

Article

Emerging Contaminants in the Effluent of Wastewater Should Be Regulated: Which and to What Extent?

Weiwei Yang ¹, Qingwei Bu ^{1,*}, Qianhui Shi ¹, Ruiqing Zhao ¹, Haitao Huang ¹, Lei Yang ², Jianfeng Tang ³ and Yuning Ma ^{4,*}

¹ School of Chemical & Environmental Engineering, China University of Mining & Technology-Beijing, Beijing 100083, China; 2110340107@student.cumtb.edu.cn (Q.S.)

² State Key Laboratory of Urban and Regional Ecology, Research Center for Eco-Environmental Sciences, Chinese Academy of Sciences, Beijing 100085, China

³ Key Laboratory of Urban Environment and Health, Institute of Urban Environment, Chinese Academy of Sciences, Xiamen 361021, China

⁴ College of Environmental and Resource Sciences, Zhejiang University, Hangzhou 310058, China

* Correspondence: qingwei.bu@cumtb.edu.cn (Q.B.); julius.yuningma@gmail.com (Y.M.)

Abstract: Effluent discharged from urban wastewater treatment plants (WWTPs) is a major source of emerging contaminants (ECs) requiring effective regulation. To this end, we collected discharge datasets of pharmaceuticals (PHACs) and endocrine-disrupting chemicals (EDCs), representing two primary categories of ECs, from Chinese WWTP effluent from 2012 to 2022 to establish an exposure database. Moreover, high-risk ECs' long-term water quality criteria (LWQC) were derived using the species sensitivity distribution (SSD) method. A total of 140 ECs (124 PHACs and 16 EDCs) were identified, with concentrations ranging from N.D. (not detected) to 706 µg/L. Most data were concentrated in coastal regions and Gansu, with high ecological risk observed in Gansu, Hebei, Shandong, Guangdong, and Hong Kong. Using the assessment factor (AF) method, 18 high-risk ECs requiring regulation were identified. However, only three of them, namely carbamazepine, ibuprofen, and bisphenol-A, met the derivation requirements of the SSD method. The LWQC for these three ECs were determined as 96.4, 1010, and 288 ng/L, respectively. Exposure data for carbamazepine and bisphenol-A surpassed their derived LWQC, indicating a need for heightened attention to these contaminants. This study elucidates the occurrence and risks of ECs in Chinese WWTPs and provides theoretical and data foundations for EC management in urban sewage facilities.

Keywords: China's WWTPs; emerging contaminants; risk; SSD; water quality criteria



Citation: Yang, W.; Bu, Q.; Shi, Q.; Zhao, R.; Huang, H.; Yang, L.; Tang, J.; Ma, Y. Emerging Contaminants in the Effluent of Wastewater Should Be Regulated: Which and to What Extent? *Toxics* **2024**, *12*, 309. <https://doi.org/10.3390/toxics12050309>

Academic Editor: Mark Taggart

Received: 26 March 2024

Revised: 22 April 2024

Accepted: 22 April 2024

Published: 24 April 2024



Copyright: © 2024 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

1. Introduction

Emerging contaminants (ECs) encompass newly discovered or recognized pollutants that pose risks to ecological environments and human health yet lack effective regulatory measures [1]. They mainly consist of PHACs, EDCs, persistent organic pollutants, and microplastics [2,3], among others. Advances in science and monitoring technology have led to increased detection of ECs in aquatic ecosystems such as rivers, lakes, and groundwater [4]. Due to the limited treatment performance of traditional water treatment processes, urban sewage still contains high concentrations of ECs even after treatment, making urban wastewater discharge a significant source of ECs [5–8]. Continuous discharge of ECs may accumulate in aquatic environments, endangering ecosystems [8]. Moreover, utilizing treated wastewater for landscaping [9], agricultural irrigation [10], and industrial reuse [11] may expose humans to ECs, thereby posing potential health risks [12,13]. Consequently, controlling EC discharge from WWTP effluent is crucial for aquatic ecosystems and human health. While governments prioritize identifying and regulating high-risk ECs [4], specific regulatory guidance is lacking. Variation in EC detection, discharge, risk, and regional

characteristics necessitates determining which ECs to regulate and to what extent in WWTP effluent discharge.

Despite numerous reports on EC occurrence and risks in WWTP effluent, most focus on limited ECs in small-scale areas, leaving nationwide or larger-scale data gaps. Deep mining of nationwide data is crucial for identifying high-risk areas and EC species, informing regulation in WWTP effluent discharge. Water quality criteria (WQC) guide water quality assessment and pollution prevention. Generally, WQC derivation methods include statistical extrapolation [14], the AF method [15], and the biotic ligand model method [16]. The AF method, while simple, is subjective, leading to conservative outcomes, primarily used for risk assessment. The biotic ligand model's incomplete theory hampers accurate baseline value derivation. In contrast, the statistical extrapolation method, with its rigorous logic and ample data, yields more objective and accurate WQC. Specifically, the statistical extrapolation method can be subdivided into species sensitivity distribution (SSD) and toxicity percentile rank (TPR) methods [14]. The SSD method, based on species sensitivity distribution theory, establishes a probability distribution model based on dose-response relationships, representing the sensitivity differences among different species and deducing the hazardous concentration for a given percentage of species, thereby protecting the ecosystem [14]. The TPR method, recommended by the US Environmental Protection Agency (US EPA) [17], considers water quality characteristics and the bioaccumulation effect of organisms but only utilizes the mean toxicity values of the four most sensitive genera. When deriving the WQC for pollutants unrelated to water quality characteristics and bioaccumulation effects, the SSD method is more capable of reflecting the overall ecological toxicity of chemicals, especially when considering the differences in species sensitivity. Therefore, WQC derived based on the SSD method hold promise in providing effective solutions for establishing discharge limits for high-risk ECs in WWTP effluent.

In this study, PHACs and EDCs were chosen as the focus, aiming to identify EC species, concentrations, risks, and high-risk areas in WWTP effluent across China, using nationwide data. High-risk ECs needing specific attention are selected, with SSD employed to calculate discharge limits. The objectives of this study include the following: (1) analyze PHACs and EDCs reported from Chinese WWTP effluent (2012–2022) to identify ECs needing attention; (2) screen high-risk ECs using the AF method; and (3) derive WQC for ECs in WWTP effluent using the SSD method.

2. Methodology

2.1. Methods of Data Collection

A comprehensive search was conducted utilizing the ISI Web of Science (<https://webofscience.clarivate.cn>, accessed on 30 December 2022) and China National Knowledge Infrastructure (CNKI) (<https://kns.cnki.net/>, accessed on 30 December 2022) to collect the relevant literature between 2012 and 2022 concerning PHACs and EDCs in WWTP effluent. The collected data focused solely on urban domestic wastewater, excluding pharmaceutical and industrial WWTPs, among others. This approach aimed to create provincial-level discharge maps specifically for PHACs and EDCs. Publications lacking clear location information were excluded from the analysis. Additionally, data from different wastewater treatment plants within the same study and data from the same wastewater treatment plant across different seasons were documented separately.

Furthermore, toxicological data on PHACs and EDCs were sourced from the ECOTOX database (<https://cfpub.epa.gov/ecotox/>) of the US EPA, accessed on 15 June 2023.

2.2. Risk Assessment Methods

To assess the ecological risk of a specific pollutant to aquatic organisms, the risk quotient (RQ) is computed by dividing the reported measured environmental concentration (MEC) by the predicted no-effect concentration (PNEC) [18]. PNEC is derived by dividing the most sensitive biological toxicity value by an AF. The selection criteria for assessment factors in the AF method are outlined in Table S4, while the PNEC values for PHACs and

EDCs are provided in Tables S5 and S6. To accurately evaluate the exposure risk of regional ECs, values such as “N.D.” (not detected), “ $<\text{LOD}$ ” (below the limit of detection), and “ $<\text{LOQ}$ ” (below the limit of quantitation) are considered as zero in the calculation. The risk exceeding rate (RER) is then calculated by determining the ratio of the number of RQs with values greater than 0.1 to the total number of RQs.

2.3. Water Quality Criteria Derivation Method

The derivation of WQC using the SSD method was conducted according to the procedures outlined in the Technical Guidelines for Deriving Water Quality Criteria for Freshwater Organisms published by the Ministry of Ecology and Environment of the People's Republic of China [19]. Initially, the SSD method was applied following the minimum data requirements specified in the freshwater biological water quality criteria derivation method. These requirements include covering at least three different trophic levels, including producers, and encompassing at least 10 species representing diverse biological groups. These groups include one species each of cyprinid fish, non-cyprinid fish, zooplankton, benthic invertebrates (e.g., mollusks, benthic crustaceans), amphibians, or other aquatic organisms belonging to different phyla from the aforementioned animals, and one species of phytoplankton or aquatic vascular plant.

For acute toxicity data, animals require exposure times of approximately 24 h for rotifers, 48 h for daphnids and midges, and 96 h for other species, while plants need an exposure time of approximately 96 h. For chronic toxicity data, animals need exposure durations of 48 h or longer for nematodes, 21 days or longer for other species, or exposure encompassing a sensitive life stage. Plants require exposure durations of 21 days or longer, or spanning at least one generation. Subsequently, the acute value for the same effect (AVE) and chronic value for the same effect (CVE) for all species of a certain EC were calculated following the Technical Guidelines for Deriving Water Quality Criteria for Freshwater Organisms [19].

The obtained AVE and CVE values were fitted using the National Ecological Environment Criteria Calculation Software [20], and four models (normal distribution, log-normal distribution, logistic distribution, and log-logistic distribution) were fitted to obtain the hazardous concentration for 5% of species derived from the toxicity data ($\text{HC}_{5\%}$), root mean square error (RSME), and P(A-D) value. P(A-D) represents the Anderson–Darling test value, where a p -value > 0.05 indicates that the fit passes the A-D test and the model conforms to the theoretical distribution; RSME represents the root mean square error, with a smaller RSME indicating a higher accuracy of model fitting. The model fitting result ($\text{HC}_{5\%}$) with $p > 0.05$ and the smallest RSME was selected to derive the WQC.

Short-term water quality criteria (SWQC) for aquatic organisms were calculated by dividing the hazardous concentration for 5% of species derived from the acute toxicity data ($\text{SHC}_{5\%}$) by the short-term assessment factor (SAF). Long-term water quality criteria (LWQC) were derived by dividing the hazardous concentration for 5% of species derived from chronic toxicity data ($\text{LHC}_{5\%}$) by the long-term assessment factor (LAF). The value of SAF or LAF was determined based on the number of data used for deriving the WQC. When the number of species included in the effective toxicity data exceeds 15, SAF or LAF is set to 2; when the number of species included in the effective toxicity data is less than or equal to 15, SAF or LAF is generally set to 3 [19].

3. Exposure and Risk of ECs

3.1. Exposure

A comprehensive dataset comprising 1178 data points related to 140 ECs was extracted from 43 available studies. Of these, 1116 data points were associated with 124 different PHACs, accounting for 94.74% of the total, and were sourced from 29 reports (Table S1). Additionally, 62 data points were related to EDCs, covering 16 EDCs, making up 5.26% of the total, and were obtained from 14 reports (Table S2). Notably, no studies reported both PHACs and EDCs simultaneously. Detailed information on both PHACs and EDCs can be

found in Table S3. The geographical coverage of these data spanned 18 provinces in China, with significant concentrations observed in the Bohai Sea Rim region, the Yangtze River Delta, and the Pearl River Delta basins (Figure S1). Among the provinces, Beijing, Jiangsu, Shanghai, Fujian, Guangdong, and Hong Kong reported both PHACs and EDCs, while others reported only one type of EC. Moreover, EDC-related data points were relatively scarce in these provinces, accounting for only 1.75% to 27.59% of the total. The concentrations of the 140 ECs in WWTP effluent ranged widely, from 0 ng/L to 706 µg/L. Specifically, the mean concentrations of pharmaceuticals varied from 0 ng/L to 5.09 µg/L, while those of EDCs ranged from 0.84 ng/L to 2.45 µg/L.

In terms of individual ECs, sulfamethoxazole exhibited the highest detection number with 46 data points and a mean detected concentration of 219 ng/L (Figure 1a). Notably, a recent study by Guo et al. highlighted sulfamethoxazole as the most frequently detected EC in Chinese surface water, with a detection concentration of 45 ng/L [4]. Moreover, sulfamethoxazole has been detected in WWTP effluent in Germany (22.9~34.9 ng/L) [21], the United States (1640 ng/L) [22], and other countries. In addition to sulfamethoxazole, ofloxacin, erythromycin, and salicylic acid also exhibited a high detection number (exceeded the overall detection frequency, 10.8), with 45, 38, and 12 data points, respectively. Their mean detected concentrations of 1151 ng/L, 1415 ng/L, and 2819 ng/L, respectively, exceeded the mean detected concentration (934 ng/L) of all ECs. Furthermore, their mean detected concentrations generally exceeded those found in Chinese surface water [18] by tenfold, as well as being higher than those in WWTP effluent in India (ofloxacin: 0~212 ng/L; erythromycin: 1~12 ng/L) [23] and the United States (erythromycin: 230 ng/L [24]; salicylic acid: 630 ng/L [25]).

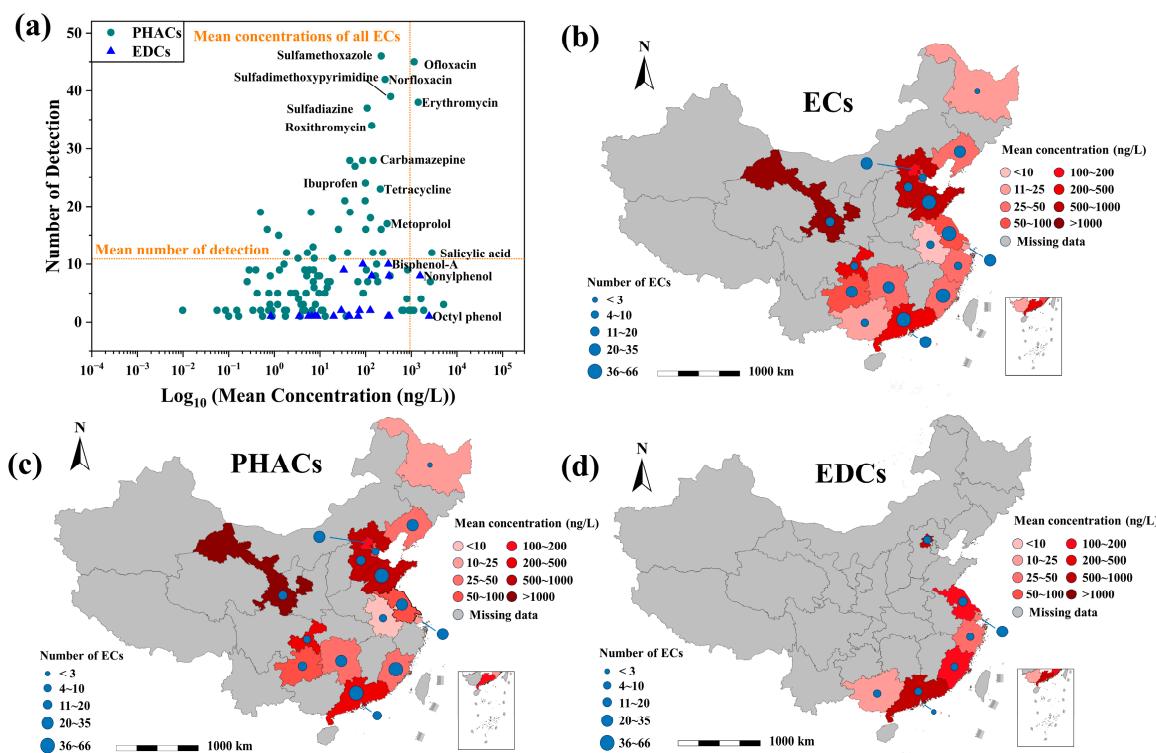


Figure 1. (a) Number of detections and mean concentration of individual ECs in the exposure database. Distribution of ECs (b), PHACs (c), and EDCs (d) by province recorded in the exposure.

The distribution of EC exposure, in terms of composition and concentration, varied significantly among different provinces' WWTP effluent (Figure 1b). Coastal provinces, except for Zhejiang, exhibited a relatively high number of EC exposure, with Guangdong Province having the highest number of exposed ECs at 66, followed by Fujian with 53 ECs, while Heilongjiang reported only one PHAC, caffeine. This variation could be attributed

to the extensive production and consumption of chemicals in economically advanced regions, alongside heightened scientific research driven by their developed economies [4]. Regarding EC concentration, Gansu, the Bohai Sea region, and the Pearl River Delta region were identified as the most severely polluted areas. The mean EC concentrations in Gansu, Hebei, Shandong, and Guangdong were 1116 ng/L, 816 ng/L, 519 ng/L, and 354 ng/L, respectively, all exceeding the mean concentration of all ECs (258 ng/L). The high concentration of ECs in Gansu was primarily due to the high concentrations of ofloxacin (mean concentration of 9240 ng/L) and sulfapyridine (mean concentration of 1150 ng/L) among PHACs, making Gansu the province with the most severe PHAC pollution (Figure 1c). Hebei and Shandong ranked second and third in terms of PHAC pollution, with mean PHAC concentrations of 862 ng/L and 586 ng/L, respectively. The PHACs in Hebei were mainly attributed to sulfonamide (mean concentration: sulfadimethoxypyrimidine, 552.5 ng/L; sulfamethoxazole, 777.5 ng/L; sulfapyridine, 442.5 ng/L; sulfadimethoxine, 745 ng/L; sulfamerazine, 1200 ng/L; sulfathiazole, 797.5 ng/L) and beta-lactam antibiotics (mean concentration: cefazolin, 797.5 ng/L; procaine hydrochloride, 1010 ng/L; cefotaxime, 672.5 ng/L; ceftriaxone, 1867.5 ng/L; cefaclor, 890 ng/L), while in Shandong, in addition to sulfonamide (mean concentration: sulfadimethoxypyrimidine, 3967.76 ng/L; sulfamethoxypyridazine, 5086.95 ng/L; sulfamethoxazole, 267.07 ng/L) and quinolone antibiotics (mean concentration: ciprofloxacin, 390.05; enoxacin, 3264.5 ng/L; sarafloxacin, 1597.2 ng/L; oxilinic acid, 622.75 ng/L), there were also non-antibiotic PHACs such as diclofenac (mean concentration of 568 ng/L), ibuprofen (mean concentration of 525 ng/L), and carbamazepine (mean concentration of 1117 ng/L). Research on EDCs was relatively scarce, mainly concentrated in the Yangtze River Delta and the Pearl River Delta regions (Figure 1d). Hong Kong had the most severe EDC pollution, with a mean concentration of 1043 ng/L, mainly composed of nonylphenol (mean concentration of 1546 ng/L) and bisphenol A (mean concentration of 540 ng/L), followed by Guangdong Province, where major EDC species included nonylphenol (mean concentration of 2512 ng/L) and bisphenol A (mean concentration of 485 ng/L), as well as octylphenol (mean concentration of 2454 ng/L).

3.2. Risk

Due to the limited availability of toxicity data for ECs, RQs were calculated for only 79 PHACs and 13 EDCs. As shown in Figure 2a, there was a significant difference in the overall risk between PHACs and EDCs, with median RQ values of 0.11 and 67.9, respectively, both exceeding 0.1, indicating unacceptable ecological risks. Specifically, a total of 479 data points of PHACs had risk values exceeding 0.1, accounting for 50.8% of the total data points for PHACs with calculable risks (Figure S2a). For EDCs, only five data points had RQ values < 0.1, while the remaining 54 data points had RQ values exceeding 0.1, accounting for 91.5% of the total data points for EDCs with calculable risks (Figure S2b).

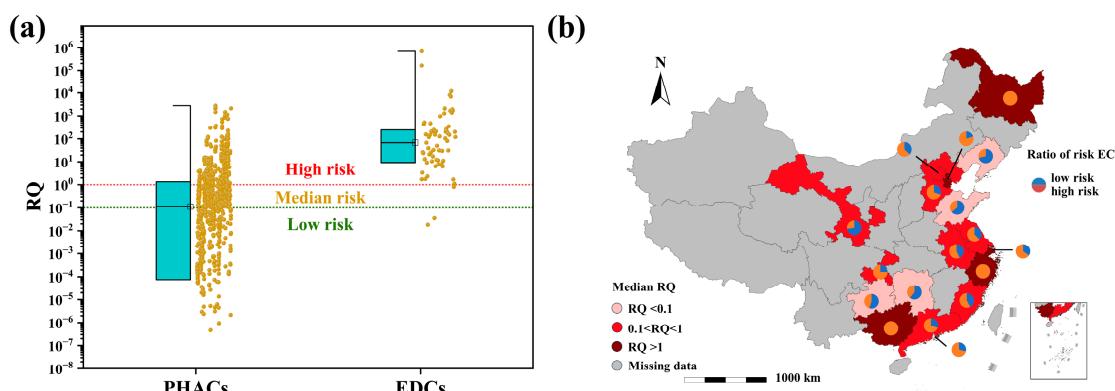


Figure 2. (a) Distribution of risk of PHACs and EDCs. (b) Distribution of risk by province, which was evaluated by median RQ.

Regarding the risk for individual provinces, except for Liaoning, Shandong, Guizhou, and Hunan, the median risk values for the other provinces were all higher than 0.1, indicating unacceptable risks. Nonetheless, the aforementioned four provinces still had 28.6%, 35.7%, 45.0%, and 38.7% of data points with an RQ > 0.1, signifying unacceptable risks (Figure 2b). Shandong Province reported an RQ for carbamazepine and ibuprofen of 1117.33 and 525.33, respectively, exceeding the critical value for unacceptable risks by more than three orders of magnitude, warranting special attention. Heilongjiang had the highest median RQ value, mainly due to the small data size (only two data points of caffeine). The median RQ of Zhejiang and Guangxi was also higher than 1, ranking among the highest in the country. This was attributed to the fact that only concentrations of EDCs were reported in these two regions, and since the PNEC for EDCs is generally low, this resulted in significantly higher median RQ values compared to other provinces. Furthermore, we also calculated RQ values for all data points of ECs (Figure S2). For PHACs, the median RQ values of 19 PHACs including sulfamethoxypyridazine, trimethoprim, ofloxacin, erythromycin, roxithromycin, spiramycin, tetracycline, ibuprofen, gemfibrozil, carbamazepine, bezafibrate, metoprolol, ketoprofen, caffeine, venlafaxine, fluoxetine, diazepam, oxazepam, and acetaminophen were all greater than 1, indicating high risk levels. For EDCs, except for chloroform and diethylstilbestrol, all other ECs had median RQ values exceeding 1, placing them in the high-risk category. These ECs pose a serious threat to aquatic organisms upon discharge after wastewater treatment and require close attention.

The identified high-risk ECs also exhibit a significant trend of risk exceeding rate (RER > 50%) and are detected frequently (exceeding the mean detection number). As illustrated in Figure 3, a total of 16 high-risk ECs were identified, comprising 14 PHACs and 2 EDCs. Among the PHACs are ofloxacin, norfloxacin, sulfamethoxazole, erythromycin, carbamazepine, roxithromycin, diclofenac, ciprofloxacin, caffeine, ibuprofen, metoprolol, bezafibrate, salicylic acid, and naproxen, while the EDCs include estrone and bisphenol A. The high ecological risks of these ECs have also been extensively documented in other studies (e.g., ofloxacin [26–29], norfloxacin [26,28,30,31], sulfamethoxazole [32–34], erythromycin [35–37], carbamazepine [32,38–41], roxithromycin [42–45], diclofenac [46–48], ciprofloxacin [49,50], caffeine [51–54], ibuprofen [38,55–57], metoprolol [58,59], bezafibrate [60,61], salicylic acid [62], naproxen [63–65], estrone [66–69], and bisphenol-A [70–75]). Moreover, these contaminants have been widely documented in surface waters across China [4,76]. Nevertheless, the current discharge standards of WWTPs in China fail to address these ECs, resulting in a lack of effective regulation over ECs with significant ecological risks.

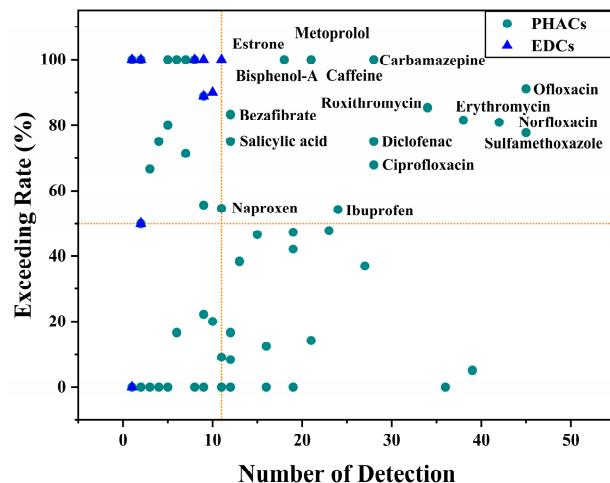


Figure 3. Risk exceeding rate (RER) and number of detections of ECs based on risk.

4. The Derivation Water Quality Criteria of ECs

Taking into account the detection frequency, mean detection concentration, high-risk exceedance rate, and the presence of locally severe ECs in WWTP effluent in China, a total of 18 ECs including ofloxacin, norfloxacin, sulfamethoxazole, sulfapyridine, erythromycin, carbamazepine, roxithromycin, diclofenac, ciprofloxacin, caffeine, ibuprofen, metoprolol, bezafibrate, salicylic acid, bisphenol-A, estrone, nonylphenol, and octylphenol were selected for deriving WQC using the SSD method. However, only carbamazepine, ibuprofen, and bisphenol-A met the data requirements for SSD derivation. The toxicity data for these three ECs were processed according to the SSD method's requirements for deriving short-term and long-term water quality standards for freshwater organisms. The processed toxicity data are detailed in Tables S7–S12.

The toxicity data were inputted into the National Ecological Environment Standard Calculation Software and fitted using four models: normal distribution, log-normal distribution, logistic, and log-logistic. The resulting HC₅, RSME, and P(A-D) values are shown in Table S13. As shown in Figure 4, the logistic model demonstrated excellent fits for the acute toxicity data of carbamazepine and ibuprofen, as well as the chronic toxicity data of ibuprofen. The log-logistic model exhibited excellent fits for the acute toxicity data of bisphenol A, the chronic toxicity data of carbamazepine, and the chronic toxicity data of bisphenol A. Further calculations revealed that the SWQC for carbamazepine, ibuprofen, and bisphenol A were 3.40 mg/L, 1.86 mg/L, and 0.89 mg/L (Table 1), respectively, which are higher than the actual concentrations of these ECs in water bodies by two to three orders of magnitude, indicating limited guidance for controlling the discharge of ECs in wastewater. However, the LWQC for carbamazepine, ibuprofen, and bisphenol A were 96.4 ng/L, 1010 ng/L, and 288 ng/L (Table 1), respectively, which are comparable to the detected concentrations of these ECs in water bodies. These LWQC can effectively reflect the exceedance of ECs in WWTP effluent. Additionally, the LWQC for carbamazepine [77] and ibuprofen [78] are consistent with those calculated by other researchers, while the LWQC for bisphenol-A [79,80] are one order of magnitude lower, which may be attributed to differences in the methodological approach employed.

The feasibility of the LWQC was further validated by integrating the reported data. As depicted in Figure 5, only the reported concentration of ibuprofen did not exceed its LWQC. However, for carbamazepine and ibuprofen, 14.3% and 45.5% of the reported data points, respectively, exceeded the corresponding LWQC. Therefore, this study concludes that the derived LWQC based on the SSD method can provide valuable reference data for controlling the discharge of ECs from WWTPs in China.

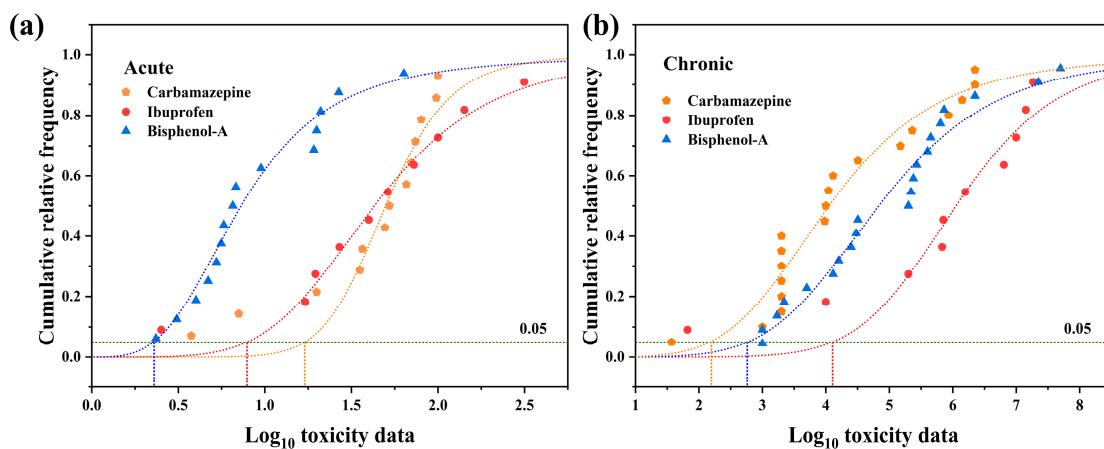
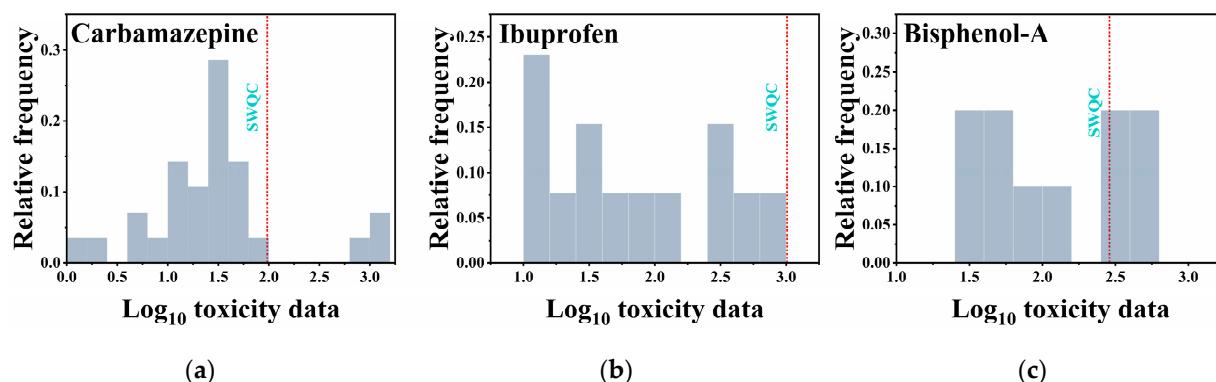


Figure 4. SSDs based on acute (a) and chronic (b) toxicity data for carbamazepine, ibuprofen, and bisphenol-A.

Table 1. Water quality criteria calculation results.

Chemicals	Model	Acute			Model	Chronic		
		SHC ₅ (mg/L)	SAF	SWQC (mg/L)		LHC ₅ (ng/L)	LAF	LWQC (ng/L)
Carbamazepine	Logistic distribution	10.19	3	3.40	Log-normal distribution	192.8	2	96.4
Ibuprofen	Logistic distribution	5.59	3	1.86	Logistic distribution	3039.9	3	1010
Bisphenol-A	Log-logistic distribution	2.66	3	0.89	Normal distribution	575.3	2	288

**Figure 5.** Logarithmic distribution of carbamazepine (a), ibuprofen (b), and bisphenol-A (c) detection data.

5. Future Prospects

Exposure data analysis indicates that the volume of data reported by WWTP effluent accounts for less than one-tenth of that reported for surface water [4]. Among the 34 provincial-level administrative regions in China, only 18 provinces reported the occurrence of ECs in WWTP effluent, with some provinces having very limited data. The reported data mainly focus on PHACs, while reports on EDCs are relatively scarce. The insufficient data significantly impair the accuracy of drawing a comprehensive and precise nationwide map of ECs in WWTP effluent, making it challenging to comprehensively and accurately understand the occurrence of ECs in WWTP effluent and the corresponding risks. Furthermore, the lack of toxicity data for some ECs prevents the calculation of their risk values, further exacerbating the limited understanding of EC risk levels in WWTP effluent. Therefore, future efforts should focus on generating more data to create a more objective and comprehensive fine-scale map of the occurrence and risk of ECs in WWTP effluent nationwide.

Regarding toxicity data, among the 18 high-risk ECs identified in this study, only three meet the basic requirements for deriving WQC using the SSD method, thus making it impossible to derive scientific and objective WQC for other high-risk ECs. In fact, we further screened the toxicity data of all PHACs with unacceptable risks based on the requirements of the SSD method. It was found that even for some PHACs with higher risk exceedance rates and detection frequencies, such as sulfamethoxazole, tetracycline, and erythromycin, although the toxicity data are adequate, WQC cannot be derived based on the SSD method. Therefore, it is necessary to derive WQC for more ECs based on more comprehensive and complete toxicity data to scientifically, accurately, objectively, and effectively control the discharge risks of ECs in WWTP effluent in the future.

6. Conclusions

In summary, we comprehensively investigated the occurrence and risks of PHACs and EDCs in WWTP effluent in China based on exposure data spanning from 2012 to 2022. Monitoring a total of 140 emerging contaminants (ECs), including 124 PHACs and 16 EDCs, revealed concentrations ranging from 0 to 706 µg/L. PHACs dominated the dataset, constituting 94.02% of the total. Through analyses encompassing overall exposure concentrations, regional risk assessment, risk exceedance rates, and detection frequencies, 18 ECs emerged as requiring close attention. These ECs were ofloxacin, norfloxacin, sulfamethoxazole, sulfapyridine, erythromycin, carbamazepine, roxithromycin, diclofenac, ciprofloxacin, caffeine, ibuprofen, metoprolol, bezafibrate, salicylic acid, bisphenol-A, estrone, nonylphenol, and octylphenol. Utilizing the SSD method, WQC were derived for three ECs meeting the derivation requirements: carbamazepine, ibuprofen, and bisphenol A, with respective LWQC of 96.4 ng/L, 1010 ng/L, and 288 ng/L. Except for ibuprofen, exposure data for carbamazepine and bisphenol A surpassed their LWQC to varying extents, underscoring the significance of these standards in regulating EC discharge in WWTP effluent. This study identifies major high-risk ECs and establishes LWQC based on nationwide data, offering a viable strategy for managing ECs discharge in WWTP effluent.

Supplementary Materials: The following supporting information can be downloaded at <https://www.mdpi.com/article/10.3390/toxics12050309/s1>: Table S1. Concentration levels of PHACs in the effluent of WWTPs in China [81–109]; Table S2. Concentration levels of EDCs in the effluent of WWTPs in China [110–123]; Table S3. Database of emerging contaminants detected in the effluent of WWTPs in China; Table S4. The selection criteria for AF in the derivation of PNEC; Table S5. PNEC of PHACs [124–181]; Table S6. PNEC of EDCs [174,182–193]; Table S7. Chronic toxicity data of carbamazepine on freshwater organisms [124,167,194–204]; Table S8. Acute toxicity data of carbamazepine on freshwater organisms [176,195,201,202,205–211]; Table S9. Chronic toxicity data of ibuprofen on freshwater organisms [167,168,212–217]; Table S10. Acute toxicity data of ibuprofen on freshwater organisms [155,176,209,211,214,217–219]; Table S11. Chronic toxicity data of bisphenol on freshwater organisms [191,220–236]; Table S12. Acute toxicity data of bisphenol on freshwater organisms [228,232,234,236–244]; Table S13. SSD fitting results of carbamazepine, ibuprofen, and bisphenol-A; Figure S1. Overview of the exposure database, including the ratio of number of detection ECs and the number of EC data by province; Figure S2. Boxplots for the calculated RQs for PHACs (a) and EDCs (b) detected in the effluent of WWTPs in China; Figure S3. The names and geographical locations of provinces in China.

Author Contributions: Conceptualization, Q.B. and Y.M.; methodology, W.Y.; software, W.Y.; validation, W.Y., Q.S. and Q.B.; formal analysis, W.Y.; investigation, W.Y.; resources, Q.B. and Y.M.; data curation, R.Z. and H.H.; writing—original draft preparation, W.Y.; writing—review and editing, Q.B., Y.M., L.Y. and J.T.; visualization, W.Y.; supervision, Q.B.; project administration, Q.B.; funding acquisition, Q.B. and Y.M. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by the National Natural Science Foundation of China (grant No. 42277406; 21777188) and Jiangsu Province Ecology and Environment Protection Key Laboratory of Groundwater Monitoring, Surveillance, and Forewarning of Pollution (Project No. GWKL2204).

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Data are contained within the article and Supplementary Materials.

Acknowledgments: We thank the anonymous reviewers for their thorough reviews and constructive comments. All individuals have consented to the acknowledgment.

Conflicts of 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.

Abbreviations

Wastewater treatment plants, WWTPs; pharmaceuticals, PHACs; endocrine-disrupting chemicals, EDCs; long-term water quality criteria, LWQC; assessment factor, AF; species sensitivity distribution, SSD; not detected, N.D.; limit of detection, LOD; limit of quantitation, LOQ; toxicity percentile rank, TPR; US Environmental Protection Agency, US EPA; acute value for the same effect, AVE; chronic value for the same effect, CVE; China National Knowledge Infrastructure, CNKI; risk quotient, RQ; measured environmental concentration, MEC; predicted no-effect concentration, PNEC; hazardous concentration for 5% of species derived from toxicity data, HC₅; root mean square error, RSME; Anderson–Darling test, P(A-D); short-term water quality criteria, SWQC; hazardous concentration for 5% of species derived from acute toxicity data, SHC₅; short-term assessment factor, SAF; hazardous concentration for 5% of species derived from chronic toxicity data, LHC₅; long-term assessment factor, LAF.

References

1. Ramírez-Malule, H.; Quiñones-Murillo, D.H.; Manotas-Duque, D. Emerging Contaminants as Global Environmental Hazards. A Bibliometric Analysis. *Emerg. Contam.* **2020**, *6*, 179–193. [[CrossRef](#)]
2. Puri, M.; Gandhi, K.; Kumar, M.S. Emerging Environmental Contaminants: A Global Perspective on Policies and Regulations. *J. Environ. Manag.* **2023**, *332*, 117344. [[CrossRef](#)] [[PubMed](#)]
3. Khan, S.; Naushad, M.; Govarthanan, M.; Iqbal, J.; Alfadul, S.M. Emerging Contaminants of High Concern for the Environment: Current Trends and Future Research. *Environ. Res.* **2022**, *207*, 112609. [[CrossRef](#)]
4. Guo, J.; Tu, K.; Chou, L.; Zhang, Y.; Wei, S.; Zhang, X.; Yu, H.; Shi, W. Deep Mining of Reported Emerging Contaminants in China’s Surface Water in the Past Decade: Exposure, Ecological Effects and Risk Assessment. *Water Res.* **2023**, *243*, 120318. [[CrossRef](#)] [[PubMed](#)]
5. Kasprzyk-Hordern, B.; Dinsdale, R.M.; Guwy, A.J. The Removal of Pharmaceuticals, Personal Care Products, Endocrine Disruptors and Illicit Drugs during Wastewater Treatment and Its Impact on the Quality of Receiving Waters. *Water Res.* **2009**, *43*, 363–380. [[CrossRef](#)] [[PubMed](#)]
6. Moldovan, Z.; Schmutzler, G.; Tusa, F.; Calin, R.; Alder, A.C. An Overview of Pharmaceuticals and Personal Care Products Contamination along the River Somes Watershed, Romania. *J. Environ. Monit.* **2007**, *9*, 986–993. [[CrossRef](#)] [[PubMed](#)]
7. Dai, G.; Wang, B.; Fu, C.; Dong, R.; Huang, J.; Deng, S.; Wang, Y.; Yu, G. Pharmaceuticals and Personal Care Products (PPCPs) in Urban and Suburban Rivers of Beijing, China: Occurrence, Source Apportionment and Potential Ecological Risk. *Environ. Sci.: Process. Impacts* **2016**, *18*, 445–455. [[CrossRef](#)] [[PubMed](#)]
8. Lin, X.; Xu, J.; Keller, A.A.; He, L.; Gu, Y.; Zheng, W.; Sun, D.; Lu, Z.; Huang, J.; Huang, X.; et al. Occurrence and Risk Assessment of Emerging Contaminants in a Water Reclamation and Ecological Reuse Project. *Sci. Total Environ.* **2020**, *744*, 140977. [[CrossRef](#)] [[PubMed](#)]
9. Bakopoulou, S.; Vasiloglou, V.; Kungolos, A. A Multicriteria Analysis Application for Evaluating the Possibility of Reusing Wastewater for Irrigation Purposes in a Greek Region. *Desalination Water Treat.* **2012**, *39*, 262–270. [[CrossRef](#)]
10. Lin, S.H.; Cheng, K.W. A New Sequencing Batch Reactor for Treatment of Municipal Sewage Wastewater for Agricultural Reuse. *Desalination* **2001**, *133*, 41–51. [[CrossRef](#)]
11. Bauer, S.; Linke, H.J.; Wagner, M. Optimizing Water-Reuse and Increasing Water-Saving Potentials by Linking Treated Industrial and Municipal Wastewater for a Sustainable Urban Development. *Water Sci. Technol.* **2020**, *81*, 1927–1940. [[CrossRef](#)] [[PubMed](#)]
12. Wei, X.; Hu, Y.; Zhu, Q.; Gao, J.; Liao, C.; Jiang, G. Co-Exposure and Health Risks of Several Typical Endocrine Disrupting Chemicals in General Population in Eastern China. *Environ. Res.* **2022**, *204*, 112366. [[CrossRef](#)] [[PubMed](#)]
13. Futran Fuhrman, V.; Tal, A.; Arnon, S. Why Endocrine Disrupting Chemicals (EDCs) Challenge Traditional Risk Assessment and How to Respond. *J. Hazard. Mater.* **2015**, *286*, 589–611. [[CrossRef](#)] [[PubMed](#)]
14. Posthuma, L.; Suter, G.W.; Traas, T.P. *Species Sensitivity Distributions in Ecotoxicology*; Taylor & Francis Ltd.: London, UK, 2001. [[CrossRef](#)]
15. Canadian Council of Minister of the Environment (CCME). *Canadian Environmental Quality Guidelines (CEQGs) Provide Science-Based Goals for the Quality of Aquatic and Terrestrial Ecosystems*; Canadian Council of Minister of the Environment: Manitoba, ON, Canada, 2018.
16. Niyogi, S.; Wood, C.M. Biotic Ligand Model, a Flexible Tool for Developing Site-Specific Water Quality Guidelines for Metals. *Environ. Sci. Technol.* **2004**, *38*, 6177–6192. [[CrossRef](#)] [[PubMed](#)]
17. USEPA. Guidelines for Deriving Numerical National Water Quality Criteria for the Protection of Aquatic Organisms and Their Uses. Available online: <https://www.epa.gov/wqc/guidelines-deriving-numerical-national-water-quality-criteria-protection-aquatic-organisms-and> (accessed on 22 March 2024).
18. Bu, Q.; Wang, B.; Huang, J.; Deng, S.; Yu, G. Pharmaceuticals and Personal Care Products in the Aquatic Environment in China: A Review. *J. Hazard. Mater.* **2013**, *262*, 189–211. [[CrossRef](#)] [[PubMed](#)]

19. Ministry of Ecology and Environment of People's Republic of China. *Technical Guideline for Deriving Water Quality Criteria for Freshwater Organisms*; Ministry of Ecology and Environment of People's Republic of China: Beijing, China, 2022.
20. National Ecological Environment Benchmark Expert Committee. *National Ecological Environment Benchmark Calculation Software Species Sensitivity Distribution Method*; Ministry of Ecology and Environment, People's Republic of China: Beijing, China, 2021.
21. Rodriguez-Mozaz, S.; Vaz-Moreira, I.; Varela Della Giustina, S.; Llorca, M.; Barceló, D.; Schubert, S.; Berendonk, T.U.; Michael-Kordatou, I.; Fatta-Kassinos, D.; Martinez, J.L.; et al. Antibiotic Residues in Final Effluents of European Wastewater Treatment Plants and Their Impact on the Aquatic Environment. *Environ. Int.* **2020**, *140*, 105733. [[CrossRef](#)] [[PubMed](#)]
22. Kwon, J.-W.; Rodriguez, J.M. Occurrence and Removal of Selected Pharmaceuticals and Personal Care Products in Three Wastewater-Treatment Plants. *Arch. Environ. Contam. Toxicol.* **2014**, *66*, 538–548. [[CrossRef](#)]
23. Balakrishna, K.; Rath, A.; Praveenkumarreddy, Y.; Guruge, K.S.; Subedi, B. A Review of the Occurrence of Pharmaceuticals and Personal Care Products in Indian Water Bodies. *Ecotoxicol. Environ. Saf.* **2017**, *137*, 113–120. [[CrossRef](#)] [[PubMed](#)]
24. Karthikeyan, K.G.; Meyer, M.T. Occurrence of Antibiotics in Wastewater Treatment Facilities in Wisconsin, USA. *Sci. Total Environ.* **2006**, *361*, 196–207. [[CrossRef](#)] [[PubMed](#)]
25. Crouse, B.A.; Ghoshdastidar, A.J.; Tong, A.Z. The Presence of Acidic and Neutral Drugs in Treated Sewage Effluents and Receiving Waters in the Cornwallis and Annapolis River Watersheds and the Mill CoveSewage Treatment Plant in Nova Scotia, Canada. *Environ. Res.* **2012**, *112*, 92–99. [[CrossRef](#)]
26. Zhao, W.; Guo, Y.; Lu, S.; Yan, P.; Sui, Q. Recent Advances in Pharmaceuticals and Personal Care Products in the Surface Water and Sediments in China. *Front. Environ. Sci. Eng.* **2016**, *10*, 2. [[CrossRef](#)]
27. Tran, N.H.; Hoang, L.; Nghiem, L.D.; Nguyen, N.M.H.; Ngo, H.H.; Guo, W.; Trinh, Q.T.; Mai, N.H.; Chen, H.; Nguyen, D.D.; et al. Occurrence and Risk Assessment of Multiple Classes of Antibiotics in Urban Canals and Lakes in Hanoi, Vietnam. *Sci. Total Environ.* **2019**, *692*, 157–174. [[CrossRef](#)]
28. Meng, F.; Sun, S.; Geng, J.; Ma, L.; Jiang, J.; Li, B.; Yabo, S.D.; Lu, L.; Fu, D.; Shen, J.; et al. Occurrence, Distribution, and Risk Assessment of Quinolone Antibiotics in Municipal Sewage Sludges throughout China. *J. Hazard. Mater.* **2023**, *453*, 131322. [[CrossRef](#)] [[PubMed](#)]
29. Zhang, L.; Zhu, Z.; Zhao, M.; He, J.; Zhang, X.; Hao, F.; Du, P. Occurrence, Removal, Emission and Environment Risk of 32 Antibiotics and Metabolites in Wastewater Treatment Plants in Wuhu, China. *Sci. Total Environ.* **2023**, *899*, 165681. [[CrossRef](#)] [[PubMed](#)]
30. Lu, S.; Lin, C.; Lei, K.; Xin, M.; Gu, X.; Lian, M.; Wang, B.; Liu, X.; Ouyang, W.; He, M. Profiling of the Spatiotemporal Distribution, Risks, and Prioritization of Antibiotics in the Waters of Laizhou Bay, Northern China. *J. Hazard. Mater.* **2022**, *424*, 127487. [[CrossRef](#)]
31. Sun, C.; Hu, E.; Liu, S.; Wen, L.; Yang, F.; Li, M. Spatial Distribution and Risk Assessment of Certain Antibiotics in 51 Urban Wastewater Treatment Plants in the Transition Zone between North and South China. *J. Hazard. Mater.* **2022**, *437*, 129307. [[CrossRef](#)] [[PubMed](#)]
32. Chaves, M.d.J.S.; Kulzer, J.; Lima, P. da R.P. de; Barbosa, S.C.; Primel, E.G. Updated Knowledge, Partitioning and Ecological Risk of Pharmaceuticals and Personal Care Products in Global Aquatic Environments. *Environ. Sci. Process. Impacts* **2022**, *24*, 1982–2008. [[CrossRef](#)]
33. Zheng, Q.; Zhang, R.; Wang, Y.; Pan, X.; Tang, J.; Zhang, G. Occurrence and Distribution of Antibiotics in the Beibu Gulf, China: Impacts of River Discharge and Aquaculture Activities. *Mar. Environ. Res.* **2012**, *78*, 26–33. [[CrossRef](#)]
34. Lin, T.; Yu, S.; Chen, W. Occurrence, Removal and Risk Assessment of Pharmaceutical and Personal Care Products (PPCPs) in an Advanced Drinking Water Treatment Plant (ADWTP) around Taihu Lake in China. *Chemosphere* **2016**, *152*, 1–9. [[CrossRef](#)]
35. Wu, C.; Huang, X.; Witter, J.D.; Spongberg, A.L.; Wang, K.; Wang, D.; Liu, J. Occurrence of Pharmaceuticals and Personal Care Products and Associated Environmental Risks in the Central and Lower Yangtze River, China. *Ecotoxicol. Environ. Saf.* **2014**, *106*, 19–26. [[CrossRef](#)]
36. Liu, J.; Lu, G.; Xie, Z.; Zhang, Z.; Li, S.; Yan, Z. Occurrence, Bioaccumulation and Risk Assessment of Lipophilic Pharmaceutically Active Compounds in the Downstream Rivers of Sewage Treatment Plants. *Sci. Total Environ.* **2015**, *511*, 54–62. [[CrossRef](#)] [[PubMed](#)]
37. Chen, H.; Liu, S.; Xu, X.-R.; Zhou, G.-J.; Liu, S.-S.; Yue, W.-Z.; Sun, K.-F.; Ying, G.-G. Antibiotics in the Coastal Environment of the Hailing Bay Region, South China Sea: Spatial Distribution, Source Analysis and Ecological Risks. *Mar. Pollut. Bull.* **2015**, *95*, 365–373. [[CrossRef](#)] [[PubMed](#)]
38. Santos, J.L.; Aparicio, I.; Alonso, E. Occurrence and Risk Assessment of Pharmaceutically Active Compounds in Wastewater Treatment Plants. A Case Study: Seville City (Spain). *Environ. Int.* **2007**, *33*, 596–601. [[CrossRef](#)] [[PubMed](#)]
39. Kondor, A.C.; Molnár, É.; Vancsik, A.; Filep, T.; Szeberényi, J.; Szabó, L.; Maász, G.; Pirger, Z.; Weiperth, A.; Ferincz, Á.; et al. Occurrence and Health Risk Assessment of Pharmaceutically Active Compounds in Riverbank Filtrated Drinking Water. *J. Water Process Eng.* **2021**, *41*, 102039. [[CrossRef](#)]
40. Wang, C.; Lu, Y.; Wang, C.; Xiu, C.; Cao, X.; Zhang, M.; Song, S. Distribution and Ecological Risks of Pharmaceuticals and Personal Care Products with Different Anthropogenic Stresses in a Coastal Watershed of China. *Chemosphere* **2022**, *303*, 135176. [[CrossRef](#)] [[PubMed](#)]
41. Ferrari, B.; Paxéus, N.; Giudice, R.L.; Pollio, A.; Garric, J. Ecotoxicological Impact of Pharmaceuticals Found in Treated Wastewaters: Study of Carbamazepine, Clofibrate Acid, and Diclofenac. *Ecotoxicol. Environ. Saf.* **2003**, *55*, 359–370. [[CrossRef](#)] [[PubMed](#)]

42. Xu, N.; Shen, Y.; Jiang, L.; Jiang, B.; Li, Y.; Yuan, Q.; Zhang, Y. Occurrence and Ecological-Risk Levels of Antibiotic Pollution in the Coastal Waters of Eastern China. *Environ. Sci. Pollut. Res.* **2023**, *30*, 71371–71381. [[CrossRef](#)]
43. Choi, K.; Kim, Y.; Jung, J.; Kim, M.-H.; Kim, C.-S.; Kim, N.-H.; Park, J. Occurrences and Ecological Risks of Roxithromycin, Trimethoprim, and Chloramphenicol in the Han River, Korea. *Environ. Toxicol. Chem.* **2008**, *27*, 711–719. [[CrossRef](#)]
44. Yu, X.; Yu, F.; Li, Z.; Zhan, J. Occurrence, Distribution, and Ecological Risk Assessment of Pharmaceuticals and Personal Care Products in the Surface Water of the Middle and Lower Reaches of the Yellow River (Henan Section). *J. Hazard. Mater.* **2023**, *443*, 130369. [[CrossRef](#)]
45. Sun, S.; Chen, Y.; Lin, Y.; An, D. Occurrence, Spatial Distribution, and Seasonal Variation of Emerging Trace Organic Pollutants in Source Water for Shanghai, China. *Sci. Total Environ.* **2018**, *639*, 1–7. [[CrossRef](#)]
46. Acuña, V.; Ginebreda, A.; Mor, J.R.; Petrovic, M.; Sabater, S.; Sumpter, J.; Barceló, D. Balancing the Health Benefits and Environmental Risks of Pharmaceuticals: Diclofenac as an Example. *Environ. Int.* **2015**, *85*, 327–333. [[CrossRef](#)] [[PubMed](#)]
47. Gopal, C.M.; Bhat, K.; Ramaswamy, B.R.; Kumar, V.; Singhal, R.K.; Basu, H.; Udayashankar, H.N.; Vasantharaju, S.G.; Praveen Kumarreddy, Y.; Shailesh; et al. Seasonal Occurrence and Risk Assessment of Pharmaceutical and Personal Care Products in Bengaluru Rivers and Lakes, India. *J. Environ. Chem. Eng.* **2021**, *9*, 105610. [[CrossRef](#)]
48. Tauxe-Wuersch, A.; De Alencastro, L.F.; Grandjean, D.; Tarradellas, J. Occurrence of Several Acidic Drugs in Sewage Treatment Plants in Switzerland and Risk Assessment. *Water Res.* **2005**, *39*, 1761–1772. [[CrossRef](#)] [[PubMed](#)]
49. Ashfaq, M.; Khan, K.N.; Rasool, S.; Mustafa, G.; Saif-Ur-Rehman, M.; Nazar, M.F.; Sun, Q.; Yu, C.-P. Occurrence and Ecological Risk Assessment of Fluoroquinolone Antibiotics in Hospital Waste of Lahore, Pakistan. *Environ. Toxicol. Pharmacol.* **2016**, *42*, 16–22. [[CrossRef](#)] [[PubMed](#)]
50. Mohd Nasir, F.A.; Praveena, S.M.; Aris, A.Z. Public Awareness Level and Occurrence of Pharmaceutical Residues in Drinking Water with Potential Health Risk: A Study from Kajang (Malaysia). *Ecotoxicol. Environ. Saf.* **2019**, *185*, 109681. [[CrossRef](#)]
51. de Souza, R.C.; Godoy, A.A.; Kummrow, F.; dos Santos, T.L.; Brandão, C.J.; Pinto, E. Occurrence of Caffeine, Fluoxetine, Bezafibrate and Levothyroxine in Surface Freshwater of São Paulo State (Brazil) and Risk Assessment for Aquatic Life Protection. *Environ. Sci. Pollut. Res.* **2021**, *28*, 20751–20761. [[CrossRef](#)] [[PubMed](#)]
52. Komori, K.; Suzuki, Y.; Minamiyama, M.; Harada, A. Occurrence of Selected Pharmaceuticals in River Water in Japan and Assessment of Their Environmental Risk. *Environ. Monit. Assess.* **2013**, *185*, 4529–4536. [[CrossRef](#)]
53. Singh, V.; Suthar, S. Occurrence, Seasonal Variations, and Ecological Risk of Pharmaceuticals and Personal Care Products in River Ganges at Two Holy Cities of India. *Chemosphere* **2021**, *268*, 129331. [[CrossRef](#)] [[PubMed](#)]
54. Li, S.; Wen, J.; He, B.; Wang, J.; Hu, X.; Liu, J. Occurrence of Caffeine in the Freshwater Environment: Implications for Ecopharmacovigilance. *Environ. Pollut.* **2020**, *263*, 114371. [[CrossRef](#)]
55. Ilechukwu, I.; Okonkwo, C.J.; Olusina, T.A.; Mpock, J.A.; Ilechukwu, C. Occurrence and Risk Assessment of Selected Pharmaceuticals in Water and Sediments of Usuma Dam, Abuja, Nigeria. *Int. J. Environ. Anal. Chem.* **2023**, *103*, 4398–4410. [[CrossRef](#)]
56. Qu, H.; Barrett, H.; Wang, B.; Han, J.; Wang, F.; Gong, W.; Wu, J.; Wang, W.; Yu, G. Co-Occurrence of Antiseptic Triclocarban and Chiral Anti-Inflammatory Ibuprofen in Environment: Association between Biological Effect in Sediment and Risk to Human Health. *J. Hazard. Mater.* **2021**, *407*, 124871. [[CrossRef](#)] [[PubMed](#)]
57. Lindqvist, N.; Tuukkanen, T.; Kronberg, L. Occurrence of Acidic Pharmaceuticals in Raw and Treated Sewages and in Receiving Waters. *Water Res.* **2005**, *39*, 2219–2228. [[CrossRef](#)] [[PubMed](#)]
58. Sörensgård, M.; Campos-Pereira, H.; Ullberg, M.; Lai, F.Y.; Golovko, O.; Ahrens, L. Mass Loads, Source Apportionment, and Risk Estimation of Organic Micropollutants from Hospital and Municipal Wastewater in Recipient Catchments. *Chemosphere* **2019**, *234*, 931–941. [[CrossRef](#)] [[PubMed](#)]
59. Godoy, A.A.; Kummrow, F.; Pamplin, P.A.Z. Occurrence, Ecotoxicological Effects and Risk Assessment of Antihypertensive Pharmaceutical Residues in the Aquatic Environment—A Review. *Chemosphere* **2015**, *138*, 281–291. [[CrossRef](#)] [[PubMed](#)]
60. Zhang, K.; Zhao, Y.; Fent, K. Cardiovascular Drugs and Lipid Regulating Agents in Surface Waters at Global Scale: Occurrence, Ecotoxicity and Risk Assessment. *Sci. Total Environ.* **2020**, *729*, 138770. [[CrossRef](#)]
61. Mijangos, L.; Ziarrusta, H.; Ros, O.; Kortazar, L.; Fernández, L.A.; Olivares, M.; Zuloaga, O.; Prieto, A.; Etxebarria, N. Occurrence of Emerging Pollutants in Estuaries of the Basque Country: Analysis of Sources and Distribution, and Assessment of the Environmental Risk. *Water Res.* **2018**, *147*, 152–163. [[CrossRef](#)]
62. Peng, X.; Ou, W.; Wang, C.; Wang, Z.; Huang, Q.; Jin, J.; Tan, J. Occurrence and Ecological Potential of Pharmaceuticals and Personal Care Products in Groundwater and Reservoirs in the Vicinity of Municipal Landfills in China. *Sci. Total Environ.* **2014**, *490*, 889–898. [[CrossRef](#)]
63. Ashfaq, M.; Nawaz Khan, K.; Saif Ur Rehman, M.; Mustafa, G.; Faizan Nazar, M.; Sun, Q.; Iqbal, J.; Mulla, S.I.; Yu, C.-P. Ecological Risk Assessment of Pharmaceuticals in the Receiving Environment of Pharmaceutical Wastewater in Pakistan. *Ecotoxicol. Environ. Saf.* **2017**, *136*, 31–39. [[CrossRef](#)]
64. Isidori, M.; Lavorgna, M.; Nardelli, A.; Parrella, A.; Previtera, L.; Rubino, M. Ecotoxicity of Naproxen and Its Phototransformation Products. *Sci. Total Environ.* **2005**, *348*, 93–101. [[CrossRef](#)]
65. Korkmaz, N.E.; Savun-Hekimoğlu, B.; Aksu, A.; Burak, S.; Caglar, N.B. Occurrence, Sources and Environmental Risk Assessment of Pharmaceuticals in the Sea of Marmara, Turkey. *Sci. Total Environ.* **2022**, *819*, 152996. [[CrossRef](#)]

66. Cao, J.; Shi, J.; Han, R.; Li, Y.; Yang, Z. Seasonal Variations in the Occurrence and Distribution of Estrogens and Pharmaceuticals in the Zhangweinanyun River System. *Chin. Sci. Bull.* **2010**, *55*, 3138–3144. [[CrossRef](#)]
67. Wang, D.; Luo, Z.; Zhang, X.; Lin, L.; Du, M.; Du Laing, G.; Yan, C. Occurrence, Distribution and Risk Assessment of Estrogenic Compounds for Three Source Water Types in Ningbo City, China. *Environ. Earth Sci.* **2015**, *74*, 5961–5969. [[CrossRef](#)]
68. Yu, Y.; Wu, L.; Chang, A.C. Seasonal Variation of Endocrine Disrupting Compounds, Pharmaceuticals and Personal Care Products in Wastewater Treatment Plants. *Sci. Total Environ.* **2013**, *442*, 310–316. [[CrossRef](#)] [[PubMed](#)]
69. Du, B.; Fan, G.; Yu, W.; Yang, S.; Zhou, J.; Luo, J. Occurrence and Risk Assessment of Steroid Estrogens in Environmental Water Samples: A Five-Year Worldwide Perspective. *Environ. Pollut.* **2020**, *267*, 115405. [[CrossRef](#)] [[PubMed](#)]
70. Liu, J.; Zhang, L.; Lu, G.; Jiang, R.; Yan, Z.; Li, Y. Occurrence, Toxicity and Ecological Risk of Bisphenol A Analogues in Aquatic Environment—A Review. *Ecotoxicol. Environ. Saf.* **2021**, *208*, 111481. [[CrossRef](#)] [[PubMed](#)]
71. Wang, Y.; Wang, Q.; Hu, L.; Lu, G.; Li, Y. Occurrence of Estrogens in Water, Sediment and Biota and Their Ecological Risk in Northern Taihu Lake in China. *Environ. Geochem. Health* **2015**, *37*, 147–156. [[CrossRef](#)] [[PubMed](#)]
72. Hu, Y.; Zhu, Q.; Yan, X.; Liao, C.; Jiang, G. Occurrence, Fate and Risk Assessment of BPA and Its Substituents in Wastewater Treatment Plant: A Review. *Environ. Res.* **2019**, *178*, 108732. [[CrossRef](#)] [[PubMed](#)]
73. Liu, R.; Luo, X.; Shu, S.; Ding, J.; Zhang, G.; Wang, Z.; Zou, H.; Zhang, Y. Impact of Rainfall on the Occurrence, Spatiotemporal Distribution, and Partition Trend of Micropollutants in Taihu Lake, China: Bisphenol A and 4-Nonylphenol as Examples. *Ecotoxicol. Environ. Saf.* **2020**, *204*, 111064. [[CrossRef](#)] [[PubMed](#)]
74. Shen, J.; Sui, Y.; Feng, J.; Wang, X.; Li, X.; Jiang, S.; Zhang, Z.; Zi, J.; Sun, T.; Gao, Y.; et al. Environmental Occurrence and Ecological Risk of Bisphenol A in Erhai Lake Basin Away From Industrial Regions in China. *Pol. J. Environ. Stud.* **2020**, *30*, 841–850. [[CrossRef](#)]
75. Catenza, C.J.; Farooq, A.; Shubear, N.S.; Donkor, K.K. A Targeted Review on Fate, Occurrence, Risk and Health Implications of Bisphenol Analogues. *Chemosphere* **2021**, *268*, 129273. [[CrossRef](#)]
76. Zhong, M.; Wang, T.; Zhao, W.; Huang, J.; Wang, B.; Blaney, L.; Bu, Q.; Yu, G. Emerging Organic Contaminants in Chinese Surface Water: Identification of Priority Pollutants. *Engineering* **2022**, *11*, 111–125. [[CrossRef](#)]
77. Wu, J.; Shi, D.; Wang, S.; Yang, X.; Zhang, H.; Zhang, T.; Zheng, L.; Zhang, Y. Derivation of Water Quality Criteria for Carbamazepine and Ecological Risk Assessment in the Nansi Lake Basin. *Int. J. Environ. Res. Public Health* **2022**, *19*, 10875. [[CrossRef](#)]
78. Huang, Q.; Bu, Q.; Zhong, W.; Shi, K.; Cao, Z.; Yu, G. Derivation of Aquatic Predicted No-Effect Concentration (PNEC) for Ibuprofen and Sulfamethoxazole Based on Various Toxicity Endpoints and the Associated Risks. *Chemosphere* **2018**, *193*, 223–229. [[CrossRef](#)]
79. Wang, L.; Wang, Z.; Liu, J.; Ji, G.; Shi, L.; Xu, J.; Yang, J. Deriving the Freshwater Quality Criteria of BPA, BPF and BPAF for Protecting Aquatic Life. *Ecotoxicol. Environ. Saf.* **2018**, *164*, 713–721. [[CrossRef](#)]
80. Wang, Y.; Na, G.; Zong, H.; Ma, X.; Yang, X.; Mu, J.; Wang, L.; Lin, Z.; Zhang, Z.; Wang, J.; et al. Applying Adverse Outcome Pathways and Species Sensitivity-Weighted Distribution to Predicted-No-Effect Concentration Derivation and Quantitative Ecological Risk Assessment for Bisphenol A and 4-Nonylphenol in Aquatic Environments: A Case Study on Tianjin City, China. *Environ. Toxicol. Chem.* **2018**, *37*, 551–562. [[CrossRef](#)]
81. Zhou, Y.; Meng, J.; Zhang, M.; Chen, S.; He, B.; Zhao, H.; Li, Q.; Zhang, S.; Wang, T. Which Type Of pollutants Need to be Controlled with Priority in Wastewater Treatment Plants: Traditional or Emerging Pollutants? *Environ. Int.* **2019**, *131*, 104982. [[CrossRef](#)]
82. Yang, Y.-Y.; Liu, W.-R.; Liu, Y.-S.; Zhao, J.-L.; Zhang, Q.-Q.; Zhang, M.; Zhang, J.-N.; Jiang, Y.-X.; Zhang, L.-J.; Ying, G.-G. Suitability of Pharmaceuticals and Personal Care Products (PPCPs) and Artificial Sweeteners (ASs) as Wastewater Indicators in the Pearl River Delta, South China. *Sci. Total Environ.* **2017**, *590–591*, 611–619. [[CrossRef](#)]
83. Tang, Y.; Guo, L.-L.; Hong, C.-Y.; Bing, Y.-X.; Xu, Z.-C. Seasonal Occurrence, Removal and Risk Assessment of 10 Pharmaceuticals in 2 Sewage Treatment Plants of Guangdong, China. *Environ. Technol.* **2019**, *40*, 458–469. [[CrossRef](#)]
84. Wang, L.; Zhu, D.; Cao, Y.; Yu, X.; Hui, Y.; Li, W.; Wang, D. Seasonal changes and ecological risk assessment of pharmaceutical and personal care products in the effluents of wastewater treatment plants in Beijin. *Acta Sci. Circumstantiae* **2021**, *41*, 2922–2932. [[CrossRef](#)]
85. Shao, T.; Ben, W.; Su, D.; Zhang, H.; Hou, P.; Qiang, Z.; Zhang, Y. Quantitative determination of typical pharmaceuticals and their metabolites in municipal wastewater treatment plants. *Acta Sci. Circumstantiae* **2020**, *40*, 2136–2141. [[CrossRef](#)]
86. Yang, Z.; Li, J.; Zhang, S.; Xiang, F.; Tang, T.; Yang, Y. Pollution Level and Ecological Risk of Typical Antibiotics in Guiyang Wastewater Treatment Plants. *Environ. Sci.* **2019**, *40*, 3249–3256. [[CrossRef](#)]
87. Ye, P.; You, W.; Yang, B.; Chen, Y.; Wang, L.; Zhao, J.; Ying, G. Pollution Characteristics and Removal of Typical Pharmaceuticals in Hospital Wastewater and Municipal Wastewater Treatment Plants. *Environ. Sci.* **2021**, *42*, 2928–2936. [[CrossRef](#)]
88. Zhang, X.; Zhao, H.; Du, J.; Qu, Y.; Shen, C.; Tan, F.; Chen, J.; Quan, X. Occurrence, Removal, and Risk Assessment of Antibiotics in 12 Wastewater Treatment Plants from Dalian, China. *Environ. Sci. Pollut. Res.* **2017**, *24*, 16478–16487. [[CrossRef](#)]
89. Yao, L.; Chen, Z.-Y.; Dou, W.-Y.; Yao, Z.-K.; Duan, X.-C.; Chen, Z.-F.; Zhang, L.-J.; Nong, Y.-J.; Zhao, J.-L.; Ying, G.-G. Occurrence, Removal and Mass Loads of Antiviral Drugs in Seven Wastewater Treatment Plants with Various Treatment Processes. *Water Res.* **2021**, *207*, 117803. [[CrossRef](#)]

90. Ashfaq, M.; Li, Y.; Wang, Y.; Chen, W.; Wang, H.; Chen, X.; Wu, W.; Huang, Z.; Yu, C.-P.; Sun, Q. Occurrence, Fate, and Mass Balance of Different Classes of Pharmaceuticals and Personal Care Products in an Anaerobic-Anoxic-Oxic Wastewater Treatment Plant in Xiamen, China. *Water Res.* **2017**, *123*, 655–667. [[CrossRef](#)]
91. Duan, L.; Zhang, Y.; Wang, B.; Deng, S.; Huang, J.; Wang, Y.; Yu, G. Occurrence, Elimination, Enantiomeric Distribution and Intra-Day Variations of Chiral Pharmaceuticals in Major Wastewater Treatment Plants in Beijing, China. *Environ. Pollut.* **2018**, *239*, 473–482. [[CrossRef](#)]
92. Gao, L.; Shi, Y.; Li, W.; Niu, H.; Liu, J.; Cai, Y. Occurrence of Antibiotics in Eight Sewage Treatment Plants in Beijing, China. *Chemosphere* **2012**, *86*, 665–671. [[CrossRef](#)]
93. Wang, W.; Zhang, W.; Liang, H.; Gao, D. Occurrence and Fate of Typical Antibiotics in Wastewater Treatment Plants in Harbin, North-East China. *Front. Environ. Sci. Eng.* **2019**, *13*, 34. [[CrossRef](#)]
94. Gan, X.; Yan, Q.; Gao, X.; Zhang, Y.; Zi, C.; Peng, X.; Guo, J. Occurrence and Fate of Typical Antibiotics in a Wastewater Treatment Plant in Southwest China. *Environ. Sci.* **2014**, *35*, 1817–1823. [[CrossRef](#)]
95. Zhao, B.; Liu, Y.; Dong, W.; Li, M.; Lu, S.; Wang, W.; Fan, Y. Occurrence and Fate of Ten Sulfonamide Antibiotics in Typical Wastewater Treatment Plants in the City of Jinan of Northeastern China. *Desalination Water Treat.* **2020**, *206*, 340–348. [[CrossRef](#)]
96. Li, Q.; Liu, H.; Liu, J.; Jia, L.; Wang, Q. Occurrence and fate of sulfonamide and β -lactam antibiotics in wastewater treatment plants in Handan. *Environ. Chem.* **2018**, *37*, 1738–1745.
97. Wu, M.; Xiang, J.; Que, C.; Chen, F.; Xu, G. Occurrence and Fate of Psychiatric Pharmaceuticals in the Urban Water System of Shanghai, China. *Chemosphere* **2015**, *138*, 486–493. [[CrossRef](#)]
98. Hu, J.; Zhou, J.; Zhou, S.; Wu, P.; Tsang, Y.F. Occurrence and Fate of Antibiotics in a Wastewater Treatment Plant and Their Biological Effects on Receiving Waters in Guizhou. *Process Saf. Environ. Prot.* **2018**, *113*, 483–490. [[CrossRef](#)]
99. Du, J.; Fan, Y.; Qian, X. Occurrence and Behavior of Pharmaceuticals in Sewage Treatment Plants in Eastern China. *Front. Environ. Sci. Eng.* **2015**, *9*, 725–730. [[CrossRef](#)]
100. Wang, Y.; Li, Y.; Hu, A.; Rashid, A.; Ashfaq, M.; Wang, Y.; Wang, H.; Luo, H.; Yu, C.-P.; Sun, Q. Monitoring, Mass Balance and Fate of Pharmaceuticals and Personal Care Products in Seven Wastewater Treatment Plants in Xiamen City, China. *J. Hazard. Mater.* **2018**, *354*, 81–90. [[CrossRef](#)]
101. Lin, H.; Li, H.; Chen, L.; Li, L.; Yin, L.; Lee, H.; Yang, Z. Mass Loading and Emission of Thirty-Seven Pharmaceuticals in a Typical Municipal Wastewater Treatment Plant in Hunan Province, Southern China. *Ecotoxicol. Environ. Saf.* **2018**, *147*, 530–536. [[CrossRef](#)]
102. Ke, R.; Jiang, Y.; Huang, Q.; Chen, L. Investigative Screening of Pharmaceuticals in a Municipal Wastewater Treatment Plant in Shanghai. *Asian J. Ecotoxicol.* **2014**, *9*, 1146–1155.
103. Yin, Z.Y.; Min, L.; Jin, L.; Wang, F.; Sun, H. HPLC-MS/MS determination of eight PPCPs in sewage and sludge from three types of sewage treatment plants. *Environ. Chem.* **2018**, *37*, 1720–1727. [[CrossRef](#)]
104. Chen, L.; Fu, W.; Tan, Y.; Zhang, X. Emerging Organic Contaminants and Odorous Compounds in Secondary Effluent Wastewater: Identification and Advanced Treatment. *J. Hazard. Mater.* **2021**, *408*, 124817. [[CrossRef](#)]
105. Li, Y.; Niu, X.; Yao, C.; Yang, W.; Lu, G. Distribution, Removal, and Risk Assessment of Pharmaceuticals and Their Metabolites in Five Sewage Plants. *Int. J. Environ. Res. Public Health* **2019**, *16*, 4729. [[CrossRef](#)]
106. Leung, H.W.; Minh, T.B.; Murphy, M.B.; Lam, J.C.W.; So, M.K.; Martin, M.; Lam, P.K.S.; Richardson, B.J. Distribution, Fate and Risk Assessment of Antibiotics in Sewage Treatment Plants in Hong Kong, South China. *Environ. Int.* **2012**, *42*, 1–9. [[CrossRef](#)] [[PubMed](#)]
107. Chunhui, Z.; Liangliang, W.; Xiangyu, G.; Xudan, H. Antibiotics in WWTP Discharge into the Chaobai River, Beijing. *Arch. Environ. Prot.* **2016**, *42*, 48–57. [[CrossRef](#)]
108. Wang, K.; Zhuang, T.; Su, Z.; Chi, M.; Wang, H. Antibiotic Residues in Wastewaters from Sewage Treatment Plants and Pharmaceutical Industries: Occurrence, Removal and Environmental Impacts. *Sci. Total Environ.* **2021**, *788*, 147811. [[CrossRef](#)] [[PubMed](#)]
109. Li, W.-L.; Zhang, Z.-F.; Ma, W.-L.; Liu, L.-Y.; Song, W.-W.; Li, Y.-F. An Evaluation on the Intra-Day Dynamics, Seasonal Variations and Removal of Selected Pharmaceuticals and Personal Care Products from Urban Wastewater Treatment Plants. *Sci. Total Environ.* **2018**, *640–641*, 1139–1147. [[CrossRef](#)] [[PubMed](#)]
110. Xu, E.G.B.; Liu, S.; Ying, G.-G.; Zheng, G.J.S.; Lee, J.H.W.; Leung, K.M.Y. The Occurrence and Ecological Risks of Endocrine Disrupting Chemicals in Sewage Effluents from Three Different Sewage Treatment Plants, and in Natural Seawater from a Marine Reserve of Hong Kong. *Mar. Pollut. Bull.* **2014**, *85*, 352–362. [[CrossRef](#)] [[PubMed](#)]
111. Liang, H.; Gong, J.; Zhou, K.; Deng, L.; Chen, J.; Guo, L.; Jiang, M.; Lin, J.; Tang, H.; Liu, X. Removal Efficiencies and Risk Assessment of Endocrine-Disrupting Chemicals at Two Wastewater Treatment Plants in South China. *Ecotoxicol. Environ. Saf.* **2021**, *225*, 112758. [[CrossRef](#)] [[PubMed](#)]
112. Wang, K.; Huang, Z.; Wang, Y.; Li, Z.; Ye, X.; Yang, S.; Huang, Z. Pollution characteristics and ecological risk assessment of typical EDCs and PPCPs in a municipal sewage treatment plant in Huizhou. *Water Wastewater* **2017**, *53*, 152–154. [[CrossRef](#)]
113. Zhou, Y.; Zha, J.; Xu, Y.; Lei, B.; Wang, Z. Occurrences of Six Steroid Estrogens from Different Effluents in Beijing, China. *Environ. Monit. Assess.* **2012**, *184*, 1719–1729. [[CrossRef](#)]

114. Xu, G.; Ma, S.; Tang, L.; Sun, R.; Xiang, J.; Xu, B.; Bao, Y.; Wu, M. Occurrence, Fate, and Risk Assessment of Selected Endocrine Disrupting Chemicals in Wastewater Treatment Plants and Receiving River of Shanghai, China. *Environ. Sci. Pollut. Res.* **2016**, *23*, 25442–25450. [[CrossRef](#)]
115. Xu, Y.; Xu, N.; Llewellyn, N.R.; Tao, H. Occurrence and Removal of Free and Conjugated Estrogens in Wastewater and Sludge in Five Sewage Treatment Plants. *Environ. Sci. Process. Impacts* **2014**, *16*, 262–270. [[CrossRef](#)]
116. Ashfaq, M.; Li, Y.; Wang, Y.; Qin, D.; Rehman, M.S.U.; Rashid, A.; Yu, C.-P.; Sun, Q. Monitoring and Mass Balance Analysis of Endocrine Disrupting Compounds and Their Transformation Products in an Anaerobic-Anoxic-Oxic Wastewater Treatment System in Xiamen, China. *Chemosphere* **2018**, *204*, 170–177. [[CrossRef](#)] [[PubMed](#)]
117. He, Y.; Chen, W.; Zheng, X.; Wang, X.; Huang, X. Fate and Removal of Typical Pharmaceuticals and Personal Care Products by Three Different Treatment Processes. *Sci. Total Environ.* **2013**, *447*, 248–254. [[CrossRef](#)] [[PubMed](#)]
118. Sun, Q.; Wang, Y.; Li, Y.; Ashfaq, M.; Dai, L.; Xie, X.; Yu, C.-P. Fate and Mass Balance of Bisphenol Analogues in Wastewater Treatment Plants in Xiamen City, China. *Environ. Pollut.* **2017**, *225*, 542–549. [[CrossRef](#)] [[PubMed](#)]
119. Wu, L.; Lu, C.; Huang, N.; Zhong, M.; Teng, Y.; Tian, Y.; Ye, K.; Liang, L.; Hu, Z. Exploration of the Effect of Simultaneous Removal of EDCs in the Treatment Process of Different Types of Wastewater. *Water Sci. Technol.* **2022**, *87*, 436–453. [[CrossRef](#)] [[PubMed](#)]
120. Yang, M.; Wang, K.; Shen, Y.; Wu, M. Evaluation of Estrogenic Activity in Surface Water and Municipal Wastewater in Shanghai, China. *Bull. Environ. Contam. Toxicol.* **2011**, *87*, 215–219. [[CrossRef](#)] [[PubMed](#)]
121. Xu, W.; Yan, W.; Huang, W.; Miao, L.; Zhong, L. Endocrine-Disrupting Chemicals in the Pearl River Delta and Coastal Environment: Sources, Transfer, and Implications. *Environ. Geochem. Health* **2014**, *36*, 1095–1104. [[CrossRef](#)] [[PubMed](#)]
122. Jiang, R.; Liu, J.; Huang, B.; Wang, X.; Luan, T.; Yuan, K. Assessment of the Potential Ecological Risk of Residual Endocrine-Disrupting Chemicals from Wastewater Treatment Plants. *Sci. Total Environ.* **2020**, *714*, 136689. [[CrossRef](#)]
123. Qiang, Z.; Dong, H.; Zhu, B.; Qu, J.; Nie, Y. A Comparison of Various Rural Wastewater Treatment Processes for the Removal of Endocrine-Disrupting Chemicals (EDCs). *Chemosphere* **2013**, *92*, 986–992. [[CrossRef](#)]
124. Triebeskorn, R.; Casper, H.; Scheil, V.; Schwaiger, J. Ultrastructural Effects of Pharmaceuticals (Carbamazepine, Clofibrate Acid, Metoprolol, Diclofenac) in Rainbow Trout (*Oncorhynchus mykiss*) and Common Carp (*Cyprinus carpio*). *Anal. Bioanal. Chem.* **2007**, *387*, 1405–1416. [[CrossRef](#)]
125. Zhu, B.; Liu, L.; Gong, Y.-X.; Ling, F.; Wang, G.-X. Triazole-Induced Toxicity in Developing Rare Minnow (*Gobiocypris rarus*) Embryos. *Environ. Sci. Pollut. Res. Int.* **2014**, *21*, 13625–13635. [[CrossRef](#)]
126. Guo, J.; Bai, Y.; Chen, Z.; Mo, J.; Li, Q.; Sun, H.; Zhang, Q. Transcriptomic Analysis Suggests the Inhibition of DNA Damage Repair in Green Alga Raphidocelis Subcapitata Exposed to Roxithromycin. *Ecotoxicol. Environ. Saf.* **2020**, *201*, 110737. [[CrossRef](#)]
127. Huggett, D.B.; Brooks, B.W.; Peterson, B.; Foran, C.M.; Schlenk, D. Toxicity of Select Beta Adrenergic Receptor-Blocking Pharmaceuticals (B-Blockers) on Aquatic Organisms. *Arch. Environ. Contam. Toxicol.* **2002**, *43*, 229–235. [[CrossRef](#)] [[PubMed](#)]
128. Baran, W.; Sochacka, J.; Wardas, W. Toxicity and Biodegradability of Sulfonamides and Products of Their Photocatalytic Degradation in Aqueous Solutions. *Chemosphere* **2006**, *65*, 1295–1299. [[CrossRef](#)] [[PubMed](#)]
129. Kwon, B.; Kho, Y.; Kim, P.-G.; Ji, K. Thyroid Endocrine Disruption in Male Zebrafish Following Exposure to Binary Mixture of Bisphenol AF and Sulfamethoxazole. *Environ. Toxicol. Pharmacol.* **2016**, *48*, 168–174. [[CrossRef](#)] [[PubMed](#)]
130. Owen, S.F.; Huggett, D.B.; Hutchinson, T.H.; Hetheridge, M.J.; McCormack, P.; Kinter, L.B.; Ericson, J.F.; Constantine, L.A.; Sumpter, J.P. The Value of Repeating Studies and Multiple Controls: Replicated 28-day Growth Studies of Rainbow Trout Exposed to Clofibrate Acid. *Enviro Toxic. Chem.* **2010**, *29*, 2831–2839. [[CrossRef](#)] [[PubMed](#)]
131. Lower, N. The Effects of Contaminants on Various Life-Cycle Stages of Atlantic Salmon (*Salmo salar* L.). Ph.D. Thesis, University of Portsmouth, Portsmouth, UK, 2008.
132. Ebringer, L.; Krajcovic, J.; Polónyi, J.; Lahitová, N.; Doušovcová, M.; Dobias, J. Tetracycline Reduces Fluoroquinolones-Induced Bleaching of Euglena Gracilis. *Mutat. Res.* **1996**, *340*, 141–149. [[CrossRef](#)]
133. Giusti, A.; Ducrot, V.; Joaquim-Justo, C.; Lagadic, L. Testosterone Levels and Fecundity in the Hermaphroditic Aquatic Snail *Lymnaea stagnalis* Exposed to Testosterone and Endocrine Disruptors. *Environ. Toxicol. Chem.* **2013**, *32*, 1740–1745. [[CrossRef](#)] [[PubMed](#)]
134. Wilkinson, R.E.; Duncan, R.R. Seashore Paspalum (*Paspalum vaginatum* Swartz) Seminal Root Response to Calcium (45 Ca²⁺) Absorption Modifiers. *J. Plant Nutr.* **1994**, *17*, 1385–1392. [[CrossRef](#)]
135. Zhang, X.; Hecker, M.; Tompsett, A.R.; Park, J.-W.; Jones, P.D.; Newsted, J.; Au, D.; Kong, R.; Wu, R.S.S.; Giesy, J.P. Responses of the Medaka HPG Axis PCR Array and Reproduction to Prochloraz and Ketoconazole. *Environ. Sci. Technol.* **2008**, *42*, 6762–6769. [[CrossRef](#)]
136. Ayanda, O.; Oniye, S.; Auta, J.; Ajibola, V.; Bello, O. Responses of the African Catfish Clarias Gariepinus to Long-Term Exposure to Glyphosate- and Paraquat-Based Herbicides. *Afr. J. Aquat. Sci.* **2015**, *40*, 261–267. [[CrossRef](#)]
137. Crago, J.; Klaper, R. Place-Based Screening of Mixtures of Dominant Emerging Contaminants Measured in Lake Michigan Using Zebrafish Embryo Gene Expression Assay. *Chemosphere* **2018**, *193*, 1226–1234. [[CrossRef](#)] [[PubMed](#)]
138. Diaz, L. Pharmaceuticals in the Environment: Sources, Fate, Effects and Risks. *Waste Manag.* **2003**, *23*, 193. [[CrossRef](#)]
139. Zhu, Y.; Yang, D.; Duan, X.; Zhang, Y.; Chen, D.; Gong, Z.; Liu, C. Perfluorooctane Sulfonate Promotes Doxycycline-Induced Liver Tumor Progression in Male KrasV12 Transgenic Zebrafish. *Environ. Res.* **2021**, *196*, 110962. [[CrossRef](#)] [[PubMed](#)]
140. Cunha, E.; Machado, J. Parturition in Anodonta Cygnea Induced by Selective Serotonin Reuptake Inhibitors (SSRIs). *Can. J. Zool.* **2011**, *79*, 95–100. [[CrossRef](#)]

141. Divo, A.A.; Geary, T.G.; Jensen, J.B. Oxygen- and Time-Dependent Effects of Antibiotics and Selected Mitochondrial Inhibitors on *Plasmodium Falciparum* in Culture. *Antimicrob. Agents Chemother.* **1985**, *27*, 21–27. [CrossRef] [PubMed]
142. Passarelli, F.; Merante, A.; Pontieri, F.E.; Margotta, V.; Venturini, G.; Palladini, G. Opioid-Dopamine Interaction in Planaria: A Behavioral Study. *Comp. Biochem. Physiol. C Pharmacol. Toxicol. Endocrinol.* **1999**, *124*, 51–55. [CrossRef] [PubMed]
143. Mennillo, E.; Pretti, C.; Cappelli, F.; Luci, G.; Intorre, L.; Meucci, V.; Arukwe, A. Novel Organ-Specific Effects of Ketoprofen and Its Enantiomer, Dexketoprofen on Toxicological Response Transcripts and Their Functional Products in Salmon. *Aquat. Toxicol.* **2020**, *229*, 105677. [CrossRef] [PubMed]
144. Bereketoglu, C.; Pradhan, A.; Olsson, P.-E. Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) Cause Male-Biased Sex Differentiation in Zebrafish. *Aquat. Toxicol.* **2020**, *223*, 105476. [CrossRef] [PubMed]
145. Lebreton, M.; Sire, S.; Carayon, J.-L.; Malgouyres, J.-M.; Vignet, C.; Géret, F.; Bonnafé, E. Low Concentrations of Oxazepam Induce Feeding and Molecular Changes in *Radix Balthica* Juveniles. *Aquat. Toxicol.* **2021**, *230*, 105694. [CrossRef]
146. Macphee, C.; Ruelle, R. Lethal Effects of 1888 Chemicals upon 4 Species of Fish from Western North America. Research technical Compelction Report, Project A-013-IDDA. Idaho Waters Digital Library, University of Idaho Library Digital Collections, 1969. Available online: <https://www.lib.uidaho.edu/digital/iwdl/items/iwdl-196913.html> (accessed on 15 June 2023).
147. Baldisserotto, B.; Brinn, R.P.; Brandão, F.R.; Gomes, L.C.; Abreu, J.S.; McComb, D.M.; Marcon, J.L. Ion Flux and Cortisol Responses of Cardinal Tetra, *Paracheirodon axelrodi* (Schultz, 1956), to Additives (Tetracycline, Tetracycline + Salt or Amquel®) Used during Transportation: Contributions to Amazonian Ornamental Fish Trade. *J. Appl. Ichthyol.* **2014**, *30*, 86–92. [CrossRef]
148. Gustafson, A.-L.; Stedman, D.B.; Ball, J.; Hillegass, J.M.; Flood, A.; Zhang, C.X.; Panzica-Kelly, J.; Cao, J.; Coburn, A.; Enright, B.P.; et al. Inter-Laboratory Assessment of a Harmonized Zebrafish Developmental Toxicology Assay—Progress Report on Phase I. *Reprod. Toxicol.* **2012**, *33*, 155–164. [CrossRef]
149. Yang, L.-H.; Ying, G.-G.; Su, H.-C.; Stauber, J.L.; Adams, M.S.; Binet, M.T. Growth-Inhibiting Effects of 12 Antibacterial Agents and Their Mixtures on the Freshwater Microalga *Pseudokirchneriella Subcapitata*. *Environ. Toxicol. Chem.* **2008**, *27*, 1201–1208. [CrossRef] [PubMed]
150. Bulut, C.; Kubilay, A.; Hanol Bektaş, Z.; Birden, B. Histopathological Effects of Formaldehyde (CH₂O) on Rainbow Trout (*Oncorhynchus mykiss* Walbaum, 1792). *J. Limnol. Freshw. Fish. Res.* **2015**, *1*, 43.
151. Park, K.; Kwak, I.-S. Gene Expression of Ribosomal Protein mRNA in *Chironomus riparius*: Effects of Endocrine Disruptor Chemicals and Antibiotics. *Comp. Biochem. Physiol. Part C Toxicol. Pharmacol.* **2012**, *156*, 113–120. [CrossRef] [PubMed]
152. Zhang, X.; Gong, Z. Fluorescent Transgenic Zebrafish Tg(Nkx2.2a:mEGFP) Provides a Highly Sensitive Monitoring Tool for Neurotoxins. *PLoS ONE* **2013**, *8*, e55474. [CrossRef] [PubMed]
153. Rocco, L.; Frenzilli, G.; Fusco, D.; Peluso, C.; Stingo, V. Evaluation of Zebrafish DNA Integrity after Exposure to Pharmacological Agents Present in Aquatic Environments. *Ecotoxicol. Environ. Saf.* **2010**, *73*, 1530–1536. [CrossRef] [PubMed]
154. Eguchi, K.; Nagase, H.; Ozawa, M.; Endoh, Y.S.; Goto, K.; Hirata, K.; Miyamoto, K.; Yoshimura, H. Evaluation of Antimicrobial Agents for Veterinary Use in the Ecotoxicity Test Using Microalgae. *Chemosphere* **2004**, *57*, 1733–1738. [CrossRef] [PubMed]
155. Han, S.; Choi, K.; Kim, J.; Ji, K.; Kim, S.; Ahn, B.; Yun, J.; Choi, K.; Khim, J.S.; Zhang, X.; et al. Endocrine Disruption and Consequences of Chronic Exposure to Ibuprofen in Japanese Medaka (*Oryzias latipes*) and Freshwater Cladocerans *Daphnia magna* and *Moina Macrocopa*. *Aquat. Toxicol.* **2010**, *98*, 256–264. [CrossRef]
156. Tojo, J.; Santamaría, M.; Ubeira, F.; Leiro, J. Efficacy of Antiprotozoal Drugs against Gyrodactylosis in Rainbow Trout (*Oncorhynchus mykiss*). *Bull. Eur. Assoc. Fish Pathol.* **1993**, *13*, 79–82.
157. Steinkey, D.; Lari, E.; Woodman, S.G.; Luong, K.H.; Wong, C.S.; Pyle, G.G. Effects of Gemfibrozil on the Growth, Reproduction, and Energy Stores of *Daphnia magna* in the Presence of Varying Food Concentrations. *Chemosphere* **2018**, *192*, 75–80. [CrossRef]
158. Oggier, D.M.; Weisbrod, C.J.; Stoller, A.M.; Zenker, A.K.; Fent, K. Effects of Diazepam on Gene Expression and Link to Physiological Effects in Different Life Stages in Zebrafish *Danio rerio*. *Environ. Sci. Technol.* **2010**, *44*, 7685–7691. [CrossRef] [PubMed]
159. Shi, H.; Sun, Z.; Liu, Z.; Xue, Y. Effects of Clotrimazole and Amiodarone on Early Development of Amphibian (*Xenopus tropicalis*). *Toxicol. Environ. Chem.* **2012**, *94*, 128–135. [CrossRef]
160. Nesbitt, R. Effects of Chronic Exposure to Ibuprofen and Naproxen on Florida Flagfish (*Jordanella floridae*) over One Complete Life-Cycle. Ph.D. Thesis, Ontario Tech University, Oshawa, ON, Canada, 2011.
161. Li, Y.; Ma, Y.; Yang, L.; Duan, S.; Zhou, F.; Chen, J.; Liu, Y.; Zhang, B. Effects of Azithromycin on Feeding Behavior and Nutrition Accumulation of *Daphnia magna* under the Different Exposure Pathways. *Ecotoxicol. Environ. Saf.* **2020**, *197*, 110573. [CrossRef]
162. Brain, R.A.; Johnson, D.J.; Richards, S.M.; Sanderson, H.; Sibley, P.K.; Solomon, K.R. Effects of 25 Pharmaceutical Compounds to *Lemna Gibba* Using a Seven-Day Static-Renewal Test. *Environ. Toxicol. Chem.* **2004**, *23*, 371–382. [CrossRef] [PubMed]
163. Nandurkar, H.P.; Zambare, S.P. Effect of Tetracycline and Chloramphenicol on Protein Contents in Different Tissues of Freshwater Bivalve, *Parreysia cylindrica* (Annandale & Prashad). *J. Am. Chem. Soc.* **2012**, *18*, 259–264. [CrossRef] [PubMed]
164. Reda, R.M.; Ibrahim, R.E.; Ahmed, E.-N.G.; El-Bouhy, Z.M. Effect of Oxytetracycline and Florfenicol as Growth Promoters on the Health Status of Cultured *Oreochromis niloticus*. *Egypt. J. Aquat. Res.* **2013**, *39*, 241–248. [CrossRef]
165. Han, G.H.; Hur, H.G.; Kim, S.D. Ecotoxicological Risk of Pharmaceuticals from Wastewater Treatment Plants in Korea: Occurrence and Toxicity to *Daphnia magna*. *Environ. Toxicol. Chem.* **2006**, *25*, 265–271. [CrossRef]
166. Biały-Bielńska, A.; Stolte, S.; Arning, J.; Uebers, U.; Böschen, A.; Stepnowski, P.; Matzke, M. Ecotoxicity Evaluation of Selected Sulfonamides. *Chemosphere* **2011**, *85*, 928–933. [CrossRef] [PubMed]

167. Overturf, M.D.; Overturf, C.L.; Baxter, D.; Hala, D.N.; Constantine, L.; Venables, B.; Huggett, D.B. Early Life-Stage Toxicity of Eight Pharmaceuticals to the Fathead Minnow, *Pimephales promelas*. *Arch. Environ. Contam. Toxicol.* **2012**, *62*, 455–464. [CrossRef]
168. Pascoe, D.; Karntanut, W.; Müller, C.T. Do Pharmaceuticals Affect Freshwater Invertebrates? A Study with the Cnidarian *Hydra vulgaris*. *Chemosphere* **2003**, *51*, 521–528. [CrossRef]
169. Parolini, M.; Quinn, B.; Binelli, A.; Provini, A. Cytotoxicity Assessment of Four Pharmaceutical Compounds on the Zebra Mussel (*Dreissena polymorpha*) Haemocytes, Gill and Digestive Gland Primary Cell Cultures. *Chemosphere* **2011**, *84*, 91–100. [CrossRef]
170. Schoenfuss, H.L.; Furlong, E.T.; Phillips, P.J.; Scott, T.-M.; Kolpin, D.W.; Cetkovic-Cvrlje, M.; Lesteberg, K.E.; Rearick, D.C. Complex Mixtures, Complex Responses: Assessing Pharmaceutical Mixtures Using Field and Laboratory Approaches. *Environ. Toxicol. Chem.* **2016**, *35*, 953–965. [CrossRef]
171. Zounková, R.; Klimešová, Z.; Nepejchalová, L.; Hilscherová, K.; Bláha, L. Complex Evaluation of Ecotoxicity and Genotoxicity of Antimicrobials Oxytetracycline and Flumequine Used in Aquaculture. *Environ. Toxicol. Chem.* **2011**, *30*, 1184–1189. [CrossRef]
172. Calleja, M.C.; Persoone, G.; Geladi, P. Comparative Acute Toxicity of the First 50 Multicentre Evaluation of In Vitro Cytotoxicity Chemicals to Aquatic Non-Vertebrates. *Arch. Environ. Contam. Toxicol.* **1994**, *26*, 69–78. [CrossRef]
173. Galus, M.; Kirischian, N.; Higgins, S.; Purdy, J.; Chow, J.; Rangaranjan, S.; Li, H.; Metcalfe, C.; Wilson, J.Y. Chronic, Low Concentration Exposure to Pharmaceuticals Impacts Multiple Organ Systems in Zebrafish. *Aquat. Toxicol.* **2013**, *132–133*, 200–211. [CrossRef]
174. Parolini, M.; Pedriali, A.; Binelli, A. Application of a Biomarker Response Index for Ranking the Toxicity of Five Pharmaceutical and Personal Care Products (PPCPs) to the Bivalve *Dreissena polymorpha*. *Arch. Environ. Contam. Toxicol.* **2013**, *64*, 439–447. [CrossRef]
175. Lister, A.L.; Van Der Kraak, G. An Investigation into the Role of Prostaglandins in Zebrafish Oocyte Maturation and Ovulation. *Gen. Comp. Endocrinol.* **2008**, *159*, 46–57. [CrossRef] [PubMed]
176. Quinn, B.; Gagné, F.; Blaise, C. An Investigation into the Acute and Chronic Toxicity of Eleven Pharmaceuticals (and Their Solvents) Found in Wastewater Effluent on the Cnidarian, *Hydra Attenuata*. *Sci. Total Environ.* **2008**, *389*, 306–314. [CrossRef] [PubMed]
177. Lützhøft, H.H.; Halling-Sørensen, B.; Jørgensen, S.E. Algal Toxicity of Antibacterial Agents Applied in Danish Fish Farming. *Arch. Environ. Contam. Toxicol.* **1999**, *36*, 1–6. [CrossRef]
178. Nunes, B.; Antunes, S.C.; Gomes, R.; Campos, J.C.; Braga, M.R.; Ramos, A.S.; Correia, A.T. Acute Effects of Tetracycline Exposure in the Freshwater Fish Gambusia Holbrookii: Antioxidant Effects, Neurotoxicity and Histological Alterations. *Arch. Environ. Contam. Toxicol.* **2015**, *68*, 371–381. [CrossRef]
179. Wollenberger, L.; Halling-Sørensen, B.; Kusk, K.O. Acute and Chronic Toxicity of Veterinary Antibiotics to *Daphnia magna*. *Chemosphere* **2000**, *40*, 723–730. [CrossRef] [PubMed]
180. Pruvot, B.; Quiroz, Y.; Voncken, A.; Jeanray, N.; Piot, A.; Martial, J.A.; Muller, M. A Panel of Biological Tests Reveals Developmental Effects of Pharmaceutical Pollutants on Late Stage Zebrafish Embryos. *Reprod. Toxicol.* **2012**, *34*, 568–583. [CrossRef] [PubMed]
181. Ando, T.; Nagase, H.; Eguchi, K.; Hirooka, T.; Nakamura, T.; Miyamoto, K.; Hirata, K. A Novel Method Using Cyanobacteria for Ecotoxicity Test of Veterinary Antimicrobial Agents. *Environ. Toxicol. Chem.* **2007**, *26*, 601–606. [CrossRef] [PubMed]
182. Selcer, K.W.; Verbanic, J.D. Vitellogenin of the Northern Leopard Frog (*Rana pipiens*): Development of an ELISA Assay and Evaluation of Induction after Immersion in Xenobiotic Estrogens. *Chemosphere* **2014**, *112*, 348–354. [CrossRef] [PubMed]
183. Liang, Y.-Q.; Xu, W.; Liang, X.; Jing, Z.; Pan, C.-G.; Tian, F. The Synthetic Progestin Norethindrone Causes Thyroid Endocrine Disruption in Adult Zebrafish. *Comp. Biochem. Physiol. Part C Toxicol. Pharmacol.* **2020**, *236*, 108819. [CrossRef] [PubMed]
184. Lee, W.; Kang, C.-W.; Su, C.-K.; Okubo, K.; Nagahama, Y. Screening Estrogenic Activity of Environmental Contaminants and Water Samples Using a Transgenic Medaka Embryo Bioassay. *Chemosphere* **2012**, *88*, 945–952. [CrossRef] [PubMed]
185. Thorpe, K.L.; Cummings, R.I.; Hutchinson, T.H.; Scholze, M.; Brighty, G.; Sumpter, J.P.; Tyler, C.R. Relative Potencies and Combination Effects of Steroidal Estrogens in Fish. *Environ. Sci. Technol.* **2003**, *37*, 1142–1149. [CrossRef] [PubMed]
186. Lei, B.; Kang, J.; Yu, Y.; Zha, J.; Li, W.; Wang, Z.; Wang, Y.; Wen, Y. Long-Term Exposure Investigating the Estrogenic Potency of Estriol in Japanese Medaka (*Oryzias latipes*). *Comp. Biochem. Physiol. Part C Toxicol. Pharmacol.* **2014**, *160*, 86–92. [CrossRef] [PubMed]
187. EG and G BIONOMICS. Initial Submission: The Chronic Toxicity of s-900d to the Water Flea (Daphnia Magna) with Cover Letter Dated 081492, USEPA: Health and Environmental Research on Line. 1992. Available online: https://hero.epa.gov/hero/index.cfm/reference/details/reference_id/1325554 (accessed on 15 June 2023).
188. Zhang, X.; Xiong, L.; Liu, Y.; Deng, C.; Mao, S. Histopathological and Estrogen Effect of Pentachlorophenol on the Rare Minnow (*Gobiocypris rarus*). *Fish. Physiol. Biochem.* **2014**, *40*, 805–816. [CrossRef]
189. Kazeto, Y.; Place, A.R.; Trant, J.M. Effects of Endocrine Disrupting Chemicals on the Expression of CYP19 Genes in Zebrafish (*Danio rerio*) Juveniles. *Aquat. Toxicol.* **2004**, *69*, 25–34. [CrossRef]
190. Villeneuve, D.L.; Garcia-Reyero, N.; Escalon, B.L.; Jensen, K.M.; Cavallin, J.E.; Makynen, E.A.; Durhan, E.J.; Kahl, M.D.; Thomas, L.M.; Perkins, E.J.; et al. Ecotoxicogenomics to Support Ecological Risk Assessment: A Case Study with Bisphenol A in Fish. *Environ. Sci. Technol.* **2012**, *46*, 51–59. [CrossRef]
191. Gagnaire, B.; Gagné, F.; André, C.; Blaise, C.; Abbaci, K.; Budzinski, H.; Dévier, M.-H.; Garric, J. Development of Biomarkers of Stress Related to Endocrine Disruption in Gastropods: Alkali-Labile Phosphates, Protein-Bound Lipids and Vitellogenin-like Proteins. *Aquat. Toxicol.* **2009**, *92*, 155–167. [CrossRef]

192. Bean, R.M.; Gibson, C.I.; Anderson, D.R. *Biocide By-Products in Aquatic Environments*; Pacific Northwest National Lab.: Richland, WA, USA, 1981. [CrossRef]
193. Croteau, M.C.; Davidson, M.; Duarte-Guterman, P.; Wade, M.; Popesku, J.T.; Wiens, S.; Lean, D.R.S.; Trudeau, V.L. Assessment of Thyroid System Disruption in *Rana pipiens* Tadpoles Chronically Exposed to UVB Radiation and 4-Tert-Octylphenol. *Aquat. Toxicol.* **2009**, *95*, 81–92. [CrossRef]
194. Jarvis, A.L.; Bernot, M.J.; Bernot, R.J. The Effects of the Psychiatric Drug Carbamazepine on Freshwater Invertebrate Communities and Ecosystem Dynamics. *Sci. Total Environ.* **2014**, *496*, 461–470. [CrossRef] [PubMed]
195. Melvin, S.D.; Cameron, M.C.; Lanctôt, C.M. Individual and Mixture Toxicity of Pharmaceuticals Naproxen, Carbamazepine, and Sulfamethoxazole to Australian Striped Marsh Frog Tadpoles (*Limnodynastes peronii*). *J. Toxicol. Environ. Health A* **2014**, *77*, 337–345. [CrossRef] [PubMed]
196. Li, Z.-H.; Velisek, J.; Zlabek, V.; Grabic, R.; Machova, J.; Kolarova, J.; Randak, T. Hepatic Antioxidant Status and Hematological Parameters in Rainbow Trout, *Oncorhynchus mykiss*, after Chronic Exposure to Carbamazepine. *Chem. Biol. Interact.* **2010**, *183*, 98–104. [CrossRef] [PubMed]
197. Fraz, S.; Lee, A.H.; Wilson, J.Y. Gemfibrozil and Carbamazepine Decrease Steroid Production in Zebrafish Testes (*Danio rerio*). *Aquat. Toxicol.* **2018**, *198*, 1–9. [CrossRef]
198. Dordio, A.V.; Belo, M.; Martins Teixeira, D.; Palace Carvalho, A.J.; Dias, C.M.B.; Picó, Y.; Pinto, A.P. Evaluation of Carbamazepine Uptake and Metabolization by *Typha* Spp., a Plant with Potential Use in Phytotreatment. *Bioresour. Technol.* **2011**, *102*, 7827–7834. [CrossRef] [PubMed]
199. Chen, H.; Zha, J.; Liang, X.; Li, J.; Wang, Z. Effects of the Human Antiepileptic Drug Carbamazepine on the Behavior, Biomarkers, and Heat Shock Proteins in the Asian Clam *Corbicula fluminea*. *Aquat. Toxicol.* **2014**, *155*, 1–8. [CrossRef]
200. Oetken, M.; Nentwig, G.; Löffler, D.; Ternes, T.; Oehlmann, J. Effects of Pharmaceuticals on Aquatic Invertebrates. Part I. The Antiepileptic Drug Carbamazepine. *Arch. Environ. Contam. Toxicol.* **2005**, *49*, 353–361. [CrossRef]
201. Zhang, W.; Zhang, M.; Lin, K.; Sun, W.; Xiong, B.; Guo, M.; Cui, X.; Fu, R. Eco-Toxicological Effect of Carbamazepine on *Scenedesmus obliquus* and *Chlorella pyrenoidosa*. *Environ. Toxicol. Pharmacol.* **2012**, *33*, 344–352. [CrossRef] [PubMed]
202. Lamichhane, K.; Garcia, S.N.; Huggett, D.B.; DeAngelis, D.L.; La Point, T.W. Chronic Effects of Carbamazepine on Life-History Strategies of *Ceriodaphnia dubia* in Three Successive Generations. *Arch. Environ. Contam. Toxicol.* **2013**, *64*, 427–438. [CrossRef] [PubMed]
203. Yan, S.; Chen, R.; Wang, M.; Zha, J. Carbamazepine at Environmentally Relevant Concentrations Caused DNA Damage and Apoptosis in the Liver of Chinese Rare Minnows (*Gobiocypris rarus*) by the Ras/Raf/ERK/P53 Signaling Pathway. *Environ. Pollut.* **2021**, *270*, 116245. [CrossRef]
204. Gust, M.; Gagné, F.; Berlioz-Barbier, A.; Besse, J.P.; Buronfosse, T.; Tournier, M.; Tutundjian, R.; Garric, J.; Cren-Olivé, C. Caged Mudsnail *Potamopyrgus antipodarum* (Gray) as an Integrated Field Biomonitoring Tool: Exposure Assessment and Reprotoxic Effects of Water Column Contamination. *Water Res.* **2014**, *54*, 222–236. [CrossRef]
205. Weigt, S.; Huebler, N.; Strecker, R.; Braunbeck, T.; Broschard, T.H. Zebrafish (*Danio rerio*) Embryos as a Model for Testing Proteratogens. *Toxicology* **2011**, *281*, 25–36. [CrossRef]
206. DeLorenzo, M.E.; Fleming, J. Individual and Mixture Effects of Selected Pharmaceuticals and Personal Care Products on the Marine Phytoplankton Species *Dunaliella tertiolecta*. *Arch. Environ. Contam. Toxicol.* **2008**, *54*, 203–210. [CrossRef] [PubMed]
207. Jos, A.; Repetto, G.; Rios, J.C.; Hazen, M.J.; Molero, M.L.; del Peso, A.; Salguero, M.; Fernández-Freire, P.; Pérez-Martín, J.M.; Cameán, A. Ecotoxicological Evaluation of Carbamazepine Using Six Different Model Systems with Eighteen Endpoints. *Toxicol. Vitr.* **2003**, *17*, 525–532. [CrossRef] [PubMed]
208. Kim, Y.; Choi, K.; Jung, J.; Park, S.; Kim, P.-G.; Park, J. Aquatic Toxicity of Acetaminophen, Carbamazepine, Cimetidine, Diltiazem and Six Major Sulfonamides, and Their Potential Ecological Risks in Korea. *Environ. Int.* **2007**, *33*, 370–375. [CrossRef]
209. Cleuvers, M. Aquatic Ecotoxicity of Pharmaceuticals Including the Assessment of Combination Effects. *Toxicol. Lett.* **2003**, *142*, 185–194. [CrossRef]
210. Li, Z.-H.; Zlabek, V.; Velisek, J.; Grabic, R.; Machova, J.; Kolarova, J.; Li, P.; Randak, T. Acute Toxicity of Carbamazepine to Juvenile Rainbow Trout (*Oncorhynchus mykiss*): Effects on Antioxidant Responses, Hematological Parameters and Hepatic EROD. *Ecotoxicol. Environ. Saf.* **2011**, *74*, 319–327. [CrossRef]
211. Richards, S.M.; Cole, S.E. A Toxicity and Hazard Assessment of Fourteen Pharmaceuticals to *Xenopus laevis* Larvae. *Ecotoxicology* **2006**, *15*, 647–656. [CrossRef] [PubMed]
212. Kaza, M.; Nałacz-Jawecki, G.; Sawicki, J. The Toxicity of Selected Pharmaceuticals to the Aquatic Plant *Lemna minor*. *Fresenius Environ. Bull.* **2007**, *16*, 524–531.
213. Dordio, A.; Ferro, R.; Teixeira, D.; Palace, A.J.; Pinto, A.P.; Dias, C.M.B. Study on the Use of *Typha* Spp. for the Phytotreatment of Water Contaminated with Ibuprofen. *Int. J. Environ. Anal. Chem.* **2011**, *91*, 654–667. [CrossRef]
214. Saravanan, M.; Devi, K.U.; Malarvizhi, A.; Ramesh, M. Effects of Ibuprofen on Hematological, Biochemical and Enzymological Parameters of Blood in an Indian Major Carp, *Cirrhinus mrigala*. *Environ. Toxicol. Pharmacol.* **2012**, *34*, 14–22. [CrossRef] [PubMed]
215. Ceballos-Laita, L.; Calvo, L.; Bes, M.; Fillat, M.; Peleato, M. Effects of Benzene and Several Pharmaceuticals on the Growth and Microcystin Production in *Microcystis aeruginosa* PCC 7806. *Limnetica* **2015**, *34*, 237–246. [CrossRef]
216. Flippin, J.L.; Huggett, D.; Foran, C.M. Changes in the Timing of Reproduction Following Chronic Exposure to Ibuprofen in Japanese Medaka, *Oryzias latipes*. *Aquat. Toxicol.* **2007**, *81*, 73–78. [CrossRef] [PubMed]

217. Pounds, N.; Maclean, S.; Webley, M.; Pascoe, D.; Hutchinson, T. Acute and Chronic Effects of Ibuprofen in the Mollusc *Planorbis carinatus* (*Gastropoda: Planorbidae*). *Ecotoxicol. Environ. Saf.* **2008**, *70*, 47–52. [[CrossRef](#)]
218. Kim, J.-W.; Ishibashi, H.; Yamauchi, R.; Ichikawa, N.; Takao, Y.; Hirano, M.; Koga, M.; Arizono, K. Acute Toxicity of Pharmaceutical and Personal Care Products on Freshwater Crustacean (*Thamnocephalus platyurus*) and Fish (*Oryzias latipes*). *J. Toxicol. Sci.* **2009**, *34*, 227–232. [[CrossRef](#)]
219. Li, M.-H. Acute Toxicity of 30 Pharmaceutically Active Compounds to Freshwater Planarians, *Dugesia japonica*. *Toxicol. Environ. Chem.* **2013**, *95*, 1157–1170. [[CrossRef](#)]
220. Lv, X.; Zhou, Q.; Song, M.; Jiang, G.; Shao, J. Vitellogenesis Responses of 17 β -Estradiol and Bisphenol A in Male Chinese Loach (*Misgurnus anguillicaudatus*). *Environ. Toxicol. Pharmacol.* **2007**, *24*, 155–159. [[CrossRef](#)]
221. Qiu, W.; Shen, Y.; Pan, C.; Liu, S.; Wu, M.; Yang, M.; Wang, K.-J. The Potential Immune Modulatory Effect of Chronic Bisphenol A Exposure on Gene Regulation in Male Medaka (*Oryzias latipes*) Liver. *Ecotoxicol. Environ. Saf.* **2016**, *130*, 146–154. [[CrossRef](#)] [[PubMed](#)]
222. Haubruege, E.; Petit, F.; Gage, M.J. Reduced Sperm Counts in Guppies (*Poecilia reticulata*) Following Exposure to Low Levels of Tributyltin and Bisphenol A. *Proc. Biol. Sci.* **2000**, *267*, 2333–2337. [[CrossRef](#)] [[PubMed](#)]
223. Hatef, A.; Zare, A.; Alavi, S.M.H.; Habibi, H.R.; Linhart, O. Modulations in Androgen and Estrogen Mediating Genes and Testicular Response in Male Goldfish Exposed to Bisphenol A. *Environ. Toxicol. Chem.* **2012**, *31*, 2069–2077. [[CrossRef](#)] [[PubMed](#)]
224. Keiter, S.; Baumann, L.; Färber, H.; Holbech, H.; Skutlarek, D.; Engwall, M.; Braunbeck, T. Long-Term Effects of a Binary Mixture of Perfluorooctane Sulfonate (PFOS) and Bisphenol A (BPA) in Zebrafish (*Danio rerio*). *Aquat. Toxicol.* **2012**, *118–119*, 116–129. [[CrossRef](#)] [[PubMed](#)]
225. Mochida, K.; Fujii, K.; Kakuno, A.; Matsubara, T.; Ohkubo, N.; Adachi, S.; Yamauchi, K. Expression of Ubiquitin C-Terminal Hydrolase Is Regulated by Estradiol-17 β in Testis and Brain of the Japanese Common Goby. *Fish. Physiol. Biochem.* **2003**, *28*, 435–436. [[CrossRef](#)]
226. Yang, F.-X.; Xu, Y.; Wen, S. Endocrine-Disrupting Effects of Nonylphenol, Bisphenol A, and p,p'-DDE on Rana Nigromaculata Tadpoles. *Bull. Environ. Contam. Toxicol.* **2005**, *75*, 1168–1175. [[CrossRef](#)]
227. Ha, M.-H.; Choi, J. Effects of Environmental Contaminants on Hemoglobin Gene Expression in *Daphnia magna*: A Potential Biomarker for Freshwater Quality Monitoring. *Arch. Environ. Contam. Toxicol.* **2009**, *57*, 330–337. [[CrossRef](#)] [[PubMed](#)]
228. Ladewig, V.; Jungmann, D.; Köhler, H.-R.; Licht, O.; Ludwichowski, K.-U.; Schirling, M.; Triebeskorn, R.; Nagel, R. Effects of Bisphenol A on Gammarus Fossarum and Lumbriculus Variegatus in Artificial Indoor Streams. *Toxicol. Environ. Chem.* **2006**, *88*, 649–664. [[CrossRef](#)]
229. Lahnsteiner, F.; Berger, B.; Kletzl, M.; Weismann, T. Effect of Bisphenol A on Maturation and Quality of Semen and Eggs in the Brown Trout, *Salmo trutta f. fario*. *Aquat. Toxicol.* **2005**, *75*, 213–224. [[CrossRef](#)] [[PubMed](#)]
230. Staples, C.A.; Tilghman Hall, A.; Friederich, U.; Caspers, N.; Klecka, G.M. Early Life-Stage and Multigeneration Toxicity Study with Bisphenol A and Fathead Minnows (*Pimephales promelas*). *Ecotoxicol. Environ. Saf.* **2011**, *74*, 1548–1557. [[CrossRef](#)]
231. Van den Belt, K.; Verheyen, R.; Witters, H. Comparison of Vitellogenesis Responses in Zebrafish and Rainbow Trout Following Exposure to Environmental Estrogens. *Ecotoxicol. Environ. Saf.* **2003**, *56*, 271–281. [[CrossRef](#)] [[PubMed](#)]
232. Jung, J.-W.; Kang, J.-S.; Choi, J.; Park, J.-W. Chronic Toxicity of Endocrine Disrupting Chemicals Used in Plastic Products in Korean Resident Species: Implications for Aquatic Ecological Risk Assessment. *Ecotoxicol. Environ. Saf.* **2020**, *192*, 110309. [[CrossRef](#)] [[PubMed](#)]
233. Zhu, L.; Yuan, C.; Wang, M.; Liu, Y.; Wang, Z.; Seif, M.M. Bisphenol A-Associated Alterations in DNA and Histone Methylation Affects Semen Quality in Rare Minnow *Gobiocypris rarus*. *Aquat. Toxicol.* **2020**, *226*, 105580. [[CrossRef](#)] [[PubMed](#)]
234. Plahuta, M.; Tišler, T.; Pintar, A.; Toman, M.J. Adverse Effects of Bisphenol A on Water Louse (*Asellus aquaticus*). *Ecotoxicol. Environ. Saf.* **2015**, *117*, 81–88. [[CrossRef](#)] [[PubMed](#)]
235. Mihaich, E.M.; Friederich, U.; Caspers, N.; Hall, A.T.; Klecka, G.M.; Dimond, S.S.; Staples, C.A.; Ortego, L.S.; Hentges, S.G. Acute and Chronic Toxicity Testing of Bisphenol A with Aquatic Invertebrates and Plants. *Ecotoxicol. Environ. Saf.* **2009**, *72*, 1392–1399. [[CrossRef](#)] [[PubMed](#)]
236. Zhang, W.; Xiong, B.; Sun, W.-F.; An, S.; Lin, K.-F.; Guo, M.-J.; Cui, X.-H. Acute and Chronic Toxic Effects of Bisphenol A on *Chlorella pyrenoidosa* and *Scenedesmus obliquus*. *Environ. Toxicol.* **2014**, *29*, 714–722. [[CrossRef](#)] [[PubMed](#)]
237. Ozmen, M.; Güngördu, A.; Erdemoglu, S.; Ozmen, N.; Asilturk, M. Toxicological Aspects of Photocatalytic Degradation of Selected Xenobiotics with Nano-Sized Mn-Doped TiO₂. *Aquat. Toxicol.* **2015**, *165*, 144–153. [[CrossRef](#)] [[PubMed](#)]
238. Watts, M.M.; Pascoe, D.; Carroll, K. Survival and Precopulatory Behaviour of *Gammarus pulex* (L.). Exposed to Two Xenoestrogens. *Water Res.* **2001**, *35*, 2347–2352. [[CrossRef](#)] [[PubMed](#)]
239. Wolkowicz, I.R.H.; Herkovits, J.; Pérez Coll, C.S. Stage-Dependent Toxicity of Bisphenol a on *Rhinella arenarum* (Anura, Bufonidae) Embryos and Larvae. *Environ. Toxicol.* **2014**, *29*, 146–154. [[CrossRef](#)]
240. Kashiwada, S.; Ishikawa, H.; Miyamoto, N.; Ohnishi, Y.; Magara, Y. Fish Test for Endocrine-Disruption and Estimation of Water Quality of Japanese Rivers. *Water Res.* **2002**, *36*, 2161–2166. [[CrossRef](#)]
241. Debenest, T.; Gagné, F.; Petit, A.-N.; André, C.; Kohli, M.; Blaise, C. Ecotoxicity of a Brominated Flame Retardant (Tetrabromo-bisphenol A) and Its Derivatives to Aquatic Organisms. *Comp. Biochem. Physiol. Part C Toxicol. Pharmacol.* **2010**, *152*, 407–412. [[CrossRef](#)] [[PubMed](#)]
242. Chan, W.K.; Chan, K.M. Disruption of the Hypothalamic-Pituitary-Thyroid Axis in Zebrafish Embryo-Larvae Following Water-borne Exposure to BDE-47, TBBPA and BPA. *Aquat. Toxicol.* **2012**, *108*, 106–111. [[CrossRef](#)] [[PubMed](#)]

243. Alexander, H.C.; Dill, D.C.; Smith, L.W.; Guiney, P.D.; Dorn, P. Bisphenol a: Acute Aquatic Toxicity. *Environ. Toxicol. Chem.* **1988**, *7*, 19–26. [[CrossRef](#)]
244. Jemec, A.; Tišler, T.; Erjavec, B.; Pintar, A. Antioxidant Responses and Whole-Organism Changes in *Daphnia magna* Acutely and Chronically Exposed to Endocrine Disruptor Bisphenol A. *Ecotoxicol. Environ. Saf.* **2012**, *86*, 213–218. [[CrossRef](#)] [[PubMed](#)]

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.