

Which Micropollutants in Water Environments Deserve More Attention Globally?

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Cite This: *Environ. Sci. Technol.* 2022, 56, 13–29



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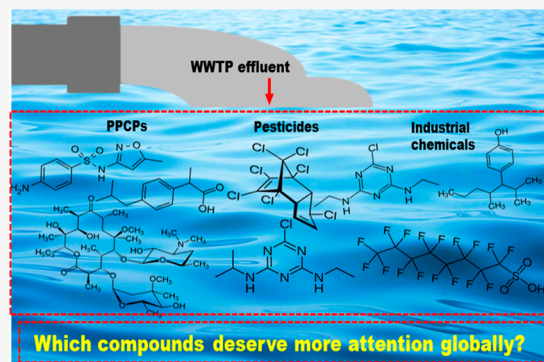
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ABSTRACT: Increasing chemical pollution of aquatic environments is a growing concern with global relevance. A large number of organic chemicals are termed as “micropollutants” due to their low concentrations, and long-term exposure to micropollutants may pose considerable risks to aquatic organisms and human health. In recent decades, numerous treatment methods and technologies have been proposed to remove micropollutants in water, and typically several micropollutants were chosen as target pollutants to evaluate removal efficiencies. However, it is often unclear whether their toxicity and occurrence levels and frequencies enable them to contribute significantly to the overall chemical pollution in global aquatic environments. This review intends to answer an important lingering question: Which micropollutants or class of micropollutants deserve more attention globally and should be removed with higher priority? Different risk-based prioritization approaches were used to address this question. The risk quotient (RQ) method was found to be a feasible approach to prioritize micropollutants in a large scale due to its relatively simple assessment procedure and extensive use. A total of 83 prioritization case studies using the RQ method in the past decade were compiled, and 473 compounds that were selected by screening 3466 compounds of three broad classes (pharmaceuticals and personal care products (PPCPs), pesticides, and industrial chemicals) were found to have risks ($RQ > 0.01$). To determine the micropollutants of global importance, we propose an overall risk surrogate, that is, the weighted average risk quotient (WARQ). The WARQ integrates the risk intensity and frequency of micropollutants in global aquatic environments to achieve a more comprehensive priority determination. Through metadata analysis, we recommend a ranked list of 53 micropollutants, including 36 PPCPs (e.g., sulfamethoxazole and ibuprofen), seven pesticides (e.g., heptachlor and diazinon), and 10 industrial chemicals (e.g., perfluorooctanesulfonic acid and 4-nonylphenol) for risk management and remediation efforts. One caveat is that the ranked list of global importance does not consider transformation products of micropollutants (including disinfection byproducts) and new forms of pollutants (including antibiotic resistance genes and microplastics), and this list of global importance may not be directly applicable to a specific region or country. Also, it needs mentioning that there might be no best answer toward this question, and hopefully this review can act as a small step toward a better answer.

KEYWORDS: micropollutants, risk assessment, prioritization, risk quotient, PPCPs



1. INTRODUCTION

Recent decades have witnessed the substantially increased production of anthropogenic chemicals. Currently, there are more than 350 000 chemicals and mixture of chemicals registered for production and use.¹ The size of the global chemical industry exceeded five trillion dollars in 2017 and is expected to double by 2030 according to the *Global Chemicals Outlook 2020 Report* by the United Nations Environment Programme.² The production and application of these chemicals result in their accidental and incidental releases into wastewater. Because current wastewater treatment processes usually have limited removal efficiencies for these chemicals,^{3,4} a portion or all of them end up in the treated effluent that is discharged into various receiving water bodies, including surface water,⁵

groundwater,⁶ and marine water.⁷ Legacy contaminants, like pesticides and polychlorinated biphenyls (PCBs), are still of concern.^{8,9} With the advancement of sampling strategies and analytical techniques in recent decades, a broad spectrum of emerging contaminants have also been detected in aquatic environments.^{10,11} The typical concentrations of these contaminants in water bodies lie in nanograms to micrograms per

Received: June 26, 2021

Revised: November 18, 2021

Accepted: December 1, 2021

Published: December 21, 2021



liter (ng/L to $\mu\text{g/L}$), and thus they are also termed as “micropollutants”. Despite their low concentrations, some micropollutants are of concern to aquatic organisms and human health.^{12,13} This is primarily attributed to the lifelong and even multigenerational exposure to micropollutants, which are usually continually produced and discharged into aquatic ecosystems. For example, triclosan, an antibacterial agent, is highly toxic to many aquatic organisms, with the lowest median effective concentration (EC_{50}) being $3.55 \mu\text{g/L}$ based on the growth inhibition to the marine phytoplankton *Dunaliella tertiolecta*.¹⁴

To control the chemical pollution, many efforts have been made to develop effective methods or technologies to remove micropollutants, such as advanced oxidation processes, biodegradation, and activated carbon adsorption.^{15–19} Typically, several micropollutants were selected for testing the removal efficiencies, which often included additional investigations such as kinetic studies, optimization of removal conditions, removal mechanism analysis, or product analysis. However, almost no study paid sufficient attention to demonstrating the rationale toward the selection of micropollutants. Many compounds can be stated to be environmentally worrisome by highlighting their toxicity, but whether their occurrence levels and distribution in global aquatic environments enable them to pose significant risks is an issue that has yet to be well addressed. In fact, it is also a prerequisite issue prior to better control of the micropollutant pollution, that is, which micropollutants or class of micropollutants deserve more attention globally and should be removed with higher priority. After all, it is impractical to equally investigate all worrisome micropollutants in aquatic environments.²⁰ Notably, although there are thousands of major micropollutants in water systems, the overall risk is usually governed by a few compounds according to the Pareto principle (i.e., 80% of the effects come from 20% of the causes).²¹

Some micropollutant prioritization methods have been proposed in the past decades. Occurrence-based approaches like chemical annual production and critical environmental concentration were reported in early studies,²² which assumed that chemicals with higher occurrence levels had higher priority for research investigation. These methods were likely to neglect some important chemicals that could cause adverse effects even at low occurrence levels. Risk-based prioritization methods that took both occurrence and hazard estimation of micropollutants into consideration were subsequently developed, like fish plasma model, risk quotient (RQ), and effect-directed analysis (EDA).²³ The U.S. Environmental Protection Agency (EPA) has also published four Contaminant Candidate Lists in drinking water since 1998 according to the contaminant’s potential for public health risk. These approaches assumed that research studies should narrow the chemical universe to the chemicals with higher risks, and risk levels could be quantified using different risk surrogates to facilitate comparison among different chemicals. Risk-based methods have been widely used in the past decades; however, the conclusions or proposed compounds with higher priority are sometimes different.²⁴ For example, the prioritized pollutants in three different countries (UK, USA, and China) somewhat varied according to the results of three individual studies.^{25–27} This indicates that chemical pollution is a large-scale environmental problem,²⁸ and the occurrence and risk levels of micropollutants could vary in different areas due to different production and use patterns.²⁹ The diversity of the existing prioritization results outlines a complex scenario that fosters the need to consider both the intensity of risk (i.e., the

magnitude of the risk level) and the spatial distribution of risk, in order to achieve a more general ranking list in global aquatic environments. Unfortunately, to our knowledge, few studies provided such prioritization results by simultaneously considering the intensity and frequency of risk on a large spatial scale.

Based on the foregoing information, this review highlights the necessity of micropollutant prioritization to identify top concerns with global environmental relevance. The selection of the target micropollutants should be based on their high-risk levels from a well-rounded evaluation framework so that resources can be allocated more efficiently in efforts to inform regulations and evaluate newly proposed control technologies. We first provide an overview of the methodology for prioritization and a detailed introduction of the RQ method. We then summarize the occurrence and hazard parameters of commonly detected micropollutants and propose a more comprehensive risk surrogate—the weighted average risk quotient (WARQ)—for prioritizing micropollutants of environmental concern. This approach is used to develop a ranked list of micropollutants to prioritize for risk management and treatment efforts.

2. OVERVIEW OF PRIORITIZATION METHODOLOGY

Various criteria and frameworks for evaluating risk levels of micropollutants have been proposed in the past decades. In general, two tiers of approaches are employed. The first-tier approach is a conceptual prioritization framework. A surrogate is applied to quantify the risk level of an individual chemical. The most commonly used one is the RQ, which can be calculated as follows:

$$\text{RQ} = \text{MEC}/\text{PNEC} \quad (1)$$

$$\text{RQ} = \text{MEC}/\text{DWEL} \quad (2)$$

where MEC (ng/L) is the measured environmental concentration for a given chemical; PNEC (ng/L) and DWEL (ng/L) are the predicted no-effect concentration and the drinking water equivalent level, respectively (see Section 3). Equations 1 and 2 have been widely used for risk assessment on environments and human health, respectively.^{30,31} For instance, Hernando et al.³² evaluated the environmental risk of pharmaceuticals in the wastewater effluent, surface water, and sediments using the RQ method, and found that four analgesics and one antiepileptic had high risk levels in both wastewater effluents and surface waters. Leung et al.³³ evaluated the life-long human health risk of 32 pharmaceuticals in China’s tap waters by calculating RQ values at different life stages. Most of the detected pharmaceuticals posed low risk on human health, but dimetridazole, thiamphenicol, sulfamethazine, and clarithromycin were found to have relatively high RQ values to infants and children. Modified frameworks based on the RQ method for risk assessment were also reported. von der Ohe et al.³⁴ developed an elaborate prioritization framework for surface waters in EU. Some traditional and emerging contaminants were first classified into six categories according to their available information. For example, category 1 was defined for compounds with sufficient occurrence and toxicity data for determining an environmental quality standard; category 2 was for compounds with comprehensive hazard assessment and few occurrence data in aquatic environments. The chemicals in each category were then prioritized according to two indicators, that is, the frequency and extent of MEC exceeding the corresponding PNEC. Similarly, Kuzmanović et al.³⁵ prioritized 200 organic micropollutants in

surface waters using a so-called “ranking index” (RI) approach, which could be regarded as an averaging process based on the RQ approach (see Section 6.1). The risk surrogate used in their study was the toxic unit (TU), which was very similar to the concept of the RQ approach. TU is calculated by dividing MEC by EC_{50} instead of PNEC, and it scales the intrinsic toxicity of a chemical to an occurrence level in aquatic environments.³⁶ Typically, for a given compound, the TU value was calculated using a single MEC, and other MEC data were discarded. However, in the RI approach, all TU values were calculated using all MEC values at different sampling sites, and different weighting indexes (W_x) were assigned to reflect the importance of the MEC values for the overall risk level.³⁵ Each compound was then prioritized according to the frequency that it might pose risk and the magnitude of the risk level. It can be found that both studies^{34,35} incorporated the detection frequency information into risk assessment, and thus they were more well-rounded than those using risk intensity only and provided a relatively full picture of the risk potential in the studied areas.

In addition to the RQ-based methods, several quantitative risk surrogates were also reported. van de Meent et al. developed a prioritization approach by considering the emission and toxic pressure of chemicals in a typical European water body at steady state.³⁷ A multimedia fate model was developed to estimate emission rates of 6409 substances in the EU list for which there were estimates of production.³⁷ Blum et al.³⁸ established a ranking score system for each compound by considering its removal efficiency in sewage treatment, bioaccumulation potential, persistence, and risk ratio. The sum of these scores was used for transparent comparison for priority setting. Similar score rankings based on persistence, bioaccumulation, and toxicity properties (PBT criteria) or other analogous parameters were also reported.^{39,40} Muñoz et al.⁴¹ reported a life cycle impact assessment (LCIA) method to quantify the environmental impacts of 98 frequently detected micropollutants in wastewater effluents. The LCIA method aimed to understand and quantify the impacts of wastewater effluents in all potential receiving ecosystems, which included ecotoxicity potential on freshwater, marine water, and terrestrial environments, and human health toxicity potential associated with soil environments. The results showed that 16 substances had significant contributions to the overall toxicity of the effluents, and 10 of them were pharmaceuticals and personal care products (PPCPs). Murray et al.²⁶ calculated the consumption rate posing health risk (CRPHR) for 71 individual chemicals, which allowed the comparison of different chemicals based on their health risk. CRPHR was only used for risk assessment on human health and was calculated from the accepted daily intake (ADI) value and median or maximum concentrations of chemicals in the freshwater environment. Compounds with CRPHR values <2 L/day were considered to have high priority for regulation and treatment, and several industrial chemicals, pesticides, and PPCPs were determined as the pollutants with high priority.

The approaches mentioned above are all based on theoretical estimation, which may serve as a first-tier judgment to provide a tentative list of priority chemicals, while further experimental validation may be required. In other words, these approaches provide a first indication of which chemicals are present at concentrations that may pose risk. Therefore, the second-tier evaluation is an experiment-based approach, such as the EDA approach. An in-depth overview of EDA has been provided elsewhere.⁴² Briefly, EDA is a process to reduce the complexity of the mixture in a real sample, and it aims at identifying the

chemicals with potential risk on the ecosystem or human health by direct experimental evidence. It involves multiple fractionations, chemical analysis, and biological tests to determine the main adverse effects of the mixture and the corresponding risk driving substances. In general, EDA is a powerful tool to provide extensive and accurate risk assessment for real water samples. However, it is relatively time-consuming and arduous, and thus it might not be practical for risk assessment in a large scale.

According to the above information, herein we focus on the prioritization studies based on the RQ method. This is because compared with the EDA method, the RQ method has a relatively simple evaluation framework. It has also been the most frequently used approach in the past decades, and it has generated comprehensive data on the risk intensity and distribution of micropollutants around the world for further analysis. A detailed introduction of the RQ method is presented below.

3. INTRODUCTION OF THE RQ METHOD

The RQ approach is usually carried out using a conceptual framework, with a lot of attention on compiling existing monitoring and (eco)toxicological data for target chemicals.⁴³ In this approach, the occurrence concentration and (eco)toxicological data are integrated using a risk surrogate, that is, RQ, which can be calculated using eqs 1 and 2.

For environmental risk assessment, PNEC is ideally derived from the species sensitivity distribution (SSD) for compounds with sufficient toxicity information. Confidence can be given to an SSD-derived PNEC if 10 chronic, no observed effect concentrations (NOECs) for different species covering more than eight taxonomic groups are available.⁴⁴ Nonetheless, for many micropollutants, there are only very few available ecotoxicity data. In such cases, the assessment factor (AF) approach recommended by the EU technique guidance document on risk assessment can be used to estimate the PNEC as follows:⁴⁵

$$\text{PNEC} = \text{NOEC}/\text{AF} \quad \text{or} \quad \text{PNEC} = \text{EC}_{50}/\text{AF} \quad (3)$$

where NOEC is the lowest no observed effect concentration, and EC_{50} is the lowest median effective concentration available for the assessed chemical. AF refers to the assessment factor, which is used to account for the uncertainty due to extrapolation between intra- or inter-species and from laboratory studies to mesocosm or field-based studies. Different effective concentrations used in eq 3 would be paired with different AFs. In terms of occurrence levels in aquatic environments (i.e., MEC), routinely monitored chemicals usually only account for a very small proportion of the contaminants loading. Therefore, for most micropollutants, their occurrence levels are collected from extensive literature reviews or direct screening-level detection in site-specific case studies.^{46,47} Theoretical calculation was also used to estimate occurrence levels of micropollutants according to their production and consumption pattern.²² Typically, there is a set of MEC values for a given chemical, and the highest or median one is often used to calculate the corresponding RQ value. RQ obtained from the highest MEC value indicates the highest risk level or the worst exposure scenario, while RQ calculated from the median MEC value reflects the overall risk level in a better way. As for the derivation of the PNEC value for the assessed chemical, the PNEC is ideally derived from as many aquatic species as possible through the SSD approach, and if this is not possible, the toxicity information on three standard test

Table 1. All Individual Prioritization Studies Based on the RQ Method with Partial Micropollutants Lists Published in Scopus Database in the Past Decade

reference	water type	risk endpoint	area	micropollutants with RQ higher than 1	notes
Afsa et al. (131)	marine water	environment	developing (Tunisia)		<i>a,c</i>
Alonso et al. (30)	surface water	environment	developing (Chile)	heptachlor, pentachlorophenol	
Aminot et al. (63)	marine water	environment	developed (EU)	benzo(a)pyrene, triclosan	
Ashfaq et al. (132)	surface water	environment	developing (Pakistan)	ibuprofen, propylphenazone	<i>a</i>
Aukidy et al. (46)	surface water	environment	developed (EU)	acetaminophen, 17 α -ethinylestradiol	<i>a</i>
Baken et al. (133)	drinking water	human health	developed (EU)	phenol, 1,4-dioxane	
Blum et al. (38)	wastewater	environment	developed (EU)	phenyldodecane, galaxolide	
Bu et al. (134)	surface water	environment	developing (China)	erythromycin, azithromycin	<i>a,b</i>
Carlson et al. (57)	surface water	environment	developed (Canada)	clarithromycin, diazinon	
Chau et al. (135)	surface water	environment	developing (Vietnam)	ampicillin, acetaminophen	
Cho et al. (58)	surface water	environment	developed (South Korea)	heptachlor, chlorpyrifos	
Di Nica et al. (5)	surface water	environment	developed (Italy)	fenbendazole, streptomycin	<i>a,b</i>
Díaz-Garduño et al. (136)	wastewater	environment	developed (Spain)	caffeine, propranolol	
Etchepare and van der Hoek (53)	wastewater	human health		benzene, dodecanoic acid	<i>d</i>
Feo et al. (137)	marine water	environment	developed (Italy)	amoxicillin, clarithromycin	<i>a</i>
Fernández-Rubio et al. (138)	marine water	environment	developed (Spain)	citalopram, fluoxetine	<i>a</i>
Flores et al. (139)	surface water	environment	developing (Chile)	amoxicillin, oxytetracycline	
Ghekiere et al. (47)	marine water	environment	developed (Belgium)	4-nonylphenol, diuron	
Ginebreda et al. (140)	surface water	environment	developed (Spain)	atorvastatin	
Gosset et al. (141)	wastewater	environment	developed (France)	atenolol, diclofenac	
Guruge et al. (142)	surface water	environment	developing (Sri Lanka)	ibuprofen, sulfamethoxazole	<i>a</i>
He et al. (143)	surface water	environment	developing (China)	estrone	
Im et al. (144)	surface water	environment	developed (South Korea)		<i>a,c</i>
Jiang et al. (7)	marine water	environment	developed (Taiwan)	codeine, ampicillin	
Jiang et al. (72)	surface water	environment	developed (Taiwan)	diclofenac, ibuprofen	<i>a</i>
Johnson et al. (25)	surface water	environment	developed (UK)	PFOS, tributyltin	
Kapelewska et al. (145)	groundwater	environment	developing (Poland)	diclofenac, benzophenone-3	
Kong et al. (11)	groundwater	human health	developing (China)	carbendazim, diuron	
Kosma et al. (49)	surface water	environment	developed (Greece)	triclosan, sulfamethoxazole	<i>a,b</i>
Kuroda et al. (146)	surface water	environment		lopinavir, umifenovir	<i>a,d</i>
Kuzmanović et al. (35)	surface water	environment	developed (EU)	diuron, caffeine	
Lai et al. (147)	surface water	environment	developed (Taiwan)	sulfamethoxazole, erythromycin	<i>a</i>
Leung et al. (33)	drinking water	human health	developing (China)		<i>a,c</i>
Li et al. (6)	groundwater	human health	developing (China)		<i>c</i>
Lin et al. (148)	groundwater	environment	developed (Taiwan)	sulfamethoxazole, erythromycin	<i>a</i>
Lin et al. (149)	surface water	environment	developing (China)	sulfamethoxazole, clarithromycin	<i>a</i>
Lin et al. (150)	surface water	environment	developing (China)	sulfamethoxazole, triclosan	<i>a</i>
Liu et al. (151)	surface water	environment	developing (China)	nonylphenol, sulfamethoxazole	
Liu et al. (152)	surface water	environment	developing (China)	estrone, benzo[a]pyrene	
Liu et al. (153)	surface water	environment	developing (China)	ibuprofen, caffeine	<i>a</i>
Ma et al. (154)	surface water	environment	developing (China)	venlafaxine, diclofenac	<i>a</i>
Manan et al. (155)	wastewater	environment	developing (Malaysia)		<i>c</i>
Mendoza et al. (54)	drinking water	human health	developed (Spain)		<i>a,c</i>
Mijangos et al. (156)	wastewater	environment	developed (Spain)	caffeine, diclofenac	<i>a</i>
Mijangos et al. (156)	surface water	environment	developed (Spain)	caffeine, diuron	
Minguez et al. (70)	surface water	environment	developed (EU)	econazole	
Minguez et al. (70)	marine water	environment	developed (EU)	clindamycin, clarithromycin	
Molnar et al. (157)	surface water	environment	developing (Hungary)	diclofenac, caffeine	<i>a</i>
Morasch et al. (71)	drinking water	environment	developed (Switzerland)	paracetamol, ciprofloxacin	
Munz et al. (79)	surface water	environment	developed (Switzerland)	diazinon, imidacloprid	
Murray et al. (26)	surface water	environment	developed (USA)	17 α -ethinylestradiol, carbamazepine	
Nantaba et al. (158)	surface water	environment	developing (Uganda)	triclosan, dibutyl phthalate	
Olalla et al. (159)	surface water	environment	developing (Antarctic)	diclofenac, ibuprofen	
Papageorgiou et al. (160)	wastewater	environment	developed (Greece)	amoxicillin, clarithromycin	<i>a,b</i>
Park et al. (39)	surface water	environment	developed (South Korea)	carbamazepine, metformin	<i>a</i>
Perazzolo et al. (161)	surface water	environment	developed (Switzerland)	diclofenac, ibuprofen	

Table 1. continued

reference	water type	risk endpoint	area	micropollutants with RQ higher than 1	notes
Picó et al. (162)	surface water	environment	developed (Saudi Arabia)	chlorpyrifos, diazinon	
Praveena et al. (59)	surface water	human health	developing (Malaysia)	ciprofloxacin, dexamethasone	^a
Praveena et al. (59)	surface water	environment	developing (Malaysia)	diclofenac, sulfamethoxazole	^a
Ramos et al. (163)	wastewater	environment	developing (Brazil)	2,4-dichlorophenol, 2,3,4,6-tetrachlorophenol	
Riva et al. (164)	surface water	environment	developed (Italy)	amoxicillin, clarithromycin	
Roos et al. (23)	surface water	environment		propranolol, naproxen	^{a,d}
Sadutto et al. (165)	surface water	environment	developed (Spain)	caffeine, tramadol	^{a,b}
Sánchez-Avila et al. (166)	marine water	environment	developed (Spain)	4-nonylphenol, bis(2-ethylhexyl) phthalate	
Santos et al. (60)	wastewater	environment	developed (EU)	diclofenac, sulfamethoxazole	^{a,b}
Schriks et al. (167)	surface and groundwater	human health			^{c,d}
Schriks et al. (167)	drinking water	human health			^{c,d}
Smital et al. (24)	surface water	environment	developed (EU)	benzo(k)fluoranthene, linear alkylbenzenesulfonates	
Sodré and Sampaio (168)	drinking water	environment	developing (Brazil)	estrone, 17 α -ethinylestradiol	
Sodré and Sampaio (168)	drinking water	human health	developing (Brazil)	17 α -ethinylestradiol, beta-estradiol	
Sousa et al. (65)	marine water	environment	developed (Portugal)	chlorpyrifos, alachlor	
Stasinakis et al. (169)	surface water	environment	developed (Greece)	4-nonylphenol, triclosan	
Tang et al. (170)	surface water	environment	developing (China)	tetracycline, benzylpenicillin	^a
Tian et al. (171)	marine water	environment	developed (USA)	PFOS, bisphenol S	
Tousova et al. (172)	surface water	environment	developing (BiH)	diazinon, diclofenac	
Thomaidi et al. (173)	wastewater	environment	developed (Greece)	amoxicillin, atorvastatin	
Verlicchi et al. (62)	surface water	environment		erythromycin, ofloxacin	^{a,d}
von der Ohe et al. (34)	surface water	environment	developed (EU)	diazinon, heptachlor	
Xie et al. (174)	marine water	environment	developing (China)	diuron, ametryn	
Wu et al. (61)	surface water	environment	developing (China)	clindamycin, clarithromycin	^a
Wu et al. (175)	drinking water	environment	developing (China)	ofloxacin, sulfamethoxazole	^b
Yan et al. (27)	surface water	environment	developing (China)	ofloxacin, norfloxacin	^b
Yang et al. (52)	groundwater	environment	developed (USA)	caffeine, sulfamethoxazole	

^aOnly PPCPs were subjected to risk assessment in this study. ^bThe RQ values were calculated for algae, *Daphnia magna*, and fish, respectively, and the highest one is used in this review. ^cNo compounds were reported to have RQ values higher than 1. ^dThe prioritization of micropollutants were obtained based on the risk assessment results from different areas.

organisms *Pimephales promelas*, *Daphnia magna*, and *Selenastrum capricornutum* could be compiled from databases or literature to determine a provisional PNEC value.⁴⁸ An AF of 1000 is often applied for acute EC₅₀ values; however, this value could be reduced as the toxicity data availability increases. For example, an AF of 100 can be applied when one chronic EC₅₀ (or LC₅₀) value against one of the three standard species is available; a further lower value of AF can be used when two or more chronic EC₅₀ (or LC₅₀) values are available.⁴⁹ A higher RQ value is indicative of a higher risk potential. Special attention should be paid to chemicals with RQ values higher than 1. An RQ value lying between 0.1 and 1 indicates a moderate risk level, and RQ \leq 0.1 indicates a low risk level.²⁷

For human health risk assessment, DWEL can be obtained using the following equation:

$$\text{DWEL} = \frac{\text{ADI} \times \text{BW} \times \text{HQ}}{\text{DWI} \times \text{AB} \times \text{FOE}} \quad (4)$$

where $\text{ADI} = \frac{\text{NOAEL or LOAEL}}{\text{UF1} \times \text{UF2} \times \text{UF3} \times \text{UF4} \times \text{UF5}}$

ADI refers to the acceptable daily intake ($\mu\text{g}/\text{kg}\cdot\text{day}$), which is a level that induces no adverse effects on the potentially exposed population. ADI can be obtained from literature or calculation. Leung et al.³³ described the detailed method for ADI calculation under different toxic effects including noncancer effects, carcinogenicity, and microbiological effects. Here we only show the calculation equation for noncancer effect (eq 4). ADI can be derived from the no observable adverse effect level

(NOAEL) or lowest observable adverse effect level (LOAEL) using eq 4. UF1 to UF5 represent uncertainty factors, which are used to account for the uncertainty due to extrapolation from effective concentrations to NOAEL, from short-term to long-term exposure, among different interspecies, among different intraspecies, and data quality, respectively. The detailed selection criteria for UFs are described elsewhere.⁵⁰ BW and DWI are respectively the median values of body weight and 95th percentile drinking water intakes of 12 age groups, which are available in the U.S. EPA *Exposure Factor Handbook*.⁵¹ HQ and AB represent the hazard quotient and gastrointestinal absorption rate, respectively, both of which are assumed to be 1. FOE is the frequency of exposure.⁵² Similarly, a higher RQ value obtained from eq 2 is also indicative of a higher risk potential.⁵³

4. OCCURRENCE AND TOXICITY IN VARIOUS WATER BODIES

After industrial, agricultural, and domestic use, a wide range of chemicals are eventually released into various receiving water bodies.^{54,55} The occurrence of these chemicals has been widely reported in aquatic environments worldwide. For example, atrazine, phenanthrene, caffeine, and fluoranthene were the most commonly detected chemicals in Europe's groundwater;⁵⁶ atrazine, carbamazepine, sulfamethazine, and gemfibrozil were frequently detected in a Canadian stream;⁵⁷ organochlorine pesticides like hexachlorobenzene, heptachlor epoxide and

dieldrin were the most frequently detected chemicals in four major rivers in Korea.⁵⁸ Overall, these frequently detected chemicals can be divided into three classes according to their origins: PPCPs, pesticides, and industrial chemicals. The occurrence levels and PNEC/ADI values of these frequently detected chemicals are summarized in [Supporting Information \(SI\) Tables S1–S3](#) and [Text S1](#).

5. PRIORITIZATION OF CHEMICALS IN AQUATIC ENVIRONMENTS

To denote the micropollutants of world-scale importance, this review summarized the prioritization results for micropollutants from various case studies, which served as a first-class prioritization database for further analysis. Five criteria were used to select the qualified case studies. Specifically, the studies should (i) conduct prioritization for micropollutants using the RQ method; (ii) be published from 2010 to 2021; (iii) investigate more than 10 compounds; (iv) not investigate inorganic chemicals (e.g., heavy metals) only; and (v) not investigate specific endpoints (e.g., endocrine disrupting effect) only. A total of 83 case studies were included (accessed on 21 March 2021), and [Table 1](#) displays all the 83 studies and their targeted water types, areas, and risk endpoints. Due to the space limit, only some micropollutants with the RQ values higher than 1 were presented, and the entire summary for the micropollutants with potential risk levels can be found in [SI Table S4](#). The 83 studies together may represent our current knowledge on the risk assessment for micropollutants using the RQ method.

The number of risk assessment studies on each category (water type, area, and risk endpoint) was first analyzed as shown in [Figure 1](#), which represents an overview of research attention

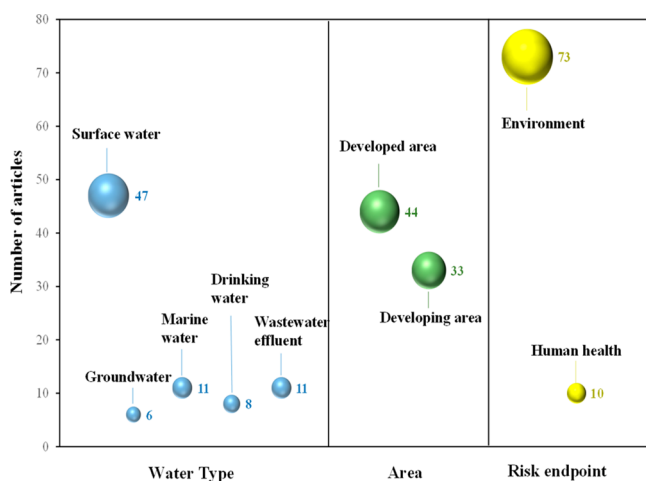


Figure 1. Number of studies conducting risk assessment using the RQ method in the past decade categorized by area (developed area and developing area), risk endpoint (environment and human health), and water type (groundwater, wastewater effluent, marine water, drinking water, and surface water). The number of studies were obtained from the Scopus database (last access on 21 March 2021).

within the past decade. Among different water types, surface water is the most investigated type. A total of 47 studies conducted risk assessments on surface water from 2010 to 2021, followed by the numbers of studies for marine water, wastewater effluent, drinking water, and groundwater. For the studied areas, they were simply classified into developed and developing areas.

More risk assessment studies were performed in developed areas (44 cases) than in developing areas (33 cases). The difference regarding the numbers of published articles on different risk endpoints is also significant. There were 73 studies focusing on risk assessment on the environment, whereas only 10 studies were conducted on risk assessment on human health. To facilitate the evaluation of the overall risk levels of micropollutants in the following part, the risk assessment results on different categories are assumed to be equally important. For example, RQ values higher than 1 from the risk assessment results on the environment and human health are assumed to contribute equally to determine the final risk levels.

The results of prioritized compounds ($RQ > 1$) identified in these case studies are also visualized in [Figure 2](#). There are as

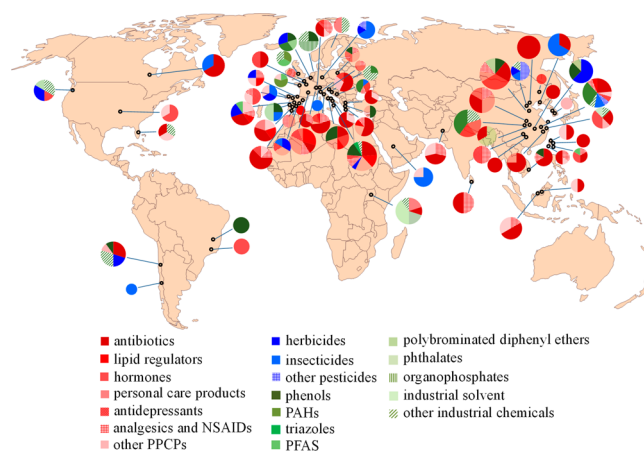


Figure 2. Micropollutant subgroups with highest priority levels ($RQ > 1$) in different areas identified in the case studies using the RQ method in the past decade. PPCPs, pesticides, and industrial chemicals were distinguished using red, blue, and green colors, respectively. Every black point represents a compiled case study. A larger circle indicates a higher number of micropollutants with RQ values higher than 1 in the corresponding case study. Detailed data are presented in [SI Table S5](#).

many as 182 micropollutants with RQ values higher than 1 (data shown in [SI Table S5](#)) reported in the past decade. To reduce the complexity, the subgroups of micropollutants instead of the specific prioritized micropollutants are presented. Different colors are used to distinguish micropollutants from three broad chemical groups (i.e., PPCPs, pesticides, and industrial chemicals), and the micropollutants from different subgroups were further characterized using different patterns. Despite that, the prioritization results are found to be relatively diverse as indicated by the varying color and pattern distributions in different areas, and a conclusion could hardly be drawn on the compounds with the highest priority levels globally. Specifically, PPCPs (red color) were more frequently reported to be prioritized compounds compared with pesticides (blue color) and industrial chemicals (green color). When it came to the analysis of the subgroups of PPCPs, pesticides, and industrial chemicals, the composition of the prioritized micropollutants (the patterns) also somewhat varied. This indicated that for the priority estimation on the global scale, it may not be representative or accurate to merely use the highest reported RQ value in the literature directly; instead, the risk distribution should also be incorporated to achieve a more “authentic” result.

Therefore, we managed to propose a more well-rounded risk surrogate for a worldwide prioritization, by considering both the risk intensity and the frequency that a compound has potential

risks in the 83 case studies. We first screened the compounds with potential risks based on their reported RQ values. Typically, only chemicals with the RQ values higher than 1 are assumed to deserve further investigation. Relatively little attention has been paid to chemicals with the RQ values ranging from 0.01 to 1, which indicates low or medium risks of the chemicals on environments. For conservative consideration and full exploitation of available data, all compounds with RQ values >0.01 were compiled. For each case study, dozens of micropollutants were usually targeted for RQ calculation, and only a proportion of them were found to have RQ values greater than 0.01. By summarizing such information for all 83 studies, a total of 473 compounds (233 PPCPs, 82 pesticides, and 158 industrial chemicals) that were screened from 3466 micropollutants (SI Table S6) were reported to have risks on aquatic environments or human health (SI Table S4). Some compounds were repeatedly reported to be risky, and thus had multiple RQ values in different areas. To normalize the importance of different RQ values on risk estimation, different rank classes were defined as shown in Table 2. Different W_x values for these

Table 2. Definition of the Four Rank Classes, Their Corresponding RQ Ranges, and Assigned Weighting Indexes

rank class (x)	RQ range	weighting index (W_x)
1	>1	1
2	0.1–1	0.5
3	0.01–0.1	0.25
4	<0.01	0

rank classes were assigned based on a previous study to distinguish the contributions of different RQ values (i.e., risk intensity) to the final risk surrogate.³⁵ For instance, an RQ value higher than 1 is indicative of a high-risk level, and the highest W_x of 1 was thus assigned. In the meantime, the frequency that an assessed compound had RQ values located in each class was determined as summarized in SI Table S7. We proposed a “weighted average RQ” (WARQ) as the overall risk surrogate for the prioritization on a global scale, which is described as follows:

$$\begin{aligned} \text{WARQ} &= \sum_{x=1}^4 \left[\left(f_{x,\text{total}} - \frac{f_{x,\text{PPCPs}}}{2} \right) \times W_x \right] \\ &= \left(f_{1,\text{total}} - \frac{f_{1,\text{PPCPs}}}{2} \right) \times 1 + \left(f_{2,\text{total}} - \frac{f_{2,\text{PPCPs}}}{2} \right) \times 0.5 \\ &\quad + \left(f_{3,\text{total}} - \frac{f_{3,\text{PPCPs}}}{2} \right) \times 0.25 + \\ &\quad \left(f_{4,\text{total}} - \frac{f_{4,\text{PPCPs}}}{2} \right) \times 0 \end{aligned} \quad (5)$$

where x refers to the rank class defined according to the RQ range; $f_{x,\text{total}}$ is the total number of studies reporting that a certain compound has RQ values in the rank class x ; $f_{x,\text{PPCPs}}$ is the total number of studies that investigated PPCPs only. The parameter $f_{x,\text{PPCPs}}$ should be involved for the priority estimation on PPCPs, because in a small half of compiled studies (29 out of 83), PPCPs were the only targets for prioritization, and other groups of micropollutants (i.e., pesticides or industrial chemicals) were not considered even though they might also have potential risks.^{59,60} Therefore, a correction factor of 0.5 is used to partially offset the contributions of these studies on determining the final

risk levels for PPCPs. This parameter is 0 for the calculation on pesticides and industrial chemicals. W_x is the weighting index for class x . A brief comparison can be made for the WARQ method and the approaches used in previous studies. The risk assessment studies published in the past decade could be divided into two types based on their studied areas. Most studies conducted risk assessments in a specific area (in a certain river or lake). For a chemical with a set of MEC data, the highest MEC was often used to calculate the RQ value for the prioritization purpose, and the other MEC values were discarded (e.g., Wu et al.⁶¹). A few studies determined the RQ values using all MEC data, and the frequencies of the RQ values higher than 1 were incorporated in priority estimation (e.g., Kuzmanović et al.³⁵). Nonetheless, it might be questionable to extrapolate the ranking results to larger spatial scales. The other type of studies reviewed the occurrence levels of micropollutants in different countries in the literature (e.g., Verlicchi et al.⁶²), while only the highest occurrence level was used to calculate the RQ values for priority comparison. This indicated that extreme local cases might have been used to represent the overall risks in global environments. By contrast, the WARQ method can be regarded as an averaging process for nearly all existing RQ values in the literature. The 83 case studies together have made up a worldwide sampling web for risk assessment, and all of them contribute partially to the final risk estimation on a global scale. Meanwhile, the WARQ method covers a more complete exploitation of existing information (with an extension of the threshold of RQ values to >0.01), and thus provides an overall risk assessment for a given chemical.

Figure 3 presents the list of overall risk ranking of micropollutants using the WARQ method. A threshold of 2 was selected for the WARQ value because it ensured that at least two individual studies reported a high potential risk level (RQ > 1) for a compound. There are 53 compounds with the WARQ values ranging from 2.25 to 21.3 (Figure 3). Micropollutants from different chemical groups (i.e., PPCPs, industrial chemicals, and pesticides) are distinguished by different colors. To our knowledge, this is the first time that a comprehensive prioritization for thousands of micropollutants in the global scale is provided. The list of risk ranking can indicate which micropollutants deserve more attention globally, and resources can then be allocated more reasonably to reduce the overall impacts of chemical pollution. It may be worth mentioning that while different assigned values of the PPCP correction factor and W_x might impact the rank order of several micropollutants in the WARQ calculation, they do not change the major conclusion of this review, that is, the 53 compounds (as summarized in Figure 3) generally have higher priority than other 420 compounds with RQ values greater than 0.01, which in turn have higher priority than other thousands of compounds with RQ values less than 0.01, because the WARQ method can essentially reflect the fact that these 53 compounds are more frequently detected in global aquatic environments and are reported to have high risk levels. Remarkably, 36 out of the priority chemicals are PPCPs, whereas only 7 and 10 are pesticides and industrial chemicals, respectively. Moreover, the top 10 substances with relatively high WARQ values all belong to PPCPs. This indicates that the overall priority of PPCPs is much higher than pesticides and industrial chemicals. This is consistent with the results in Figure 2 and the fact that PPCPs are used in larger amounts and are continuously discharged into aquatic environments, as signified by their higher detection frequencies and occurrence levels (see SI Tables S1–S3). In addition, this review primarily focuses on the risk assessment of micropollutants in water compartments,

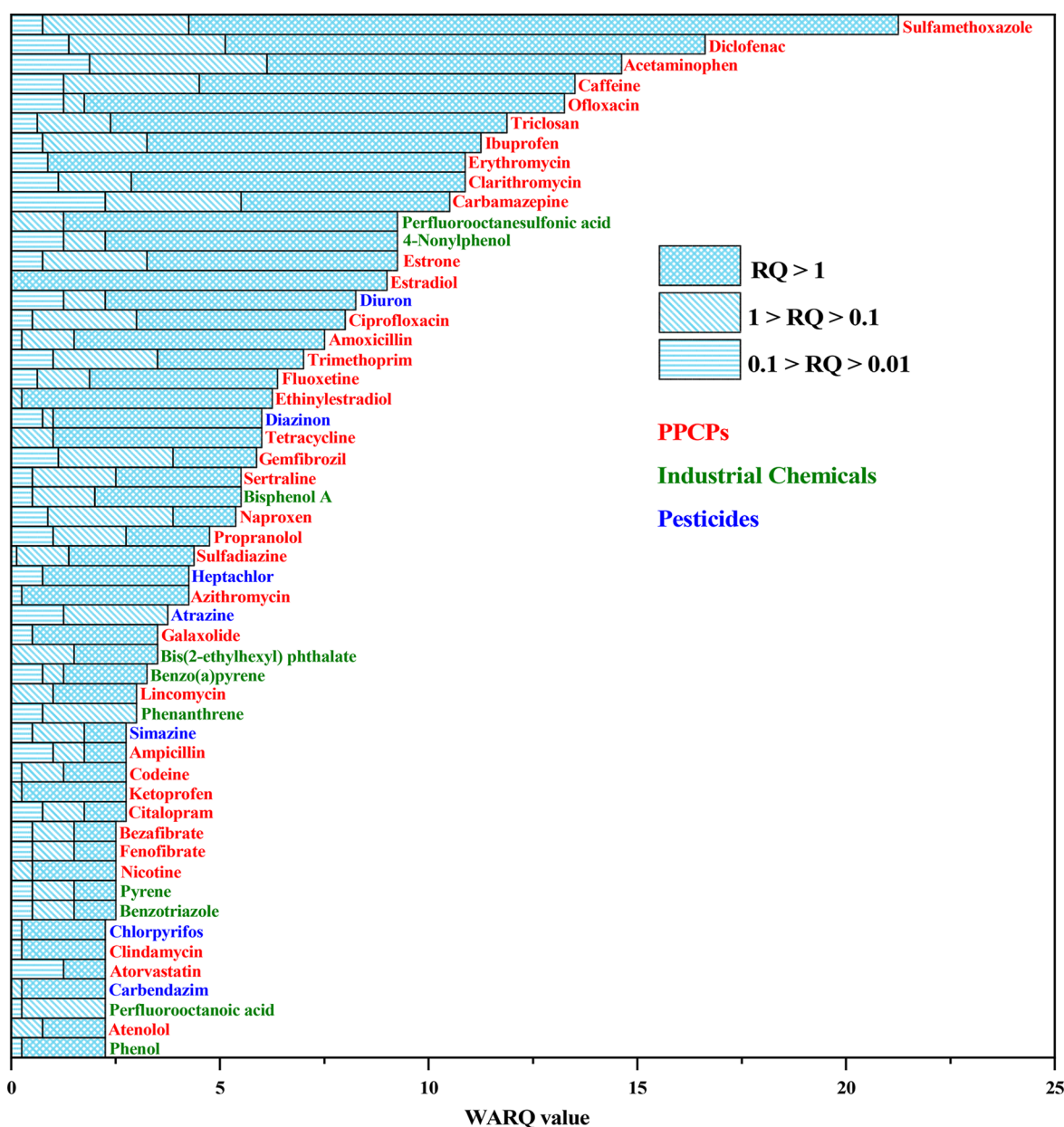


Figure 3. Micropollutants list with relatively high priority based on the prioritization results using the RQ method reported from 2010 to 2021. For each compound, the contributions of different RQ ranges to final calculation of the WARQ value are represented by different patterns. Micropollutants from three broad chemical classes are distinguished by different colors. Red indicates PPCPs; green for industrial chemicals; and blue for pesticides.

whereas pesticides and industrial chemicals may present at higher levels in the sediments or tissues in aquatic biota. Further studies on their risks in benthic ecosystems and in aquatic organisms are warranted to verify if the risk levels of the prioritized pesticides and industrial chemicals in sediment or biota are higher than those in water.^{27,63}

Figure 4 also shows the composition of prioritized PPCPs. The largest proportion is antibiotics, followed by lipid regulators, nonsteroidal anti-inflammatory drugs (NSAIDs), hormones, antidepressants, stimulants, anticonvulsants, a synthetic musk, and an opiate. In addition, half of the top 10 compounds are antibiotics, and the highest WARQ value is also recorded for an antibiotic, sulfamethoxazole (with a WARQ value of 21.3). This indicates that antibiotics is the subgroup of most concern, which can also be found in Figure 2. In terms of pesticides, there are three herbicides, three insecticides, and one

fungicide (Figure 3). The highest WARQ value corresponds to an herbicide, diuron (with a WARQ value of 8.25). Similarly, the 10 prioritized industrial chemicals include three phenols, three polycyclic aromatic hydrocarbons (PAHs), two per- and polyfluoroalkyl substances (PFASs), one phthalate, and one triazole. The highest value is recorded for perfluorooctanesulfonic acid (PFOS) and 4-nonylphenol (both with a WARQ value of 9.25).

Although the WARQ approach provides a universal prioritization result for thousands of micropollutants, its scope and limitation should also be clarified. First, the WARQ method relies on the existing information on risk assessment, indicating that the prioritization result based on the WARQ approach is inherently restricted on known chemicals. Second, this review summarizes the risk assessment results from case studies worldwide, and hence it aims at determining substances of

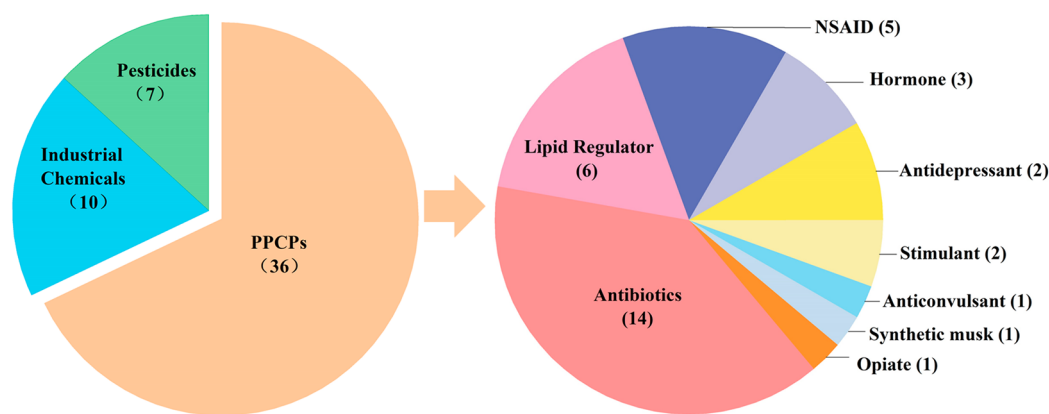


Figure 4. Distribution of prioritized micropollutants listed in Figure 3 on different chemical groups and subgroups of PPCPs. The distributions on different subgroups of pesticides, and industrial chemicals are not included due to the small number of prioritized micropollutants in these two chemical groups. The numbers in brackets indicate the quantity of prioritized micropollutants in each category.

worldwide importance to formulate more “realistic” and relevant concerns to cope with in future studies, instead of establishing policy regulations that may have distinct site-specific features. This is important for the efficient allocation of resources to address current knowledge gaps and environment problems. Third, the WARQ values are partly related to the total number of studies that reported a compound with a potential risk. Accordingly, a small number of compounds could be credited with higher priority partially due to their higher numbers of reports in the database. This is because we intentionally attribute some importance to risk frequencies on the final priority determination. Although 83 case studies had been conducted in the past decade, their prioritization results were somewhat different among different studies. For many micropollutants, their frequencies with the RQ values larger than 1 are not high enough. This WARQ method involves the RQ values in the range of 0.01 to 1 to enlarge the database in order to reduce the degree of arbitrariness and uncertainty.

6. DISCUSSION

The WARQ method was developed based on the RQ approach, and thus the prioritization result of this review is intrinsically impacted by the quality of the RQ values, which in turn relies heavily on the robustness of effect and exposure data. Uncertainty and variability are essential issues in this conceptual framework. Therefore, the aspects for improving the exposure and hazard assessment are elaborated below in order to strengthen the quality and credibility of the RQ-based risk assessment.

6.1. Improvement Needs for Exposure Assessment.

Despite the great development of analytical techniques in the past decades, there are numerous chemicals with occurrence levels lower than their limits of quantification (LOQ). It is debatable how to treat those data, which is of great significance particularly when the PNEC or DWEL value of a certain compound is lower than its LOQ. In most cases, the undetectable level is assumed to be half of the LOQ or zero to facilitate the calculation of RQ. There may be a false estimation of the risk level due to the ambiguity of whether these chemicals are present or not in the samples. This highlights the importance of using substitution methods for detection limits⁶⁴ and developing state-of-the-art detection techniques. The progress of instrumental analysis methods is well summarized elsewhere.^{65–67} An alternative is to develop theoretical models to

predict the concentrations of chemicals in aquatic environments. Compared with direct measurement of the concentration, modeling is much faster and cheaper if the models have been set up with high accuracy. Also, modeling can easily provide the occurrence information on micropollutants in a large space and time span. However, the results usually vary substantially among different models and thereby do not always reflect the reality because of the inherent uncertainty of modeling.^{68,69} For a better exposure assessment, an advisable strategy is to combine those two complementary approaches together (i.e., prediction and measurement for occurrence levels lower and higher than LOQ, respectively), which has been adopted in some risk assessment studies.^{70,71}

Moreover, the fluctuation of the chemical concentrations over time in a pollution hotspot is also of concern. On the one hand, analytical measurement usually only presents a snapshot rather than a continuous picture of the pollution. Weather conditions, hydrologic conditions, and random spills may contribute to the variation of the chemical concentrations. A typical chemical group with a distinct occurrence pattern is pesticides, which are periodically applied in the growing season of crops. A rainfall event can readily lead to the peak occurrence of pesticides in the water systems. However, the short-term peak occurrence may be neglected by the monitoring exercise with a relatively low temporal resolution, while it is often believed that the peak instead of the average concentration may be more relevant to the risk assessment for conservative consideration. An interesting study also compared the occurrence levels of 31 micropollutants in the surrounding aquatic environments before and after a youth festival.⁷² The results showed that the concentrations of several PPCPs especially illicit drugs increased substantially. This indicates that different sampling strategies should be used for different chemical groups. For many cases, time-integrated sampling may be appropriate as it provides the information on long-term concentrations,^{73,74} while event-based sampling may be more suitable for pesticides or illicit drugs. On the other hand, since a sequence of occurrence data is available, there are different criteria on which value should be used for RQ calculation. The maximum level is often used, because the corresponding RQ value predicts the risk level under the worst scenario. But it is difficult to characterize the overall dynamic contamination in an area. Besides, it relies heavily on a single concentration, which means that the risk assessment may be largely misled by an unconscious “false” detection performance.

Therefore, a collective concentration reflecting the overall occurrence level is also widely used. For example, 50th, 90th, or 95th percentile concentration is adopted to calculate the RQ value in some case studies,²⁵ and the detailed selection of a representative percentile may be dependent on the political decision. By contrast, a more reasonable approach is to develop a risk surrogate considering the contributions of all occurrence data. As mentioned above, Kuzmanović et al.³⁵ developed a risk surrogate RI to incorporate the detection frequency information on chemicals. In this approach, all MEC values obtained from different sample sites were used to calculate TUs, which were then divided into six classes. Different W_x values that reflected the contributions of different classes on the overall risk level were arbitrarily allocated to different TU ranges. This approach gives a solution to utilize the vast occurrence data in a better way. It can also be used for the risk assessment of those chemicals with high toxicity but with relatively rare occurrence information, as the result would be substantially different from using any single MEC value.

The bioavailability of micropollutants in water bodies is also a significant factor impacting the “real” exposure level. Bioavailability is usually carefully considered on the risk assessment of metals due to their varying dominant species under different hydrologic conditions. However, it should also be involved for organic chemicals especially for those with relatively low pK_a values. In addition, chemicals with high octanol–water partitioning coefficients (K_{ow}) (>5) tend to be accumulated in sediments or aquatic organisms,³¹ and their overall risks may be largely underestimated if merely the dissolved concentrations in the aqueous phase are considered. Instead, sediment or biotic samples should be used to determine their MEC values and hence risk levels on the whole aquatic ecosystem. The bioavailability issues can be solved by evaluating risk levels using pollutant concentrations inside aquatic organisms.⁷⁵ The internal concentration intrinsically reflected the bioavailability process, and it is consistent with the critical body residue (CBR) concept proposed for ecotoxicity evaluation.⁷⁶ It is usually believed that the concentrations at target domains of toxic action and the degree of interactions between toxicants and cell components control the magnitude of biological responses.^{77,78} The internal concentration is a more accurate surrogate of the toxicant concentration at a target site than the external concentration, and it is less likely to be impacted by pH or coexisting macromolecules in the exposure medium. In real cases, short-term sampling represents the snapshot of the exposure, whereas the internal concentration can reflect the overall exposure over time. For example, Munz et al.⁷⁹ evaluated the risk levels of organic micropollutants in Gammarids using their internal concentrations, and hence the EC_{50} value was changed to internal EC_{50} , which was the external EC_{50} value multiplied by the bioconcentration factor. The results revealed a much higher toxic pressure compared to traditional external-concentration-based approaches.

6.2. Improvement Needs for Hazard Assessment.

Sufficient toxicity data usually cannot be obtained for many chemicals.⁸⁰ It has been reported that nearly half of chemicals were unevaluated in plenty of prioritization exercises due to the inadequate data.⁸¹ To provide a reliable risk assessment of a chemical, the toxicity information on at least three standard aquatic organisms (fish, *Daphnia magna*, and algae) should be available. Toxicity data for risk assessment are usually collected from the extensive literature review or some databases, like the ECOTOX database⁸² and the screening information data sets.⁸³

Recently, Posthuma et al. estimated the chronic aquatic NOEC values for 7500 compounds, and the results could serve as an important toxicity database to refer to.⁸⁴ Currently missing toxicity data are usually provided by model predictions. For example, a k nearest neighbors (KNN) method can be used to estimate the toxicity of an untested chemical from its similar compound with available toxicity information.⁸⁵ Specifically, for an untested chemical, three similar compounds are selected via the atom-centered fragments (ACF)-based approach.⁸⁶ The weighted average of the EC_{50} values of the three compounds is calculated and used as the provisional toxicity data. Quantitative structure activity relationship (QSAR) models can also be applied for estimating the baseline toxicity on the three standard test organisms.⁸⁷ However, some problems still exist for the predicted toxicity data. The reliability should be validated prior to application on risk assessment. For example, some well-studied chemicals may be selected for comparing their predicted EC_{50} values with experimental ones. Besides, to determine a conservative PNEC value with limited toxicity data, the lowest EC_{50} value among the three standard test organisms should be selected, while it might be a problem if the predicted EC_{50} value is lower than other experiment values. Related criteria considering the data quality of the prediction model and the experimental bioassay should be defined to address such issues.

For those compounds with available toxicity data on the three standard test species, future research attention should be focused on establishing a toxicity database on more advanced endpoints. The SSD method should be adopted for determining the PNEC for prioritized chemicals rather than using the AF approach with single species data.⁴⁴ The SSD approach eliminates some degree of arbitrariness in selection of AF and sensitive species, and it has been recommended by many official regulatory institutions like the U.S. EPA. The detailed workflow for the SSD approach is provided elsewhere.⁸⁸ The PNEC values based on the SSD method can be found in a database established by Posthuma et al.,⁸⁴ which includes the data of over 12 000 chemicals. The mesocosm study and mixture toxicity of micropollutants might also be investigated to simulate a more “realistic” exposure scenario way for those compounds with high priority.^{89–92}

Besides to the apical toxicity (e.g., survival of aquatic organisms), hazard assessment may also be extended to other more specific endpoints. Currently, cell-based bioassays have been developed for covering all steps of the toxicity pathway, and high-throughput screening using cell-based methods are greatly promising to prioritize chemicals for further tests.^{93,94} Biomonitoring using a panel of in vitro bioassays has also been viewed as an appealing tool to better benchmark water quality.^{95,96} Careful attention should be paid in comparing the RQ values across the micropollutants, because the PNECs or DWELs might be derived from different effect endpoints, which might have varying impacts (severe or mild) on the tested organisms. However, the related data are quite limited for most micropollutants. Besides, two new forms of pollutants challenge the traditional risk assessment, in which the risk potential of a compound is derived from its toxicity property only. The first is antibiotic resistance genes (ARGs), which has been regarded as a growing threat to public health in recent years due to frequent or even imprudent use of antibiotics.^{97,98} ARGs are naturally present in the strains of fungi and bacteria, whereas the increasing use of antibiotics may accelerate the evolution and dissemination of ARGs,⁹⁹ leading to ARGs contamination in aquatic environments.^{100–103} Moreover, it has been docu-

mented that many ARGs exist in mobile genetic elements, which arguably can be transferred to human commensal bacteria and pathogens.¹⁰⁴ Considering that antibiotics is usually the only method to treat infectious diseases, it might pose a risk on public health if human commensal bacteria and pathogens acquire antibiotic resistance. Many efforts have been made to eliminate the potential risks of ARGs.^{105,106} The other challenge on traditional hazard assessment is microplastics. The term “microplastics” was first proposed in 2004, referring to the plastic fragments with a size of around 20 μm .¹⁰⁷ The scope was expanded to 5 mm later.¹⁰⁸ Microplastics have been reported to be ubiquitous in aquatic environments, especially in the marine ecosystem.¹⁰⁹ Once ingested by zooplankton, barnacles, fish, or even whales, microplastics themselves can cause adverse effects such as decreased ingestion capacity and limitation of development and growth.^{110,111}

Transformation of micropollutants also impacts the results of risk assessment. The transformation processes in natural or engineered waters do not always lower the overall toxicity.^{112,113} For example, Wang et al. identified 50 transformation products from 21 pesticides and pharmaceuticals using nontarget analysis in three wastewater treatment plants, and 25 of them were predicted to be more toxic than their parent compounds.¹¹⁴ Besides, disinfection byproducts (DBPs), a group of compounds featured by relatively high toxicity can also form from disinfection of wastewater effluents.^{115–120} DBPs have been widely recognized as a public health or ecosystem issue due to their potential cytotoxicity, genotoxicity, carcinogenicity, developmental toxicity, and growth inhibition.^{78,121–129} However, the transformation products in either natural environments or water/wastewater treatment plants were often not considered in risk assessment, and thus they are not included in the prioritization in this review.

The RQ-based risk assessment provides a tentative prioritization order for the chemicals of concern, and the results need validating by further experimental evidence. It usually completely relies on the existing chemical monitoring data, suggesting that the prioritization order from the RQ-based method is restricted in the scope of the known chemicals as well as the predetermined endpoints. It is very likely that some important and unknown chemicals that contribute to the unexplained effects are neglected.¹³⁰ Therefore, a more reasonable risk assessment procedure would be that the RQ-based approach serves as the first estimation to indicate whether the risk presents or not, and experiment-based methods like EDA should be employed when needs arise.

7. RECOMMENDATIONS

The selection of representative micropollutants for evaluating the effectiveness of newly proposed methods or technologies is of great significance on reducing overall chemical pollution in global aquatic environments, while the attention assigned to this problem in the past decade is inconsistent with its importance. Through reviewing various prioritization approaches and searching on the Scopus database, this review compiled 83 prioritization case studies for micropollutants using the RQ method published in the past 10 years. A total of 473 compounds screened from thousands of micropollutants were reported to have risks, but the prioritization results varied somewhat among different areas. Therefore, we proposed a risk surrogate WARQ to provide a universal prioritization on the global scale by incorporating their risk intensity and frequency simultaneously. A ranked list comprising 53 micropollutants was

recommended to be the priority of concern in global aquatic environments, and future studies on their reduction and removal are warranted. This review provides a tentative answer for this important yet complicated problem, that is, which micropollutants or class of micropollutants should be removed or treated with higher priority. However, it should also be recognized that the relatively small prioritization database and the inherent limitations of the RQ method prevent us from drawing a better conclusion at present, but hopefully this review can attract more attention on this challenging problem and act as a small step toward a more satisfying answer.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acs.est.1c04250>.

Details about the information on the occurrence levels, PNEC and ADI values of frequently detected PPCPs, pesticides, and industrial chemicals in Supporting Information I (PDF)

Compiled case studies, micropollutants with RQ values higher than 1, the list of micropollutants involved in case studies, and micropollutants with potential risks reported in the past decade in Supporting Information II (Tables S4–S7) (XLSX)

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Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

The work was fully supported by grants from the Research Grants Council of the Hong Kong SAR, China (Projects 16212518, 16210221, T21-711/16-R, and T21-705/20-N).

ABBREVIATIONS

ADI	accepted daily intake
ARGs	antibiotic resistance genes
AF	assessment factor
ACF	atom-centered fragments
BW	body weight
CRPHR	consumption rate posing health risk
CBR	critical body residue
DBPs	disinfection byproducts
DWEL	drinking water equivalent level
DWI	drinking water intakes
EDA	effect-directed analysis
FOE	frequency of exposure
AB	gastrointestinal absorption rate
HQ	hazard quotient
KNN	<i>k</i> nearest neighbors
LCIA	life cycle impact assessment
LOQ	limits of quantification
LOAEL	lowest observable adverse effect level
MEC	measured environmental concentration
EC50	median effective concentration
NOECs	no observed effect concentrations
NSAIDs	nonsteroidal anti-inflammatory drugs
NOAEL	no observable adverse effect level
Kow	octanol–water partitioning coefficients
PFASs	per- and poly-fluoroalkyl substances
PFOS	perfluorooctanesulfonic acid
PBT	persistence, bioaccumulation, and toxicity
PPCPs	pharmaceuticals and personal care products
PCBs	polychlorinated biphenyls
PAHs	polycyclic aromatic hydrocarbons
PNEC	predicted no-effect concentration
QSAR	quantitative structure activity relationship
RI	ranking index
RQ	risk quotient
SSD	species sensitivity distribution
TU	toxic unit
UF	uncertainty factors
WARQ	weighted average risk quotient
W_x	weighting indexes

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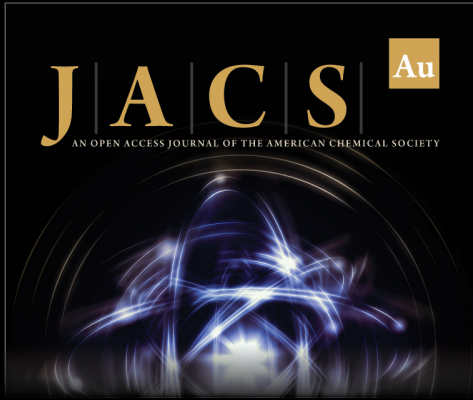
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