Na et al., 2013
Paracetamol	Fish (*Epinephelus awoara*)	Muscle (dw)		**3162**	Xie et al., 2019
	Plant (*Potamogeton* sp.)	Whole organism (dw)	45.9		Wilkinson et al., 2018
	Plant (*Callitriche* sp.)	Whole organism (dw)	22.5		Wilkinson et al., 2018
	Periphyton	Whole organism (dw)	22.1		Wilkinson et al., 2018

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Table 2 (*continued*)

Pharmaceutical	Organism	Tissue; dry weight (dw) or wet weight (ww)	BAF	BCF	Reference
	Aquatic snails (*Bithynia tentaculate*)	Whole organism (dw)	37.0		Wilkinson et al., 2018
	Crustaceans (*Gammarus pulex*)	Whole organism (dw)	26.4		Wilkinson et al., 2018
	Clam (*Corbicula fluminea*)	Whole organism (ww)	1000		Burket et al., 2020
Paroxetine	Zebrafish (*Danio rerio*)	Whole organism (ww)		10.0–25	Molina-Fernández et al., 2021
	Zebrafish (*Danio rerio*)	Whole organism (ww)		7.6–9.53	Molina-Fernández et al., 2021
Phenazone	Fish Predicted (BCFBAF v3.10)	–		3.16	Reis et al., 2021
Phenylbutazone	Fish Predicted (BCFBAF v3.10)	–		56.49	Reis et al., 2021
Prednisone	Fish Predicted (BCFBAF v3.10)	–		4.27	Reis et al., 2021
Propranolol	Mussel (*Lasmigona costata*)	Tisseus (gill, digestive gland (excluding stomach and its contents), and gonadal tissues (ww))	1059–1939		De Solla et al., 2016
	Crustacean (*D. magna*)	Whole organism (ww)		18–83	Ding et al., 2016
	Fish (*Hemiculter leucisculus*)	Liver (ww)	1000–**4000**		Liu et al., 2015
	Fish (*Hemiculter leucisculus*)	Brain (ww)	500–1000		Liu et al., 2015
	Fish (*Hemiculter leucisculus*)	Gill (ww)	500		Liu et al., 2015
	Fish (*Carassius auratus*)	Brain (ww)	200		Liu et al., 2015
	Fish (*Carassius auratus*)	Gill (ww)	133		Liu et al., 2015
Rosuvastatin	Bluegill sunfish (*Lepomis macrochirus*)	Liver (ww)		0–0.20	Zhao et al., 2017
	Bluegill sunfish (*Lepomis macrochirus*)	Bile (ww)		0–6.70	Zhao et al., 2017
	Bluegill sunfish (*Lepomis macrochirus*)	Plasma		0.40–0.56	Zhao et al., 2017
	Bluegill sunfish (*Lepomis macrochirus*)	Gut (ww)		0.79–1.30	Zhao et al., 2017
	Bluegill sunfish (*Lepomis macrochirus*)	Gill (ww)		0–0.14	Zhao et al., 2017
Roxithromycin	Crustacean (*D. magna*)	Whole organism (ww)		13.4–93.5	Ding et al., 2016
	Fish (*Hemiculter leucisculus*)	Liver (ww)	729–**7091**		Liu et al., 2015
	Fish (*Hemiculter leucisculus*)	Brain (ww)	497–**2091**		Liu et al., 2015
	Fish (*Hemiculter leucisculus*)	Muscle (ww)	21–1273		Liu et al., 2015
	Fish (*Hemiculter leucisculus*)	Gill (ww)	41–1636		Liu et al., 2015
	Fish (*Carassius auratus*)	Liver (ww)	725–920		Liu et al., 2015
	Fish (*Carassius auratus*)	Brain (ww)	566–630		Liu et al., 2015
	Fish (*Carassius auratus*)	Muscle (ww)	142–282		Liu et al., 2015
	Fish (*Carassius auratus*)	Gill (ww)	225–540		Liu et al., 2015
Salicylic acid	Shrimp (Young *Fenneropenaeus penicillatus*)	Whole organism (ww)		661	Chen et al., 2015
	Crab (Adult Calappa philargius)	Whole organism (ww)		536	Chen et al., 2015
	Molluscs (Adult *Meretrix lusoria*)	Whole organism (ww)		1854	Chen et al., 2015
	Fish (Adult *Trachinotus ovatus*)	Muscle (ww)		1238	Chen et al., 2015
	Fish (Adult *Lutjanus russelli*)	Muscle (ww)		1103	Chen et al., 2015
Sertraline	Zebrafish (*Danio rerio*)	Whole organism (ww)		37.5–50	Molina-Fernández et al., 2021
	Zebrafish (*Danio rerio*)	Whole organism (ww)		36.7–48.9	Molina-Fernández et al., 2021
	A. Common carp (*Cyprinus carpio*)	Liver (ww)	870		Grabicová et al., 2020
	B. Pikeperch (*Sander lucioperca*)	Liver (ww)	490		Grabicová et al., 2020
	A. Common carp (*Cyprinus carpio*)	Kidney (ww)	400		Grabicová et al., 2020
	B. Pikeperch (*Sander lucioperca*)	Kidney (ww)	490		Grabicová et al., 2020
	A. Common carp (*Cyprinus carpio*)	Brain (ww)	**2400**		Grabicová et al., 2020
	B. Pikeperch (*Sander lucioperca*)	Brain (ww)	710		Grabicová et al., 2020
	A. Common carp (*Cyprinus carpio*)	Muscle (ww)	65		Grabicová et al., 2020
	B. Pikeperch (*Sander lucioperca*)	Muscle (ww)	38		Grabicová et al., 2020
	Stone moroko (*Pseudorasbora parva*)	(ww)	100		Grabicová et al., 2020
	Plankton	(ww)	**6000**		Grabicová et al., 2020

Table 2 (*continued*)

Pharmaceutical	Organism	Tissue; dry weight (dw) or wet weight (ww)	BAF	BCF	Reference
	Caged goldfish (*Carassius auratus*)	Plasma	109–659		Muir et al., 2017
	Wild carp (*Cyprinus carpio*)	Plasma	120–349		Muir et al., 2017
	Brown trout (*Salmo trutta*)	Liver (ww)	880–**2400**		Grabicova et al., 2017
	Brown trout (*Salmo trutta*)	Kidney (ww)	**2800–4400**		Grabicova et al., 2017
	Brown trout (*Salmo trutta*)	Brain (ww)	240		Grabicova et al., 2017
	Common carp (*Cyprinus carpio* L.)	Liver (ww)	430–**140,000**		Sims et al., 2020
	Plant (*A. platanoides*)	Pooled samples (dw)	**2200**		Boström et al., 2017
	Crustacean (*A. aquaticus*)	Whole organism (ww)	360		Boström et al., 2017
	Insect (*N. glauca*)	Whole organism (ww)	26		Boström et al., 2017
	Fish (*P. pungitus*)	–	49		Boström et al., 2017
	Clam (*Corbicula fluminea*)	Whole organism (ww)	650		Burket et al., 2020
	Mussel (*Lasmigona costata*)	Tisseus (gill, digestive gland (excluding stomach and its contents), and gonadal tissues (ww))	**19,565–51,231**		De Solla et al., 2016
	Fish (smallmouth bass)	Brain (dw)	24–27		Arnnok et al., 2017
	Fish (smallmouth bass)	Gonad (dw)	27		Arnnok et al., 2017
	Fish (largemouth bass)	Brain (dw)	68		Arnnok et al., 2017
	Fish (rudd)	Brain (dw)	18		Arnnok et al., 2017
	Fish (rock bass)	Brain (dw)	29		Arnnok et al., 2017
	Fish (rock bass)	Gonad (dw)	14–15		Arnnok et al., 2017
	Fish (white bass)	Brain (dw)	23		Arnnok et al., 2017
	Fish (white bass)	Gonad (dw)	2		Arnnok et al., 2017
	Fish (walleye)	Brain (dw)	15–29		Arnnok et al., 2017
	Fish (walleye)	Gonad (dw)	2		Arnnok et al., 2017
	Baetidae	Whole organism (ww)	**3026–9211**		Haddad et al., 2018
	Cottus bairdii	Whole organism (ww)	66–**6947**		Haddad et al., 2018
	Lymnaeidea & Physidae	Whole organism (ww)	**15,789**		Haddad et al., 2018
	Periphyton	Whole organism (ww)	600–**19,737**		Haddad et al., 2018
	Salmo trutta	Whole organism (ww)	160–**3751**		Haddad et al., 2018
	Trichoptera	Whole organism (ww)	224–**11,053**		Haddad et al., 2018
Sotalol	Mussel (*M. galloprovincialis*)	Whole organism (dw)		18.8–59.2	Serra-Compte et al., 2018
Spectinomycin	Shellfish (*Mytilus edulis*)	Whole organism (dw)		**2512**	Xie et al., 2019
Sulfacetamide	Clams (*Crassostrea gigas*, *Patinopecten yessoensis*, *Chlamys farreri*)	Whole organism (ww)	1401		Na et al., 2013
Sulfadiazine	Clams (*Crassostrea gigas*, *Patinopecten yessoensis*, *Chlamys farreri*)	Whole organism (ww)	**10,757**		Na et al., 2013
	Shrimp (Young *Fenneropenaeus penicillatus*)	Whole organism (ww)		1392	Chen et al., 2015
	Fish (Adult *Trachinotus ovatus*)	Muscle (ww)		781	Chen et al., 2015
Sulfadimethoxine	Clams (*Crassostrea gigas*, *Patinopecten yessoensis*, *Chlamys farreri*)	Whole organism (ww)	0		Na et al., 2013
Sulfadoxine	Clams (*Crassostrea gigas*, *Patinopecten yessoensis*, *Chlamys farreri*)	Whole organism (ww)	0		Na et al., 2013
Sulfameter	Clams (*Crassostrea gigas*, *Patinopecten yessoensis*, *Chlamys farreri*)	Whole organism (ww)	**92,034**		Na et al., 2013
Sulfamethazine	Clams (*Crassostrea gigas*, *Patinopecten yessoensis*, *Chlamys farreri*)	Whole organism (ww)	**3501**		Na et al., 2013
	Caged goldfish (*Carassius auratus*)	Plasma	197–546		Muir et al., 2017
	Fish marine medaka (*Oryzias melastigma*)	Female gills (ww)		0.74–5.54	Zhao et al., 2016
	Fish marine medaka (*Oryzias melastigma*)	Female liver (ww)		1.08–26.30	Zhao et al., 2016
	Fish marine medaka (*Oryzias melastigma*)	Female bile (ww)		10.69–42.95	Zhao et al., 2016
	Fish marine medaka (*Oryzias melastigma*)	Female gonad (ww)		0.70–8.05	Zhao et al., 2016
	Fish marine medaka (*Oryzias melastigma*)	Female muscle (ww)		0.15–4.10	Zhao et al., 2016
	Fish marine medaka (*Oryzias melastigma*)	Male gills (ww)		0.57–7.95	Zhao et al., 2016
	Fish marine medaka (*Oryzias melastigma*)	Male liver (ww)		1.03–60.64	Zhao et al., 2016
	Fish marine medaka	Male bile (ww)		2.78–145.36	Zhao et al., 2016

(*continued on next page*)

Table 2 (*continued*)

Pharmaceutical	Organism	Tissue; dry weight (dw) or wet weight (ww)	BAF	BCF	Reference
	(*Oryzias melastigma*)				
	Fish marine medaka (*Oryzias melastigma*)	Male gonad (ww)		3.4–27.45	Zhao et al., 2016
	Fish marine medaka (*Oryzias melastigma*)	Male muscle (ww)		0.07–0.73	Zhao et al., 2016
Sulfamethiazole	Clams (*Crassostrea gigas*, *Patinopecten yessoensis*, *Chlamys farreri*)	Whole organism (ww)	2332		Na et al., 2013
Sulfamethoxazole	Limpet (*Ancylus fluviatilis*)	Whole organism (dw)	15.3–19.7		Ruhí et al., 2016
	Caddisfly (*Hydropsyche* sp.)	Whole organism (dw)	15.3–19.8		Ruhí et al., 2016
	Flatworm (*Phagocata vitta*)	Whole organism (dw)	15.3–19.9		Ruhí et al., 2016
	Predicted	–	1		Ruhí et al., 2016
	Fish (Young *Lutjanus russelli*)	Muscle (dw)		185	Chen et al., 2015
	Fish (*Epinephelus awoara*)	Muscle (dw)		1000	Xie et al., 2019
	Fish (*Ephippus orbis*)	Muscle (dw)		178	Xie et al., 2019
	Fish (*Culter alburnus*)	Muscle (dw)		398	Xie et al., 2019
	Shellfish (Ostrea gigas)	Whole organism (dw)		1000	Xie et al., 2019
	Shellfish (Mimachlamys nobilis)	Whole organism (dw)		126	Xie et al., 2019
	Shellfish (*Mytilus edulis*)	Whole organism (dw)		13	Xie et al., 2019
	Mussel (*M. galloprovincialis*)	Whole organism (dw)		6.2–9.0	Serra-Compte et al., 2018
	Bluegill sunfish (*Lepomis macrochirus*)	Muscle (ww)		0–0.99	Zhao et al., 2017
	Bluegill sunfish (*Lepomis macrochirus*)	Liver (ww)		0–4.48	Zhao et al., 2017
	Bluegill sunfish (*Lepomis macrochirus*)	Brain (ww)		0–2.45	Zhao et al., 2017
	Bluegill sunfish (*Lepomis macrochirus*)	Bile (ww)		0–0.49	Zhao et al., 2017
	Bluegill sunfish (*Lepomis macrochirus*)	Plasma		0	Zhao et al., 2017
	Bluegill sunfish (*Lepomis macrochirus*)	Gut (ww)		0.90–3.41	Zhao et al., 2017
	Bluegill sunfish (*Lepomis macrochirus*)	Gill (ww)		0–0.36	Zhao et al., 2017
	Clams (*Crassostrea gigas*, *Patinopecten yessoensis*, *Chlamys farreri*)	Whole organism (ww)	350		Na et al., 2013
Sulfamethoxypyridazine	Clams (*Crassostrea gigas*, *Patinopecten yessoensis*, *Chlamys farreri*)	Whole organism (ww)	**7023**		Na et al., 2013
Sulfamonomethoxine	Clams (*Crassostrea gigas*, *Patinopecten yessoensis*, *Chlamys farreri*)	Whole organism (ww)	**3076**		Na et al., 2013
Sulfathiazole	Clams (*Crassostrea gigas*, *Patinopecten yessoensis*, *Chlamys farreri*)	Whole organism (ww)	488		Na et al., 2013
Sulfisoxazole	Clams (*Crassostrea gigas*, *Patinopecten yessoensis*, *Chlamys farreri*)	Whole organism (ww)	0		Na et al., 2013
Telmisartan	A. Common carp (*Cyprinus carpio*)	Liver (ww)	7.8		Grabicová et al., 2020
	B. Pikeperch (*Sander lucioperca*)	Liver (ww)	6.6		Grabicová et al., 2020
	A. Common carp (*Cyprinus carpio*)	Kidney (ww)	0.65		Grabicová et al., 2020
	B. Pikeperch (*Sander lucioperca*)	Kidney (ww)	11		Grabicová et al., 2020
	B. Pikeperch (*Sander lucioperca*)	Brain (ww)	0.44		Grabicová et al., 2020
	Stone moroko (*Pseudorasbora parva*)	(ww)	12		Grabicová et al., 2020
	Plankton	(ww)	91		Grabicová et al., 2020
Temazepam	European perch (*Perca fluviatilis*)	Muscle (ww)		24–25	Cerveny et al., 2021b
	European perch (*Perca fluviatilis*)	Brain (ww)		83–100	Cerveny et al., 2021b
	Dragonfly larvae (*Sympetrum* sp.)	Whole organism (ww)		0.39–0.44	Cerveny et al., 2021b
	Bluegill sunfish (*Lepomis macrochirus*)	Muscle (ww)		1.08–5.69	Zhao et al., 2017
	Bluegill sunfish (*Lepomis macrochirus*)	Liver (ww)		9.17–25.5	Zhao et al., 2017

Table 2 (*continued*)

Pharmaceutical	Organism	Tissue; dry weight (dw) or wet weight (ww)	BAF	BCF	Reference
	Bluegill sunfish (*Lepomis macrochirus*)	Brain (ww)		4.42–15.1	Zhao et al., 2017
	Bluegill sunfish (*Lepomis macrochirus*)	Bile (ww)		**2350–4940**	Zhao et al., 2017
	Bluegill sunfish (*Lepomis macrochirus*)	Plasma		3.85–7.92	Zhao et al., 2017
	Bluegill sunfish (*Lepomis macrochirus*)	Gut (ww)		23.9–139.5	Zhao et al., 2017
	Bluegill sunfish (*Lepomis macrochirus*)	Gill (ww)		2.56–5.81	Zhao et al., 2017
	Sea trout (*Salmo trutta*)	Muscle (ww)		7.68	McCallum et al., 2019
Terbinafine	Plankton	(ww)	340		Grabicová et al., 2020
Tetracycline	Clams (*Crassostrea gigas*, *Patinopecten yessoensis*, *Chlamys farreri*)	Whole organism (ww)	1677		Na et al., 2013
Tramadol	A. Common carp (*Cyprinus carpio*)	Liver (ww)	2.8		Grabicová et al., 2020
	B. Pikeperch (*Sander lucioperca*)	Liver (ww)	2.4		Grabicová et al., 2020
	A. Common carp (*Cyprinus carpio*)	Kidney (ww)	5.9		Grabicová et al., 2020
	B. Pikeperch (*Sander lucioperca*)	(ww)	6.2		Grabicová et al., 2020
	Stone moroko (*Pseudorasbora parva*)	(ww)	3.8		Grabicová et al., 2020
	Plankton	(ww)	29		Grabicová et al., 2020
	Brown trout (*Salmo trutta*)	Liver (ww)	1.2–5.0		Grabicova et al., 2017
	Brown trout (*Salmo trutta*)	Kidney (ww)	10–110		Grabicova et al., 2017
	Common carp (*Cyprinus carpio* L.)	Liver (ww)	2.6–16		Sims et al., 2020
Trimethoprim	Fish predicted	–	1		Lagesson et al., 2016
	Invertebrate predicted	–	0.2		Lagesson et al., 2016
	Shrimp (Young *Fenneropenaeus penicillatus*)	Whole organism (ww)		63	Chen et al., 2015
	Fish (Young *Lutjanus russelli*)	Muscle (ww)		**6488**	Chen et al., 2015
	Fish (*Epinephelus awoara*)	Muscle (dw)		1413	Xie et al., 2019
	Fish (*Ephippus orbis*)	Muscle (dw)		1259	Xie et al., 2019
	Shellfish (*Ostrea gigas*)	Whole organism (dw)		794	Xie et al., 2019
	Shellfish (*Mimachlamys nobilis*)	Whole organism (dw)		794	Xie et al., 2019
	Shellfish (*Mytilus edulis*)	Whole organism (dw)		1585	Xie et al., 2019
	Shellfish (*Bufonaria perelegans*)	Whole organism (dw)		398	Xie et al., 2019
	Plankton	(ww)	42		Grabicová et al., 2020
	Wild carp (*Cyprinus carpio*)	Plasma	129–377		Muir et al., 2017
Venlafaxine	Limpet (*Ancylus fluviatilis*)	Whole organism (dw)	0.559–1.319		Ruhí et al., 2016
	Caddisfly (*Hydropsyche* sp.)	Whole organism (dw)	0.559–1.319		Ruhí et al., 2016
	Flatworm (*Phagocata vitta*)	Whole organism (dw)	0.559–1.319		Ruhí et al., 2016
	Predicted	–	1.55		Ruhí et al., 2016
	Mussel (*Mytilus galloprovincialis*)	Whole organism (dw)		265	Gomez et al., 2021
	Loach (*Misgurnus anguillicaudatus*)	Liver (ww)		0.04–0.14	Qu et al., 2019
	Loach (*Misgurnus anguillicaudatus*)	Liver (ww)		0.06–0.92	Qu et al., 2019
	A. Common carp (*Cyprinus carpio*)	Liver (ww)	16		Grabicová et al., 2020
	B. Pikeperch (*Sander lucioperca*)	Liver (ww)	5		Grabicová et al., 2020
	A. Common carp (*Cyprinus carpio*)	Kidney (ww)	26		Grabicová et al., 2020
	B. Pikeperch (*Sander lucioperca*)	Kidney (ww)	9.2		Grabicová et al., 2020
	B. Pikeperch (*Sander lucioperca*)	Brain (ww)	12		Grabicová et al., 2020
	B. Pikeperch (*Sander lucioperca*)	Muscle (ww)	0.4		Grabicová et al., 2020
	Stone moroko (*Pseudorasbora parva*)	(ww)	3.8		Grabicová et al., 2020
	Plankton	(ww)	180		Grabicová et al., 2020
	Mussel (*M. galloprovincialis*)	Whole organism (dw)		213–528	Serra-Compte et al., 2018
	Brown trout (*Salmo trutta*)	Liver (ww)	13–15		Grabicova et al., 2017

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Table 2 (*continued*)

Pharmaceutical	Organism	Tissue; dry weight (dw) or wet weight (ww)	BAF	BCF	Reference
	Brown trout (*Salmo trutta*)	Kidney (ww)	22–44		Grabicova et al., 2017
	Brown trout (*Salmo trutta*)	Muscle (ww)	3.3		Grabicova et al., 2017
	Common carp (*Cyprinus carpio* L.)	Liver (ww)	15–51		Sims et al., 2020
	Caged goldfish (*Carassius auratus*)	Plasma	5–31		Muir et al., 2017
	Wild carp (*Cyprinus carpio*)	Plasma	5–32		Muir et al., 2017
	Juvenile meagre (*Argyrosomus regius*)			64.6	Maulvault et al., 2018
	Fish (smallmouth bass)	Gonad (dw)	1		Arnnok et al., 2017
	Fish (smallmouth bass)	Liver (dw)	7–20		Arnnok et al., 2017
	Fish (smallmouth bass)	Muscle (dw)	1		Arnnok et al., 2017
	Fish (largemouth bass)	Gonad (dw)	3–4		Arnnok et al., 2017
	Fish (largemouth bass)	Liver (dw)	3		Arnnok et al., 2017
	Fish (largemouth bass)	Muscle (dw)	1–2		Arnnok et al., 2017
	Fish (rudd)	Muscle (dw)	1		Arnnok et al., 2017
	Fish (rock bass)	Liver (dw)	4		Arnnok et al., 2017
	Fish (rock bass)	Muscle (dw)	1		Arnnok et al., 2017
	Fish (white bass)	Gonad (dw)	6		Arnnok et al., 2017
	Fish (white bass)	Liver (dw)	1		Arnnok et al., 2017
	Fish (white perch)	Liver (dw)	11		Arnnok et al., 2017
	Fish (white perch)	Muscle (dw)	1		Arnnok et al., 2017
	Fish (walleye)	Gonad (dw)	7–14		Arnnok et al., 2017
	Fish (walleye)	Muscle (dw)	1		Arnnok et al., 2017
	Fish (steelhead)	Muscle (dw)	1		Arnnok et al., 2017
	Fish (yellow perch)	Gonad (dw)	9		Arnnok et al., 2017
	Fish (yellow perch)	Liver (dw)	84–150		Arnnok et al., 2017
	Bifilm		**2316**		Mastrángelo et al., 2022
Verapamil	B. Pikeperch (*Sander lucioperca*)	Liver (ww)	700		Grabicová et al., 2020
	B. Pikeperch (*Sander lucioperca*)	Kidney (ww)	870		Grabicová et al., 2020
	Plankton	(ww)	**9100**		Grabicová et al., 2020
	Fish, channel catfish	Plasma		0.7	Nallani et al., 2016
	Fish, channel catfish	Heart (ww)		5.2	Nallani et al., 2016
	Fish, channel catfish	Muscle (ww)		1.3	Nallani et al., 2016
	Fish, channel catfish	Gill (ww)		6.7	Nallani et al., 2016
	Fish, channel catfish	Kidney (ww)		46.5	Nallani et al., 2016
	Fish, channel catfish	Liver (ww)		13.4	Nallani et al., 2016
	Fish, fathead minnow	Heart (ww)		14.6	Nallani et al., 2016
	Fish, fathead minnow	Muscle (ww)		17.3–23.1	Nallani et al., 2016
	Fish, fathead minnow	Gill (ww)		29.3–40.3	Nallani et al., 2016
	Fish, fathead minnow	Kidney (ww)		34.4–74	Nallani et al., 2016
	Fish, fathead minnow	Liver (ww)		40–75	Nallani et al., 2016

In bold values classified as accumulative.

burdens were strongly dependent on pH and increased with increasing pH values. The fractions of neutral species, which are more lipophilic than the corresponding ionic species, increase with increasing pH levels. Because almost 80 % of all pharmaceuticals are ionizable (Manallack, 2008), thus having a pH-dependent neutral species distribution, the K_{ow} may be a less reliable predictor of bioaccumulation than for neutral organic chemicals. There is no apparent relationship between BCF values and log K_{ow} for PhACs (Duarte et al., 2022). The statistical correlation between accumulation data reported in Table 2 (BCF and BAF) and log Kow was $R^2 < 0.1$. Therefore, understanding and establishing a framework for the bioaccumulative behaviour of PhACs is crucial for assessing risks for aquatic ecosystems.

Bioconcentration is also controlled by organism tissue components other than lipids. For example, Arnnok et al. (2017) and Lu et al. (2018) found higher bioaccumulation patterns in brain, liver or gill tissue compared with muscle tissue, indicating the possibility of distribution variance across tissues. The data are not normalized for lipids because, as the authors explain, it is not appropriate to do this for ionizable compounds (Haddad et al., 2018; Ramirez et al., 2009; Grabicová et al., 2020). In fact, a new "non-classical" bioaccumulation behaviour is observed where some authors have suggested that proteins may have a significant effect on the PhAC bioaccumulation process (Duarte et al., 2022; Maculewicz et al., 2022). Kowalska et al. (2021) demonstrated higher affinity of drug metabolites for blood proteins than for lipids. Haddad et al. (2018) showed that normalization of ionizable PhACs to neutral lipid fractions is inappropriate.

Special attention is also being paid to metabolites and transformation products. These can be just as dangerous, if not more so, than their parent compounds (Świacka et al., 2022; Maculewicz et al., 2022). Metabolites usually have high hydrolytic stability and this increases the likelihood that they will accumulate in the tissues of organisms (Kowalska et al., 2021). An example of this is antidepressants. A study conducted by Arnnok et al. (2017) reported a high bioaccumulation (BCF up to 3000) of norsertraline (sertraline metabolite). This metabolite accumulates mainly in the liver and brain of fish. The BCF for sertraline (more lipophilic) was lower than 100. The authors attribute this to the metabolization of sertraline by fish, although they also state that further studies are needed to confirm the process. The same mechanism was not observed for norfluoxetine (the main metabolite of fluoxetine) whose BCF was <130. A study developed by Zhao et al. (2016), in medaka (*O. melastigma*) after exposure to sulfamethazine showed that its metabolite (acetylsulfamethazine) accumulated more readily in the organism (mainly in the gonad), presenting a different distribution pattern from that of the parent compound.

Reported investigations also suggest the probability of misestimating the risks to aquatic organisms when not considering certain environmental scenarios. The presence of other substances, for instance, seems to affect PhAC bioaccumulation in organisms. Co-exposure of Cu and diclofenac

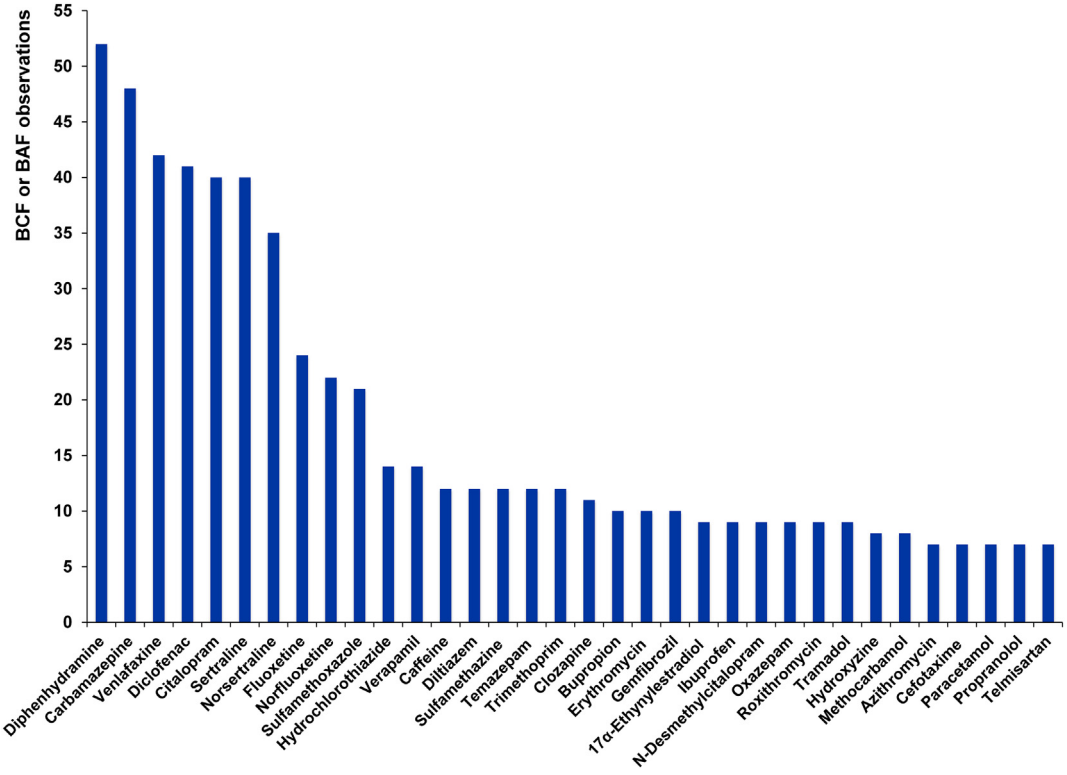

Fig. 2. PhACs most frequently studied in bioaccumulation assays.

(100 and 1000 μg/L) significantly decreased drug accumulation in crucian carp compared to single exposure to diclofenac (Xie et al., 2020). The mixture at higher levels also led to severer hepatic oxidative stress. However, co-exposure studies are relatively recent and in some cases contradictory. Zhang et al. (2019) found that the presence of microplastics increases the bioaccumulation of roxithromycin in red tilapia fish tissue, while the study by Wang et al. (2020) indicated that co-exposure with nanoplastics leads to reduced bioaccumulation and accelerated biodegradation of ibuprofen in freshwater algae. These results suggest the likelihood of erroneously estimating risks to aquatic organisms without taking environmental factors into account. Thus, when BAF data are available they should be considered the better source of information of the bioaccumulative potential of a substance. According with reported data, BAF values are superior to BCF values, highlighting the importance of field studies for reliable assessment under real conditions (Fig. 3). For example, for citalopram and its main metabolite, the mean BAF values are almost 100 and 1000 times higher respectively than the corresponding BCF values. This was also observed by Arnot and Gobas (2006) when both factors were compared for a total of 350 organic substances.

While the majority of PhACs are relatively water soluble and are generally non-bioaccumulative, resident biota can be chronically exposed to them due to the continuous release of these active compounds into ecosystems. Overall, a substance is usually considered very bioaccumulative if BAF values are >5000 L kg^{-1} in aquatic organisms, and as bioaccumulative if the BAF values are between 2000 and 5000 L kg^{-1} (Government of Canada, 2000). Some authors have used this general classification given that, in practice, there is no unified classification criterion for the bioaccumulation potential of PhACs (Burket et al., 2020; de Solla et al., 2016; Chen et al., 2015; Na et al., 2013). According to reported data, although most PhACs are considered non-bioaccumulative (BAF < 2000 L kg^{-1}), we found that 38 out of 113 PhACs identified in this review ever exceed the BAF of 2000 criterion (although it was <12 % and 6 % of the BAF and BCF data). In a study with 20 antibiotics in the coastal environment of Dalian (China) using three clam species as target aquatic organisms, Na et al. (2013) categorized sulfamethazine, sulfamethiazole, sulfamonomethoxine, and doxycycline as potentially bioaccumulative, while sulfadiazine, sulfameter, sulfamethoxypyridazine, and chloramphenicol were bioaccumulative.

Like BCF data, reported BAF data vary between studies and organisms. One of the main reasons for this variability is ecosystem type. The spatial and temporal variability associated with sampling is a major difficulty in obtaining reliable bioaccumulation information from field data. The steady-state assumption may not always be correct. For the evaluation to be representative, long-term conditioning of the study area is recommended (Burkhard et al., 2013; Arnot and Gobas, 2006; US-EPA, 2000). Reported studies describe between five (Xie et al., 2019) and twenty (Na et al., 2013) sampling areas and a sampling frequency between one (Chen et al., 2015) and two (Na et al., 2013). However, it is very difficult to carry out true random sampling as a consequence of the high economic and ecological costs (Świacka et al., 2022). BAF data are complex and seem organ, species and compound-specific. A large study conducted by Huerta et al. (2018) investigated the prevalence of PhACs in fish representing different trophic niches from 25 U.S. rivers and streams. The results suggested that the uptake of PhACs may be selective. Freshwater omnivorous fish accumulated a greater variety of PhACs of different therapeutic categories than the co-habitant carnivores and invertivores. Rojo et al. (2019) obtained similar conclusions.

Grabicová et al. (2020) reproduced a common aquaculture practice to evaluate the accumulation of PhACs in common prey of one omnivorous and one piscivorous fish for a period of 6 months. The authors found different bioaccumulation rates of PhACs between fish species. It is also interesting to note that in this study the highest levels of PhACs were found in plankton with BAF > 4000. In addition, organ-specific bioaccumulation was very clear for sertraline among other PhACs (brain > liver > kidney) for both species, while low concentrations were found in muscle tissue. Bao et al. (2020) reported differences in PhAC bioaccumulation among 5 wild fish species from Taihu Lake (China). Medroxy-progresterone was the PhAC with the highest BAF (1474 L kg^{-1}) in *C. carpio*, hexesestrol (1400 L kg^{-1}) in *C. auratus*, dienoestrol (893 L kg^{-1}) in *H. molitrix* and *A. nobilis*, and D-norgestrel (2460 L kg^{-1}) in *Anabarilius* sp. Similar results

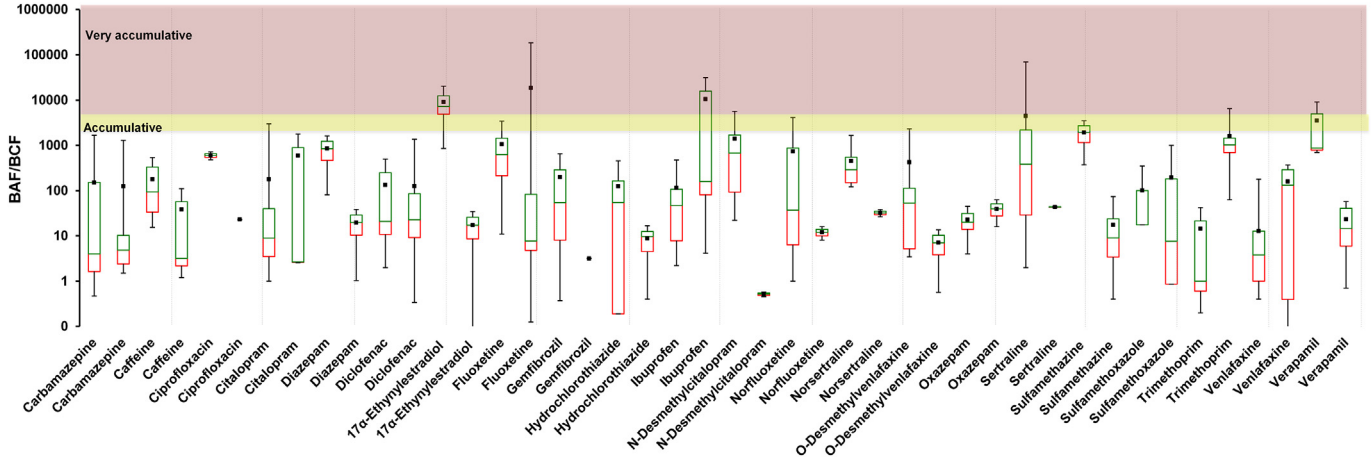

Fig. 3. Box-and-whisker plots of BAF (left box) and BCF (right box) observations of PhACs.

were also obtained by Du et al. (2014), Haddad et al. (2018) and Rojo et al. (2019). It has also been reported that kinetic differences and particular metabolic biotransformation can lead to differences in the bioaccumulation potential of certain life-stages (Świacka et al., 2022).

Finally, an important limitation is that most of the studies only determined PhACs in biota and water and did not examine suspended solids or sediments on which the more hydrophobic PhACs will be adsorbed. In a screening study considering 66 PhACs in the Tejo Estuary, Fonseca et al. (2021) reported that only 2 compounds were found simultaneously in water and biota, demonstrating the complex dynamics and behaviour of PhACs. Nevertheless, higher detection frequencies were observed in benthic and demersal species living directly on or just above the substrate, supporting the combined roles of sediment and dietary routes of PhAC uptake. Many other studies (Oetken et al., 2005; Lagesson et al., 2016; Xie et al., 2017; Wilkinson et al., 2018) have emphasized that filter-feeding organisms concentrate higher amounts of PhACs, due to their higher polluted environment and ingestion of organic matter from sediments.

5.1. Food web transfer

An important aspect to be addressed in the present review is the transfer of PhACs to the food web. The data on trophic transfer of PhACs are still very limited (Ruan et al., 2020; Du et al., 2014; Ruhí et al., 2016; Lagesson et al., 2016) although a general trend indicates that lower trophic position organisms bioaccumulate PhACs to a greater extent than higher trophic position organisms (Ding et al., 2015; Vernouillet et al., 2010; Xie et al., 2017; Du et al., 2014; Ruhí et al., 2016). Detritivores and herbivores, benthic primary consumers at lower trophic levels, were confirmed as the primary bioaccumulators of PhAC contamination in a semi-natural pond ecosystem (Lagesson et al., 2016). PhACs were quantified at concentration levels ranging from <0.03 to 5.88 ng g^{-1} w.w. in 24 species of molluscs, crustaceans and fish in a subtropical marine food web (Ruan et al., 2020). Trophic dilution was observed. Generally, invertebrate organisms had higher concentration levels than fish (TMFs 0.164 and 0.517 for atenolol and chloramphenicol, respectively). This can be explained by the fact that higher-level organisms have a greater capacity to metabolize substances. Similarly, trophic dilution was reported for 6 antidepressants (TMFs 0.01–0.71) in a semi-arid urban river, influenced by snowmelt and downstream from a municipal effluent discharge. The results were comparable at all locations and in all seasons, regardless of the different exposure conditions and concentrations (Haddad et al., 2018). Du et al. (2014) reported that PhACs accumulated in higher concentrations in invertebrates compared to fish in samples from an effluent-dependent stream. The authors reported a TMF of 0.38 and 1.17 for diphenhydramine and carbamazepine, respectively. The compounds detected in all the analysed species showed that none of them experienced trophic biomagnification. The study carried out by Xie et al. (2017) in the second largest lake in China (Taihu Lake) revealed the presence of antibiotics, NSAIDs and hormones in plankton, zoobenthos, shrimp and fish, the second of these recording the highest concentrations. No biomagnification was observed.

These results support the data that waterborne and not dietary exposures represent the primary route of fish uptake. Nevertheless more research is needed on the use of TMFs in bioaccumulation assessments and regulatory considerations (Świacka et al., 2022; Haddad et al., 2018).

6. Conclusions

This review summarizes all the recent advances examining bioaccumulation of PhACs in aquatic organisms. A total of 231 BCFs and 531 BAF determined for 113 PhACs have been collected. Without a doubt, there is much more data on fish and molluscs (63 % of the collected data) compared with crustaceans (10 %), insects (8 %) and algae or larvae (6 %). Large differences in reported data (organ, species and compound-specific) have been found. Some PhACs such as the antidepressant group, diphenhydramine, diclofenac or carbamazepine have been extensively studied in comparison with other groups of pharmaceuticals.

The results of the literature survey showed that, despite the number of works published on bioaccumulation in aquatic organisms which corroborate the importance of this topic, some aspects still require additional consideration.

1) There is an urgent need for more data on certain therapeutic groups of PhACs, such as anticancer drugs. In addition, certain PhACs can accumulate significantly in the body of aquatic organisms through biotransformation of the parent compound, without being present in the water at all. Metabolization and biotransformation have been shown to be an important exposure pathway, contributing significantly to direct uptake from the water. Therefore, PhAC metabolites should be given more attention in future research, as many can exert pharmacological effects comparable to parent drugs.
2) Water characteristics such as temperature and pH or DOM have been shown to significantly affect bioconcentration of certain PhACs in aquatic organisms. While physico-chemical properties of water vary greatly, knowledge about their role in the uptake, metabolic transformation, and excretion of PhACs is still limited. Temperature, for instance, is cause for concern given that this factor is a fundamentally important environmental variable influencing standard metabolic rates, for example in fish (Clarke and Johnston, 1999; Killen et al., 2010; Ohlberger et al., 2012). On the other hand, improving scientific knowledge requires stricter adherence to standard protocols and better documentation of the key experimental parameters. The complexity and variability of the results will be reduced with compliance to specific criteria.

3) BCF data from PhACs have been poorly correlated with lipophilicity. It seems that ionizable chemicals follow a new "non-classical" bioaccumulation behaviour where proteins may have a significant effect on the process. Therefore, it is extremely important to conduct further studies using a broader group of compounds to elucidate these relationships and assess to what extent their affinity for blood proteins translates into their potential for bioaccumulation.
4) Recent co-exposure studies have also flagged the likelihood of underestimating the risks to aquatic organisms by not taking into account an environmental scenario since, in the natural environment, PhACs occur as complex mixtures and in the company of other contaminants that could cause a dissimilar effect on the organism. Reported BAF values are superior to laboratory BCF values, highlighting the importance of field studies for reliable assessment and the best reflection of natural conditions. Some practices, such as taking into account long-term average conditions of the studied area, or the use of well-calibrated passive samplers, are crucial for reliable results and accurately calculated field-derived BCF values, respectively.
5) Finally, and regarding trophic transfer in aquatic ecosystems, benthic primary consumers at lower trophic levels concentrate higher amounts of PhACs due to the higher polluted environment and the ingestion of organic matter from sediments. Waterborne rather than dietary exposure represent the primary route of uptake of fish although, to date, the studies are too limited and the data insufficient to draw clear conclusions. Further research should be also conducted to study the bioaccumulation of PhACs in non-target species and other trophic positions.

CRediT authorship contribution statement

María del Carmen Gómez Regalado: Methodology, resources and conceptualization; Julia Martín: Methodology, resources, conceptualization, writing, review & editing; Juan Luis Santos: Conceptualization, Supervision, review & editing; Irene Aparicio: Conceptualization, Supervision, writing, review & editing; Esteban Alonso: Conceptualization, Supervision, Funding acquisition and Project administration; Alberto Zafra-Gómez: Conceptualization, writing, review & editing, supervision, funding acquisition and project administration.

Data availability

Data will be made available on request.

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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