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Original Article

Seasonal Variation and Potential Environmental Risk of Pharmaceutical Residues in West Lake and Yen So Lake, Hanoi

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Abstract: This study investigated the occurrence and seasonal variation of 16 pharmaceutical residues including paracetamol (analgesic), ciprofloxacin, ofloxacin, norfloxacin (quinolones), sulfamethoxazole, trimethoprim (sulfonamides), carbamazepine (anticonvulsant), azithromycin, clarithromycin, roxithromycin, spiramycin (macrolides), cefotaxim (cephalosporins), tetracycline, doxycycline, oxytetracycline (tetracyclines), lincomycin (lincosamides) in surface water collected from West Lake (WL) and Yen So Lake (YSL), Hanoi. A total of 20 surface water samples were collected from each lake with a frequency of 5 samples every 3 months. The observation was performed for both rainy and dry seasons from January 2020 to December 2020 during the pandemic of Covid-19. The laboratory analyses revealed that pharmaceutical residues were widely distributed in these lakes. The total pharmaceutical concentration in YSL (21.3 – 49.9 µg/L) was higher than that in WL (15.7 – 38.6 µg/L). Among these, norfloxacin was detected at the highest concentration ranging from 0.83 – 21.2 µg/L and 0.61 – 17.3 µg/L in WL and YSL respectively while cefotaxime was not detected in WL and in 7/20 samples collected in YSL with concentration ranging from 0.05 – 2.1 µg/L. Total pharmaceutical concentrations were mostly observed significantly higher in the wet season than in the dry season for both lakes. The potential ecological risks of these compounds were also evaluated. Results showed that those compounds displayed from negligible to high risk. The result could provide the valuable situation of pharmaceutical residues in two main lakes in Hanoi and enhance the security information for humans living around these lakes.

Keywords: Pharmaceutical residues, seasonal variation, UPLC-MS/MS, surface water, ecological risks.

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1. Introduction

Pharmaceuticals have been widely used to save millions of lives through the prevention and treatment of diseases. Many studies have shown that these substances can cause harmful effects on organisms living in the environment, and more importantly, can lead to an increase in antibiotic resistance [1]. In the late 1990s, reports began to appear about the detection of pharmaceuticals and cosmetics in water sources, including groundwater and surface water [2, 3]. Initially, pharmaceutical residues (PRs) were of little concern because the concentrations of these substances were lower than those detected by laboratory analytical instruments or because the contaminants were believed to have been diluted by natural water and removed from water treatment plants. After use, pharmaceutical residues are expected to be discharged to the environment via wastewater treatment plants (WWTPs) [4, 5]. Previous studies reported that the WWTPs were effective for some pharmaceutical groups such as analgesics [6], fluoroquinolones [7, 8], sulfonamides [6, 9, 10] but were not for such compounds as carbamazepine [11, 12], erythromycin [6]. In addition, the WWTPs in Vietnam have abilities to treat around 10% of municipal wastewater, and wastewater is directly discharged to the environment via urban canals, rivers, lakes, and reservoirs [13, 14]. The interest gradually increased as three classes of drugs including endocrine, antibiotic, and antidepressant were found and reported [15]. Antibiotic resistance was recently a global problem and was particularly serious in Vietnam where the use of antibiotics is often uncontrolled [13, 16]. The occurrence of PRs was monitored in many developed countries as observed and reported such as China [17], Portugal [18], France [19], Germany [20, 21], and Japan [22]. In addition, several studies presented the levels of PRs in the water bodies of Vietnam. Among the works, the monitoring was mostly conducted on antibiotics in different water bodies including urban rivers and lakes [23-25], the Red River delta [26, 27], the Mekong delta [28, 29], and hospital waste treatment plants [14]. These studies showed that the PRs existed at varied concentrations from ng L^{-1} in rivers to µg L^{-1} ^{in} urban lakes, canals, and hospitals. However, these studies temporarily presented the contamination level at a period. Many factors affect the occurrence of PRs in water including the dilution factors in the rainy season, photo-degradation, activities of microbial, the seasonal diseases. This research aimed to investigate the seasonal variation of 16 PRs in West Lake and Yen So Lake which are two biggest lakes in Hanoi capital. In addition, ecological potential risks were also assessed through the Risk Quotients (RQs).

2. Materials and Methods

2.1. Chemicals, Reagents, and Materials

All target compounds (paracetamol – PAR, >99%; ciprofloxacin – CIP, >98%; ofloxacin – OFL, ≥98%; norfloxacin – NOR, ≥98%; sulfamethoxazole – SMX, ≥98%; trimethoprim – TMP, ≥98.5%; carbamazepine – CBZ, ≥98%; azithromycin – AZI, ≥98%; clarithromycin – CLA, ≥95%; roxithromycin - ROX, 95 – 102%; spiramycin – SPI, ≥90%; cefotaxime – CEF, ≥97%; tetracycline – TET, 98 – 102% doxycycline – DOX, ≥95%; oxytetracycline – OTC, 95 – 102%; lincomycin – LIN, 96 – 102%; were purchased from Sigma-Aldrich (Singapore). Organic solvents (acetonitrile - ACN, methanol -MeOH) and Na_2-EDTA were purchased from Fisher Scientific. Internal standard, ofloxacin-D_3 (OFL - D_3) 0.1 mg/mL in methanol, Paracetamol-D_4 (PAR-D_4) 1.0 mg/mL in methanol and sulfamethoxazole-$^{13}C_6$ (SMX-$^{13}C_6$) 1.0 mg/mL in methanol were purchased from Toronto Research Chemicals (TRC, Toronto, Canada). Formic acid (FA) (100%, Optima MS grade) and 25% ammonium hydroxide solution (reagent grade) were provided by Merck (Germany). Oasis hydrophilic-lipophilic balance (HLB, 6 cc, 200 mg) solid phase extraction cartridges were purchased from Waters (USA). The ultrapure water (UPW, 18.2 MΩ.cm) was produced from the GENPURE UV water purification system (Thermoscientific, England) and was used throughout this study.

2.2. Studied Sites and Sample Collection

This study focuses on monitoring the contamination level of PRs in two biggest lakes located in Hanoi's capital during the pandemic of COVID-19. The WL located in the North of Hanoi is the biggest natural lake in Hanoi with more than 530 ha of surface area while the YSL located in the South of Hanoi was renewed with a surface of 132 ha (a complex of 5 small lakes). These lakes receive a significant volume of municipal wastewater from hotels, restaurants, households, and even hospitals. The monitoring was performed from January 2020 to December 2020 with a frequency of every 3 months. There were a total of 20 surface water samples collected from each lake (5 fixed stations for each) according to the protocol from Vietnamese standard TCVN No.6663 - 6:2018. The sampling location was mapped as in Figure 1.

Figure 1. Sampling locations in West Lake and Yen So Lake.

At each sampling station, 1 L of surface water was collected and kept in glass bottles pre-baked at 450 ^{o}C for 6 h to eliminate impurities and rinsed several times with field samples. Samples were then transferred in cold conditions (icebox) to the laboratory within the day. At the laboratory, samples were filtered using a GF/F filter (Whatman, Ø=47 mm, pore size < 0.7 µm, pre-baked at 450 ^{o}C, 6 hour) with the help of a vacuum pump. The filtered samples were stored at 4 ^{o}C and analyzed within 48 hours or stored at -80 ^{o}C for further analysis.

2.3. Analytical Methods

2.3.1. Chromatographic Conditions

An ultra-high performance liquid chromatograph (ACQUITY UPLC, H-class, Waters, USA) combined with a mass spectrometer in tandem (Xevo - TQD, Waters, USA) was used for the analysis. The target analytes were separated on a reserved phase C18 column (BEH, C18, 100 × 2.1 mm, 1.7 µm particle size). The mobile phases consisted of 0.5% formic acid in UPW (phase A) and 0.5% formic acid in ACN (phase B). The gradients were started at 90% phase A followed by a linear decrease to 65% at 10 minutes, then linearly dropped down to 5% from 10 to 11 minutes and kept at this condition for 2 minutes before returning to the initial condition for the next injection. The total time of each analysis lasted for 16 minutes. The flow rate and the column temperature were constantly kept at 0.3 mL.min^{-1} and 35 ^{o}C, respectively. The injection volume was set at 10 µL using an auto-sampler. The analytes were identified and quantified by a multiple reaction monitoring (MRM) mode followed by positive electrospray ionization (+ESI). Each compound was tracked using two MRM transitions: the higher signal was employed for quantification, while the lower signal served for confirmation. The target analyte identification relied on their retention time, two transitions, and the relative ratio of two transitions. The source parameters were also optimized to achieve the optimal conditions such as desolvation temperature at 500 °C, source temperature at 150 °C, desolvation gas flow at 1000 L h^{-1}, cone gas flow at 10 L h^{-1}, and capillary voltage at 3.0 kV. All cone voltages (CV) and collision energies (EV) applied to individual analytes are detailed in Table 1.

2.3.2. Sample Preparation

The preparation of samples was adapted from our previous studies [30, 31]. Briefly, surface water samples were thawed and left at room temperature before experimenting. Isotope-labeled internal standards (OFL-D_3, PAR-D_4, SMX-$^{13}C_6$) were added to the sample to obtain a final concentration of 50 µg/L. The HLB SPE cartridges were conditioned with 5 mL of ACN and then with 5 mL UPW at pH 5. After the conditioning step, 200 mL of surface water samples to which 8.32 mL of 0.25 M EDTA was added at pH 5 were percolated through the cartridge at a flow rate of 10 - 12 mL/min. Afterward, HLB SPE cartridges were washed with 5 mL of ultrapure water at pH 5 to remove interferences and dried for 60 min under vacuum to remove excess water. The elution step was performed with 5 mL of the H_2O/ACN mixture (40/60, v/v. The eluents were evaporated under a gentle stream of nitrogen until dryness and then reconstituted to 1 mL of H_2O/ACN (90/10, v/v). Finally, the solutions were filtered using a syringe with a 0.2 µm pore size and injected into the UPLC-MS/MS system under optimal operating conditions.

Table 1. Operating conditions for all target analytes on MSMS detector. (*) quantification ions

Compound	Retention time (min)	Precursor ion (m/z)	Product ions (m/z)	CV (V)	CE (eV)
AZI	9.61	375	116.3	35	25
			158.1*		25
CBZ	12.62	236.9	178.9	42	34
			193.7*		36
CEF	3.92	456	396.1	30	46
			125.3*		8
CIP	5.56	332.1	288.1	42	18
			314.1*		22
CLA	13.07	748.5	158	30	30
			590.4*		20
DOX	4.4	445.1	428.1	35	25
			410.1*		20
LIN	3.05	407.2	359.1	42	24
			126.2*		20
NOR	5.28	320.2	276.1	40	22
			302.0*		22
OFL	5.37	362.3	261.3	25	20
			318.3*		20
OTC	3.78	461.1	426.1*	30	20
			443.2		13
PAR	2.43	151.9	92.8	30	22
			109.9*		18
ROX	13.08	837.5	158	30	35
			679.3*		20
SMX	7.57	253.9	92	34	26
			155.9*		16

SPI	3.29	843	174.0*	64	44
			100		38
TET	4.42	445.1	154.1*	36	28
			98		42
TMP	5.14	291	229.9	28	24
			260.9*		24
OFL-D_3	5.37	365	321.1	55	20
PAR-D_4	2.43	156	114	30	15
SMX-$^{13}C_6$	7.57	260	98.1	38	28

2.3.3. Method Validation, Quality Control

The method validation was evaluated for various parameters, including linear range, method detection limit (MDL), instrument detection limit (IDL), and correlation [32]. The linear range was investigated over a six-point calibration ranging from 5 to 500 µg/L. The linearity of all target analytes was in the range of 0.990 – 0.999. MDLs and MQLs were determined using a signal-to-noise ratio of 3 and 10, respectively, and on a real sample matrix. If any compound was not detected in the real sample, the MDL and MQL were calculated based on the spiked sample. The sample volume for extraction was 200 mL. The MDLs were from 0.9 ng/L (CLA) to 203ng/L (DOX). The quality control was examined by injecting a 200 µg/L standard after every 10 injections to control the signal stability. A solvent injection was also injected after every 5 samples to ensure no cross-contamination during the analysis. The spiked samples at 50 ng/L in ultrapure water were performed in triplicate by the same protocol to investigate the recovery. The recoveries of target analytes were from 71 – 125% which is in the acceptable range for analyzing pharmaceutical residues in surface water [33, 34]

2.4. Ecological Risk Assessment

The ecological risk assessment of PRs was evaluated based on Risk quotients (RQs) that were calculated as quotients of Maximum Measured Environmental Concentration (MEC_{max}) and Predicted No Effect Concentration (PNEC) (eq. 1). The lowest threshold values of PNEC for freshwater ecosystems were sourced from the NORMAN Ecotoxicology Database [35].

Eq1: $$RQ = \frac{MEC\ max}{lowest\ PNEC}$$

RQs were classified as negligible risk (RQ<0.01), low risk (0.01<RQ≤0.1), moderate risk (0.1<RQ≤1), and high risk (RQ>1) [36].

3. Results and Discussion

3.1. Occurrence of Pharmaceutical Residues

The total concentration of 16 pharmaceutical residues from WL and YSL was demonstrated in Figure 2. The median concentrations of pharmaceuticals in the surface water of WL are mainly around 20 µg/L, whereas in YSL, the median concentrations are higher at around 30 µg/L. The spread of the concentrations in WL indicates less variability of pharmaceutical residues. In contrast, YSL has a wide distribution, which points to greater variability in the concentration levels, possibly due to differing pollution sources or environmental conditions. This suggests that there may be greater variability and a higher concentration of certain pharmaceutical compounds in YSL compared to WL, on average. Notably, fluoroquinolones and macrolides are the most frequently detected compounds in both lakes, exhibiting significant concentrations. Furthermore, SUL shows a relatively high concentration in YSL but is almost absent in WL. Duong et al., (2021) also found that the concentration of 15 antibiotics was significantly higher in YSL compared to WL, with values ranging from 101 to 1,753 ng/L in YSL and 40.3 to 674.0 ng/L in WL. This discrepancy is likely due to YSL receiving larger volumes of both treated and untreated wastewater from major urban rivers such as the Set, Kim Nguu, and To Lich Rivers, while WL experiences lower levels of such contamination [24]. In addition, similar concentration levels of PRs in urban rivers and lakes in Hanoi were also reported [14, 25, 37].

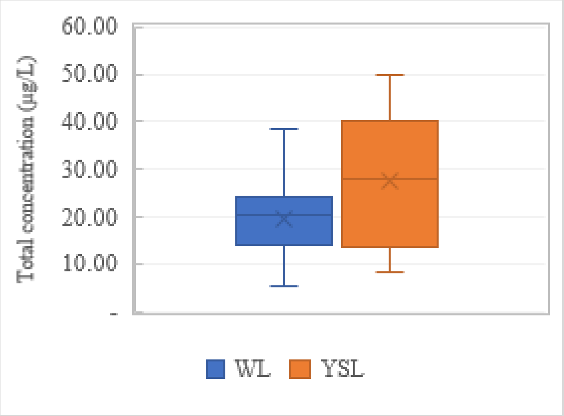

Figure 2. The total concentration of 16 pharmaceutical compounds in WL and YSL.

3.2. Seasonal Variation

Quinolones: Three fluoroquinolones (OFL, CIP, NOR) were detected at 0.39 - 12.35 µg/L, depending on the specific compound, lake, and season. All the compounds exhibited a very high detection frequency (DF), from 90% to 100%. Fluoroquinolones in Lake Victoria, Uganda also showed similar detection frequencies but at relatively lower concentrations [38]. NOR was the most prevalent, with concentrations ranging from 6.68 - 12.35 µg/L in WL and 6.31 - 12.21 µg/L in YSL. This compound showed a clear seasonal variation, with concentrations nearly doubling during the wet season compared to the dry season in both lakes. The concentration of NOR peaks in rainy months. In contrast, OFL and CIP were found at lower concentrations and minor seasonal change. OFL also showed a tendency to increase during the wet season as seen in WL where mean concentrations reached 0.50 µg/L. Meanwhile, OFL concentrations in YSL decreased slightly from 1.73 to 1.01 µg/L, a reduction of approximately 0.5% from the dry to the wet season. Similarly, CIP concentrations also declined slightly from the dry to the wet season in both lakes. Overall, these variations suggest that seasonal changes significantly influence the distribution of fluoroquinolones in these lakes, with wet season conditions generally leading to higher concentrations for most compounds, except in specific cases like OFL and CIP in YSL.

Macrolides: Macrolides were the most frequently detected antibiotics, with a DF of 100%, except SPI in WL. In general, the average concentrations of macrolide antibiotics were relatively low from 0.16 µg/L (SPI) to 2.06 (ROX), with slightly higher levels detected in YSL compared to WL. These concentration levels were coherent with the previous research [23, 25]. In WL, most macrolides exhibited an increasing trend during the wet season. The only exception was SPI, where the concentrations did not change much under the influence of the season. A similar pattern was observed in YSL, where all macrolides except AZI had higher concentrations in the wet season. AZI, on the other hand, decreased from an average concentration of 1.98 µg/L in the dry season to 1.47 µg/L in the wet season. While seasonal factors generally lead to higher concentrations of macrolides, specific compounds like SPI and AZI may respond differently, indicating a more complex interaction with environmental conditions or the use in treating diseases.

Tetracyclines: The average concentrations of tetracyclines were detected between 0.44 and 1.83 µg/L, but they exhibited a high frequency of detection, exceeding 90%. These antibiotics were also detected with high frequency but low concentrations in Baiyangdian Lake [39]. The occurrence at low concentrations may be because tetracyclines are not as widely available in Vietnam as other antibiotics including beta-lactams, macrolides, and fluoroquinolones, and their high potential for interactions with the surrounding environment, such as photo-degradation, complex formation with metal cations, and sorption to sediments [25]. This group of compounds showed minimal seasonal variation, particularly in YSL where the concentrations of TET, OTC, and DOX are slightly higher in the wet season. However, in WL, the seasonal influence was more pronounced for TET and OTC, though they exhibited different trends. TET had a higher average concentration in the dry season (1.44 µg/L) and a lower concentration in the wet season (0.51 µg/L). Conversely, OTC concentrations increased from 0.99 µg/L in the dry season to 1.31 µg/L in the wet season. Overall, while tetracyclines generally maintain stable concentrations, specific compounds like TET and OTC may be more sensitive to seasonal changes, particularly in WL.

Sulfonamide: SMX and TMP were detected frequently, with detection frequencies (DF) exceeding 80%, and both exhibited higher concentrations in, YSL compared to WL. Similarly, SMX and TRI were also reported with similar mean concentrations, 0.258 µg/L, and 0.128 µg/L, respectively, in the Asia and Pacific regions [40]. Their seasonal concentration trends were also similar. In WL, no significant variation was observed between the dry and wet seasons. However, in YSL, SMX shows a significant seasonal variation, with a much higher concentration in the dry season (5.54 µg/L to 1.07 µg/L in the wet season). Meanwhile, TMP decreases in the wet season (0.37 to 0.19 µg/L). The opposite trend of SMX and TMP may be due to the differing concentrations in the input in wet seasons [41]. SMX and TMP are more concentrated during the dry season in YSL, while seasonal effects are less pronounced in WL.

Table 2. Seasonal variation of pharmaceutical residues
(FQs: Fluoroquinolones; MCs: Macrolides; SNs: Sulfonamides; TETs: Tetracyclines)

Groups	Analytes	WL (µg/L)		YSL (µg/L)	
		Dry (n=10)	Wet (n=10)	Dry (n=10)	Wet (n=10)
FQs	OFL	0.39(0.18-0.59)	0.5(0.26-0.74)	1.73(0.35-3.65)	1.01(0.5-1.82)
	CIP	2.49(ND-9.69)	1.29(0.03-2.82)	3.45(0.48-15.33)	3.03(0.66-12.87)
	NOR	6.68(0.83-21.16)	12.35(7.65-19.24)	6.31(0.61-15.07)	12.21(8.39-17.29)
MCs	AZI	0.80(0.33-1.50)	1.12(0.72-1.76)	1.98(1.04-4.25)	1.47(0.85-2.53)
	CLA	0.58(0.04-1.56)	1.07(0.81-1.92)	1.14(0.02-3.21)	1.72(0.96-2.81)
	ROX	0.95(0.07-2.24)	1.77(1.4-3.38)	1.06(0.12-2.75)	2.06(1.40-3.40)
	SPI	0.29(ND-1.25)	0.24(0.09-0.93)	0.16(ND-0.66)	0.30(0.03-1.11)
SNs	SMX	0.3(0.16-0.43)	0.27(0.12-0.59)	5.54(0.08-14.08)	1.07(0.08-3.32)
	TMP	0.07(0.03-0.15)	0.07(0.04-0.11)	0.37(0.07-0.71)	0.19(0.06-0.41)
TETs	TET	1.44(ND-8.17)	0.51(0.31-0.66)	0.44(0.26-0.66)	0.51(0.1-0.71)
	OTC	0.99(0.78-1.31)	1.31(0.92-1.89)	1.25(0.74-1.63)	1.44(0.24-2.12)
	DOX	1.31(1.02-1.87)	1.4(0.11-1.93)	1.7(0.93-2.18)	1.83(0.15-3.2)
Others	PAR	0.28(ND-0.82)	0.3(0.04-1.86)	0.35(0.13-0.93)	0.85(0.02-5.61)
	CBZ	0.44(0.33-0.58)	0.3(0.06-0.53)	0.85(0.54-1.33)	0.59(0.21-1)
	CEF	ND	ND	0.13(ND-0.3)	1.19(0.21-2.16)
	LIN	0.19(0.02-0.35)	9.8	0.03(0.01-0.06)	0.21(0.01-0.68)

Other pharmaceutical residues (PAR, CBZ, CEF, LIN): The anticonvulsant CBX was detected in all samples with concentrations consistently below 1.33 µg/L. CBX was also reported with similar frequencies in Lake Mälaren, Sweden but at low concentrations, ranging from 83.6 to 99.7 ng/L [42]. Similar results were found with concentrations ranging from 3.3 to 128.2 ng/L in the Nansi Lake Basin [43]. Despite higher concentrations in YSL than in WL, both exhibited a trend of lower concentrations during the wet season. This decrease was modest, with the average concentration dropping from 0.44 µg/L to 0.30 µg/L in WL and from 0.85 µg/L to 0.59 µg/L in YSL. It highlights the omnipresence of CBX in both lakes, while also indicating that seasonal variation affects its levels more in YSL. PAR also showed high detection frequencies, with DF = 90% in WL and 100% in YSL. However, in WL, this substance did not exhibit significant changes between the dry and wet seasons. In YSL, by contrast, the average concentration during the wet season (0.85 µg/L) was markedly higher than in the dry season (0.35 µg/L), suggesting a strong seasonal influence in this lake. The remaining two substances, LIN and CEF, had the lowest detection frequencies. CEF was only detected in YSL, with a DF of 20%. The low concentration of cephalosporins antibiotics in water environments may be due to the susceptibility to attenuation mechanisms such as hydrolysis and photolysis [44]. This compound exhibited a clear seasonal variation, with a higher average concentration in the wet season (1.19 µg/L) compared to the dry season (0.13 µg/L). LIN, on the other hand, had a DF of just 15% in WL but also showed a significant seasonal effect. Its average concentration increased dramatically from 0.19 µg/L in the dry season to 9.8 µg/L in the wet season. In YSL, LIN was detected more frequently, with a DF of 60%, and similarly exhibited a seasonal increase, rising from 0.03 µg/L in the dry season to 0.21 µg/L in the wet season. These findings suggest that LIN and CEF, though detected less frequently, are highly influenced by seasonal changes, with concentrations notably higher during the wet season, especially in YSL.

3.3. Ecological Risk Ssessments

The ecological risks were assessed based on the risk quotient, calculated from the maximum measured environmental concentration. The RQs were evaluated in Table 3. In YSL, a total of 11 substances exhibited risk quotient deemed to be of significant concern, with concentrations surpassing the lowest PNEC by factors ranging from 2 to an alarming 155 times. Among these substances, ciprofloxacin (CIP) stood out, reaching particularly hazardous levels, underscoring the critical need for further investigation and mitigation in this environment. By contrast, WL showed high-risk factors for 8 substances, with NOR presenting the most serious potential for environmental harm. The findings indicate that both lakes are subject to considerable pharmaceutical contamination, but the degree of risk in YSL appears to be notably more pronounced. A closer examination reveals that antibiotics, particularly those belonging to the fluoroquinolone, macrolide, and tetracycline families, alongside sulfonamides (SUL) and cephalosporins (CEF), exert significant ecological pressure on both lakes. These classes of pharmaceuticals, known for their persistence and bioactivity in aquatic environments, pose an undeniable threat to the health of the ecosystems. Notably, in YSL, substances such as ofloxacin (OFL), SUL, and CEF demonstrated even higher risk factors compared to WL, suggesting that YSL is subject to more intense pollution, likely due to greater exposure to pharmaceutical discharges, either from urban runoff or other anthropogenic sources.

In contrast, only a small number of pharmaceuticals were classified as having low-risk factors, primarily in WL. Among these, cephalexin (CEF) and trimethoprim (TRI) stood out, with their concentrations remaining relatively low and well below the risk thresholds established by the PNEC. This marked difference between the lakes may suggest a more favorable environmental status for WL, where pollution levels are relatively lower, and the ecosystem appears to be more resilient to pharmaceutical contamination. The ecosystems of WL and YSL both are under pharmaceutical pollution; however, it is very alarming in YSL, as more substances are found to have a high-risk quotient. Such high concentrations and related risk quotients in YSL do require immediate concern and point to the need for more stringent regulatory measures, better waste management practices, and further monitoring activities to protect the aquatic environment from further degradation. WL would relatively be at a better state, though not free from pharmaceutical contamination, and calls for continued vigilance to avoid further deterioration.

Table 3. The maximum MEC, lowest PNEC, and their RQs in the WL and the YSL

Compounds	MEC max (µg/L)		Lowest PNEC freshwater (µg/L)	RQ code	
	WL	YSL		WL	YSL
PAR	1.86	5.61	14.1	🟧	🟧
OFL	0.74	3.65	1.4	🟧	🟥
CIP	9.69	15.33	0.1	🟥	🟥
NOR	21.26	17.29	0.2	🟥	🟥
SUL	0.59	14.08	0.6	🟧	🟥
TMP	0.15	0.41	120.0	🟩	🟩
CAR	0.58	1.33	2.0	🟧	🟧
AZI	1.76	4.25	0.0	🟥	🟥
CLA	1.92	3.21	0.1	🟥	🟥
ROX	3.38	3.40	0.0	🟥	🟥
SPI	1.25	0.66	0.1	🟥	🟥
TET	8.17	0.71	0.1	🟥	🟥
OXY	1.89	2.12	10.0	🟧	🟧
DOX	1.93	3.20	0.2	🟥	🟥
CEF	ND	2.16	1.2	🟩	🟥
LIN	0.35	0.68	4.0	🟨	🟧

🟥	🟧	🟨	🟩
High risk ($RQ>1$)	Medium risk ($0.1 < RQ \leq 1$)	Low risk ($0.01<RQ\leq0.1$)	Negligible risk $RQ\leq0.01$

4. Conclusion

This study evaluated the occurrence and seasonal variation of 16 pharmaceutical residues belonging to 8 groups in surface water collected from two biggest lakes in Hanoi. Of these, 14/16 compounds were found at high detection frequency except CEF (not detected in WL, 4/20 samples in YSL) and LIN (detected in only 3/20 samples from WL and 12/20 samples from YSL). The concentration of detected PRs was typically in µg/L level. The highest concentration was found for NOR (12.21 µg/L, DF = 100%). Higher concentration levels were mostly observed in the wet season than in the dry season except for some compounds (CBZ, CIP, SMX, and TMP) which were observed as a reversed trend. The RQs calculated for all PRs varied from 0 (TMP) to 224 (AZI), suggesting that their potential for ecological risk was from negligible to significant risks. This study contributes valuable information toward enhancing comprehension regarding the occurrence and potential risks associated with PRs in surface water in closed systems of Hanoi. Long-term monitoring is recommended to control the water quality from these two lakes which serve as a detention basin for millions of inhabitant surrounding.

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