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Evaluation the pharmaceutical residue risks in Tigris River in Wasit Governorate, Iraq

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Abstract

The objective of the present study was to evaluate the risks associated with pharmaceutical residues in the surface water of the Tigris River located in the Wasit Governorate of Iraq. This research provided a comprehensive analysis encompassing physical, chemical, and microbiological parameters of the surface water along the Tigris River during the study period from October 2023 to July 2024. The findings included minimum, maximum, average, and standard deviation values for each parameter assessed. Given the critical issue of pharmaceutical contamination in the aquatic environment of the Tigris River, a total of 17 different pharmaceuticals were identified in the surface water of the Wasit Governorate, Iraq. The pharmaceuticals classified as high risk (HQ ≥ 1.0) include acetaminophen (an analgesic), caffeine (a stimulant), ibuprofen, clofibric acid, sulfachloropyridazine, thiabendazole, hydrochlorothiazide, paraxanthine, and paroxetine. Given their considerable ecological risk, these pharmaceuticals warrant an in-depth evaluation. This process should involve continuous monitoring of their levels in surface water, a careful assessment of the risks posed to aquatic organisms (addressing both chronic and acute toxicity), and the investigation of potential removal strategies from surface water, as well as sustainable management practices.

Keywords: Assessment of pharmaceutical residues; Associated risks; Tigris River; Wasit Governorate; Iraq

1. Introduction

Pharmacologically active compounds (PhACs) are essential for the restoration and preservation of human health, as they are widely employed in the diagnosis, treatment, alleviation, and prevention of various diseases. These compounds can be classified into different therapeutic categories based on their functions and mechanisms of action within the body, such as anti-inflammatories, lipid regulators, antibiotics, antidepressants, chemotherapeutic agents, and endocrine regulators. In recent decades, advancements in medicine have led to a substantial rise in the global usage of PhACs [1,2].

In 2003, the estimated global consumption of antibiotics was already between 100,000 and 200,000 tons. By 2014, worldwide pharmaceutical revenues surpassed one trillion US dollars. Among the most commonly utilized therapeutic classes are chemotherapeutic agents, antibiotics, and anti-inflammatory medications. By 2015, revenues from cancer treatments approached $79 billion on a global scale. Other significant therapeutic categories include analgesics, antihypertensives, and antidiabetic medications [3,4].

The properties of pharmaceutical active compounds (PhACs) play a crucial role in improving human health; however, they also present a risk as potential environmental contaminants. After ingestion, these compounds are not fully metabolized and are excreted through urine and feces. Consequently, PhACs enter municipal sewage systems, flow into wastewater treatment plants (WWTP), and eventually reach receiving water bodies, as traditional treatment methods are inadequate for their total elimination [5,6]. Significant sources of contamination by pharmaceutical active compounds (PhACs) also encompass discharges from pharmaceutical production facilities and agricultural practices

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involving livestock. A multitude of research studies have recorded the occurrence of PhACs in the effluents of wastewater treatment plants (WWTPs) and in both natural surface water and groundwater, with concentration levels ranging from nanograms per liter (ng/L) to micrograms per liter (µg/L) [6,7]. In his research, Godoy (2014) compiled findings from various scholars who examined the occurrence of pharmaceuticals in aquatic ecosystems between 2003 and 2011 across several countries, including the United Kingdom, India, Spain, the United States, France, Brazil, Austria, and Sweden. More than 30 distinct active compounds from 14 different categories of pharmaceuticals have been identified [8,9].

The World Health Organization (WHO, 1999) characterizes risk assessment as a methodical approach that facilitates the quantitative evaluation and forecasting of negative health impacts on a specific population due to exposure to a substance at a specified concentration. The European Medicines Agency (EMEA) and the US Food and Drug Administration (FDA) have developed protocols for performing environmental risk assessments (ERA) for both novel and existing chemicals. These protocols are based on the relationship between exposure and effect, which is measured using the hazard quotient (HQ). This quotient is derived from the ratio of the measured environmental concentration (MEC) to the predicted non-effect concentration (PNEC). An elevated HQ signifies a greater likelihood that the pharmaceutical active compound (PhAC) may result in toxicological effects [10,11].

The methodology for risk assessment is crucial in evaluating whether the presence of pharmaceutical and personal care products (PhACs) in surface water poses a threat to both aquatic ecosystems and human health. This evaluation is vital for determining the necessity of regulatory measures by environmental agencies and legislation. However, despite its significance, there is a notable scarcity of studies addressing the toxicological risk assessment of PhACs in the international literature [12,13]. Furthermore, existing research is often constrained by the geographic areas studied and the quality of the toxicological data available [14,15]. Some investigations have indeed conducted risk assessments of PhACs in surface waters.

Pharmaceuticals and personal care products (PhACs) predominantly enter aquatic ecosystems via the effluent released from wastewater treatment facilities (WWTP)[16,17]. Other sources of contamination include untreated or insufficiently treated discharges from the pharmaceutical industry and healthcare facilities, improper medication disposal, waste and effluents from livestock operations, as well as the disposal of untreated sewage [18,19]. Upon entering the environment, pharmaceutical and personal care products (PhACs) can experience natural attenuation processes. These processes may include dilution, sorption, or chemical transformation, all of which are affected by the physical and chemical properties of the compounds, such as their water solubility, lipophilicity, and vapor pressure. Additionally, environmental factors such as pH, temperature, and ionic strength play a significant role in these processes [20,21]. The negative effects of these substances have been recorded in global literature since the 1990s, demonstrating their ability to harm ecosystems even at concentrations as minimal as nanograms per liter [22,23]. Drinking water treatment plants (DWTP) can act as a safeguard against the reintroduction of pharmaceutical contaminants (PhACs) into the human body; however, current research indicates that these treatment methods do not consistently ensure the total elimination of PhACs [24,25,26].

Clinical testing offers an extensive insight into the biological impacts of pharmaceuticals on human subjects; however, uncertainties persist concerning the environmental hazards posed by pharmaceutical contaminants (PhACs). These uncertainties stem from a lack of comprehensive understanding regarding their environmental fate and behavior, which encompasses factors such as uptake, metabolism, and excretion rates (pharmacokinetics), in addition to their target affinity and functional effects (pharmacodynamics) [27,28]. Additionally, the long-term effects of indirect exposure through drinking water are not well understood.

The movement towards conducting specific ecological risk assessments for pharmaceuticals began in the late 1960s, when the US Food and Drug Administration (FDA) required a basic evaluation of new medications as a component of the licensing procedure in the United States. This process has undergone numerous revisions and enhancements over the years, ultimately resulting in the guidelines presented in the document entitled 'Guidance for Industry: Environmental Assessment of Human Drugs and Biologics Applications' [29,30]. These principles continue to be relevant in the present day. Concurrently, the European Medicines Agency (EMEA) has developed guidelines for performing risk assessments. Originally founded on Directive 65/65/EEC and later revised in 93/39/EEC, the methodology has undergone ongoing improvements, culminating in the release of the "Guideline on the Environmental Risk Assessment of Medicinal Products for Human Use." [31,32].

After ingestion, pharmaceutical active compounds (PhACs) are metabolized and then excreted in both their original form and as a range of metabolites. The effectiveness of their removal in wastewater treatment plants (WWTP) and drinking water treatment plants (DWTP) varies considerably, which can be attributed to their unique physicochemical

properties and degradability [33,34]. Inadequate removal procedures result in the identification of pharmaceutical active compounds (PhACs) in both surface and potable water sources. Recent studies have uncovered the existence of PhACs in aquatic ecosystems, with concentrations varying from nanograms per liter (ng/L) to micrograms per liter (µg/L). A review conducted in 2011 by the German Federal Environment Agency (UBA) reported on environmental monitoring activities in Germany, which revealed a total of 156 pharmaceuticals present in surface water, groundwater, and drinking water [35,36]. On an international level, numerous review articles have underscored the monitoring of PhACs in aquatic systems across the European Union the United, China, and the United Kingdom [37,38,39] , illustrating the frequency of detection of these compounds. Godoy (2014) [22] aggregated data from 2003 to 2011 across the United Kingdom, India, Spain, the United States, France, Brazil, Austria, and Sweden, demonstrating the pervasive contamination of natural waters by PhACs. According to the findings of Petrie et al. (2015), the therapeutic classes that have been most extensively studied include non-steroidal anti-inflammatory drugs (NSAIDs), beta-blockers, antidepressants, and antibiotics.

2. Material and methods

Figure 1 Sampling site of Tigris River, along of Wasit Governorate

Water samples were obtained from the Tigris River within the Wasit Governorate during the designated study period. The samples were collected in bottle containers that had been thoroughly cleaned by washing with a non-ionic detergent, rinsing with tap water, soaking in a 5% HNO_3 solution for 24 hours, and finally rinsing with deionised water before use. Prior to sampling, the bottles were rinsed three times with the water to be sampled before being filled. Each sample was properly identified and labeled at the point of collection and subsequently transported to the laboratory for analysis. All physical, chemical, and microbial analyses were conducted in accordance with standard methods for water and wastewater (APHA, 2017) [10].

The chromatographic injections were conducted utilizing High-Performance Liquid Chromatography (HPLC) with the Agilent 1260 Infinity system (USA), featuring an automatic injector valve with a capacity of 20 µL. The UV-visible photodiode array detector, model Surveyor PDA, was equipped with a quartz cell that has an optical path length of 5.0 cm, ensuring superior data quality. The 1260 Infinity II Diode Array Detector HS provides enhanced sensitivity and improved data quality, instilling greater confidence in the results. The HPLC system was outfitted with a C18 ODS column measuring 250 × 4.6 mm (internal diameter), complemented by a guard column of C18 ODS measuring 10 × 4.0 mm (internal diameter). Both columns contained particles with a pore size of 5 microns and a carbon content of 15.5%. Prior to the first injection and following the final injection of the day, the column was thoroughly cleaned with ultrapure water for duration of 30 minutes at a flow rate of 0.5 mL min^{-1}. The initial conditioning of the stationary phase involved the passage of the mobile phase through the column for 25 minutes at a flow rate of 1.2 mL min^{-1}. Following the injection of standards or samples (20 µL), the separation process commenced. The temperature was maintained at 25 °C, with a detection wavelength set at 222 nm. After each analytical run, the column was reconditioned for 10 minutes using the mobile phase at a flow rate of 1.0 mL min^{-1}. The concentrations of the various pharmaceuticals examined were determined using a calibration curve derived from the linear equation y = mx + c. The antibiotics analyzed in this study fall within the same range as the prepared standard curve, thereby facilitating their concentration calculations.

3. Results and discussion

The study aimed to evaluate the risks associated with some pharmaceutical residue in the Tigris River along of Wasit Governorate, Iraq.

Table 1 Physical & chemical analysis of Tigris River water, Wasit Governorate, Iraq during the study (Min-Max, Avg and Sd) (Oct. 2023 to Jul. 2024)

No.	Water Parameter	Unit	Months (2023-2024)			
			Min.	Max.	Avg.	Sd
1	Temperature	0C	11	34	23	7.7
2	pH	-	6.8	8.1	7.8	23.1
3	DO	mg/l	5.4	7.2	6.5	13.4
4	Turbidity	NTU	244	359	275	31.2
5	Conductivity	µS/cm	612	1080	852	24.2
6	TDS	mg/l	368	648	514	24.1
7	Total Hardness	mg/l	206	388	278	14.2
8	Calcium hardness	mg/l	132	224	178	13.8
9	Magnesium hardness	mg/l	74	164	100	14.1
10	Chloride	mg/l	64	112	86	19.2
11	Sulphate	mg/l	74.1	266	184	41.2
12	Alkalinity	mg/l	89	132	114	19.4
13	Ammonia	mg/l	0.3	0.71	0.52	52.1
14	Nitrite	mg/l	0.02	0.06	0.05	13.1
15	Nitrate	mg/l	0.68	1.47	1.12	14.6
16	Phosphate	mg/l	0.2	0.31	0.19	11.3
17	Silicate	mg/l	6.31	12.2	8.4	29.6
18	Aluminum (residual)	mg/l	0.02	0.08	0.06	4.8
19	Iron	mg/l	0.14	0.48	0.38	47.2
20	Manganese	mg/l	0.03	0.14	0.1	14.8

21	TSS	mg/l	184	243	198	34.5
22	COD	mg/l	5.2	11.3	7.8	14.8
23	BOD	mg/l	3.8	8.6	6.2	11.2
24	Total Bacterial Count	CFU/ml	23500	114600	79200	43.8
25	Total Coliform	CFU/ml	5800	14600	11200	34.6
26	Fecal Coliform	CFU/ml	1850	4600	3450	29.4
27	Total Algal count	U/ml	312	945	614	23.6
28	Parasite	U/l	3	13	7	18.2

Tables (1) illustrate the physical, chemical, and microbiological analyses of the surface water from the Tigris River, located in the Wasit Governorate, were conducted during the study period from October 2023 to July 2024. The results presented the minimum, maximum, average, and standard deviation for each parameter assessed. The pH levels of the water were found to range between 6.8 and 8.1, with an average of 7.8 and a standard deviation of 23.1. The dissolved oxygen (DO) values varied from 5.4 to 7.2 mg/l, yielding an average of 6.5 mg/l and a standard deviation of 13.4.

Furthermore, turbidity measurements indicated a range from 244 to 359 NTU, with an average of 275 NTU and a standard deviation of 31.2. The conductivity and total dissolved solids (TDS) values were recorded between 612 and 1080 µS/cm and 368 to 648 mg/l, respectively, with average values of 852 µS/cm and 514 mg/l, and standard deviations of 24.2 and 13.4.

In terms of ammonia concentration, the data revealed a range from 0.3 to 0.71 mg/l, with an average of 0.52 mg/l and a standard deviation of 52.1. The chemical oxygen demand (COD) and biochemical oxygen demand (BOD) values ranged from 5.2 to 11.3 mg/l and 3.8 to 8.6 mg/l, respectively, with average values of 7.8 mg/l and 6.2 mg/l, and standard deviations of 14.8 and 11.2.

Lastly, the bacteriological analysis showed that the total bacterial count varied from 5800 to 114600 CFU/ml, with an average of 79200 CFU/ml and a standard deviation of 43.8. The total algal count ranged from 312 to 945 U/ml, with an average of 614 U/ml and a standard deviation of 23.6.

Table 2 Pharmaceuticals residue in the Tigris River water, Wasit Governorate, Iraq (Oct. 2023 to Jul. 2024)

No.	**Pharmaceutical Compounds**	**Unit**	**Months (2023-2024)**									
			Oct.	**Nov.**	**Dec.**	**Jan.**	**Feb.**	**Mar.**	**Apr.**	**May.**	**Jun.**	**Jul.**
1	Acetaminophen	ng/l	0.01	0.012	0.01	0.032	0.018	0.012	0.019	0.033	0.041	0.025
2	Ibuprofen		12	28	31	24	39	33	54	19	28	37
3	Propranolol		64	69	74	28	35	51	63	54	59	44
4	Clofibric Acid		312	422	248	315	355	389	511	431	458	418
5	Gemfibrozil		2100	1840	2300	1680	1940	1995	1789	1774	1815	1984
6	Citalopram		52	111	148	143	68	74	92	115	119	143
7	Fluvoxamine		43	55	38	42	49	57	55	62	79	74
8	Paroxetine		3.2	4.6	4.1	5.3	2.9	2.8	3.3	5.8	11.2	6.2
9	Primidone		714	533	415	322	465	611	721	522	487	429
10	Cetirizine		3400	3800	4200	3600	5100	4250	4300	4800	5600	6100
11	Enrofloxacin		355	911	477	548	912	1300	1412	925	846	733
12	Sulfachloropyridazine		43	58	28	36	37	24	19	18	23	14
13	Thiabendazole		18	19	23	14	11	9	14	18	19	23

14	Diazepam		23	28	34	24	26	18	19	15	11	18
15	Hydrochlorothiazide		21	14	15	28	31	34	24	28	27	13
16	Caffeine		246	311	428	358	529	346	338	337	248	349
17	Paraxanthine		14	16	11	25	29	31	23	21	25	26

Table (2) illustrate the analysis of pharmaceutical residues in the surface water of the Tigris River, located within the Wasit Governorate, was conducted over the study period from October 2023 to July 2024. The findings presented the minimum, maximum, average, and standard deviation for each pharmaceutical compound examined. Specifically, the residue levels of Acetaminophen ranged from 0.01 to 0.04 ng/l, with an average concentration of 0.02 ng/l and a standard deviation of 0.01. In contrast, the residue levels of Ibuprofen varied from 12.0 to 54.0 ng/l, yielding an average of 30.5 ng/l and a standard deviation of 11.56.

Table 3 Pharmaceuticals residue data analysis in the Tigris River water, Wasit Governorate, Iraq (Oct. 2023 to Jul. 2024)

No.	**Pharmaceutical Compounds**	**Unit**	**Min**	**Max**	**Avg**	**Sd**
1	Acetaminophen	ng/l	0.01	0.04	0.02	0.01
2	Ibuprofen		12.00	54.00	30.50	11.56
3	Propranolol		28.00	74.00	54.10	14.82
4	Clofibric Acid		248.00	511.00	385.90	78.66
5	Gemfibrozil		1680.00	2300.00	1921.70	182.69
6	Citalopram		52.00	148.00	106.50	33.92
7	Fluvoxamine		38.00	79.00	55.40	13.44
8	Paroxetine		2.80	11.20	4.94	2.51
9	Primidone		322.00	721.00	521.90	128.70
10	Cetirizine		3400.00	6100.00	4515.00	876.88
11	Enrofloxacin		355.00	1412.00	841.90	336.64
12	Sulfachloropyridazine		14.00	58.00	30.00	13.53
13	Thiabendazole		9.00	23.00	16.80	4.71
14	Diazepam		11.00	34.00	21.60	6.75
15	Hydrochlorothiazide		13.00	34.00	23.50	7.44
16	Caffeine		246.00	529.00	349.00	82.50
17	Paraxanthine		11.00	31.00	22.10	6.56

Acetaminophen enters the environment primarily through wastewater. Approximately 9 percent of the acetaminophen consumed by an individual is excreted unchanged in urine, leading to its introduction into wastewater systems. Additionally, improper disposal of excess or expired medications contributes to its presence in wastewater. While some acetaminophen is removed during wastewater treatment processes, it can also degrade in surface water due to sunlight exposure. Nevertheless, new wastewater continuously introduces acetaminophen into surface water, suggesting its long-term presence at low concentrations [11,22].

The analysis further revealed that the residue levels of Propranolol in water ranged from 28.0 to 74.0 ng/l, with an average of 54.1 ng/l and a standard deviation of 14.82. Clofibric acid exhibited residue levels from 248.0 to 511.0 ng/l, with an average of 385.9 ng/l and standard deviations of 24.2 and 78.66.

Moreover, the residue levels of Gemfibrozil were found to range from 1680 to 2300 ng/l, with an average concentration of 1921.7 ng/l and a standard deviation of 182.69. Citalopram levels varied from 52.0 to 148.0 ng/l, resulting in an average of 106.5 ng/l and a standard deviation of 33.92. Additionally, the Citalopram residue was noted to range from 38.0 to 79.0 ng/l, with an average of 55.4 ng/l and a standard deviation of 13.44. Lastly, the residue levels of Paroxetine ranged from 2.8 to 11.2 ng/l, with an average of 4.94 ng/l and a standard deviation.

Various sources contribute to the introduction of metabolized ibuprofen into the environment, leading to its accumulation in natural matrices. This metabolized form is primarily released into the water systems of various communities, where it accumulates in aquatic ecosystems or soil. Additionally, unused expired medications are frequently disposed of in household waste, ultimately reaching municipal landfills, where they pose a potential risk of soil contamination. Ibuprofen is also utilized in veterinary medicine, and following its administration, it is excreted into the environment through animal urine or feces. Several studies have investigated the toxicological effects of ibuprofen on freshwater fish species. One particular study indicated that exposure to ibuprofen resulted in alterations in the kidneys of freshwater Oncorhynchus mykiss, including hyalinosis, heightened oxidative stress, and modifications in the expression of heat shock protein 70 [23,29]. Furthermore, it adversely affected their liver, leading to dystrophy, cellular congestion, and inflammation. In bivalve mollusks (Unio tumidus), which are commonly employed as bioindicators of freshwater quality, exposure to a sub-chronic environmental concentration of ibuprofen (0.8 µg/L) over a period of 14 days resulted in a decrease in protein carbonyl concentration, induction of cholinesterase, and a reduction in lysosomal integrity within their digestive glands.

Table 4 Risk analysis of pharmaceuticals residue in the Tigris River water, Wasit Governorate, Iraq (Oct. 2023 to Jul. 2024)

No.	Pharmaceutical Compounds	Level of Compounds (ng/l)	Average daily dose (mg/day)	HQ	Potentiality (N/R)
1	Acetaminophen	0.02	4000	200000.00	R
2	Ibuprofen	30.5	3200	104.92	R
3	Propranolol	54.1	60	1.11	R
4	Clofibric Acid	385.9	500	1.30	R
5	Gemfibrozil	1921.7	600	0.31	N
6	Citalopram	106.5	30	0.28	N
7	Fluvoxamine	55.4	50	0.90	N
8	Paroxetine	4.94	10	2.02	R
9	Primidone	521.9	500	0.96	N
10	Cetirizine	4515	5	0.00	N
11	Enrofloxacin	841.9	20	0.02	N
12	Sulfachloropyridazine	30	900	30.00	R
13	Thiabendazole	16.8	25	1.49	R
14	Diazepam	21.6	10	0.46	N
15	Hydrochlorothiazide	23.5	25	1.06	R
16	Caffeine	349	400	1.15	R
17	Paraxanthine	22.1	150	6.79	R

N: No risks present; R: high risks present

Beta-blockers, a category of pharmaceuticals and personal care products, are primarily utilized in the treatment of cardiovascular conditions. Due to incomplete metabolic processes in humans, these substances often enter the sewage system in their original form or as metabolites, and they have been identified in wastewater systems across various regions. As emerging contaminants in aquatic environments, beta-blockers consistently find their way into municipal sewage treatment facilities. Calleja et al. reported the detection of propranolol (PRO, a representative beta-blocker) in effluent samples from eight wastewater treatment plants in different parts of the United States, with the highest

concentration recorded at 1900 ng•L^{-1}. Furthermore, the peak concentrations of PRO in surface waters in the United States and Germany were found to be 1.9 mg•L^{-1} and 0.59 mg•L^{-1}, respectively. Due to their high solubility in water and low biodegradability, beta-blockers that enter aquatic systems can persist for extended periods, posing ecological risks. Propranolol, the most frequently detected beta-blocker in aquatic environments, has been shown to have detrimental effects on aquatic life. De Oliveira's study exposed daphnia to PRO at a concentration of 128 µg•L^{-1}, revealing a significant reduction in their reproductive rates. Additionally, a 21-day chronic ecotoxicity assessment conducted by Archer et al. 2017 indicated that PRO at a concentration of 26 µg•L^{-1} could adversely affect the growth rate, heart rate, abdominal appendage movement frequency, and deformity rate of juvenile daphnia. The prolonged presence of beta-blockers in the environment not only contributes to chemical pollution but also poses potential ecotoxicological risks to organisms, significantly impacting ecosystems. Therefore, it is imperative to address the issue of water pollution caused by beta-blockers and to explore effective treatment technologies to mitigate this problem [4,12].

The fundamental purpose of research is to guarantee the ongoing productivity of established techniques or methods of application. As advancements are made, it is essential to evaluate not only the effectiveness of the new processes but also their health and environmental implications. Clofibrate serves as a lipid regulator, while its metabolite, Clofibric acid (CA), tends to accumulate significantly in both surface and groundwater. A considerable portion of xenobiotic toxins originates from pharmaceutical, personal care, and municipal waste discharges. When these wastes are inadequately managed, they do not integrate into the soil but instead remain trapped in aquatic environments. These biochemically active compounds exhibit a remarkable resistance to metabolic breakdown, rendering them persistent water pollutants. The degradation rate of CA is so minimal that it poses a substantial environmental threat [14,25].

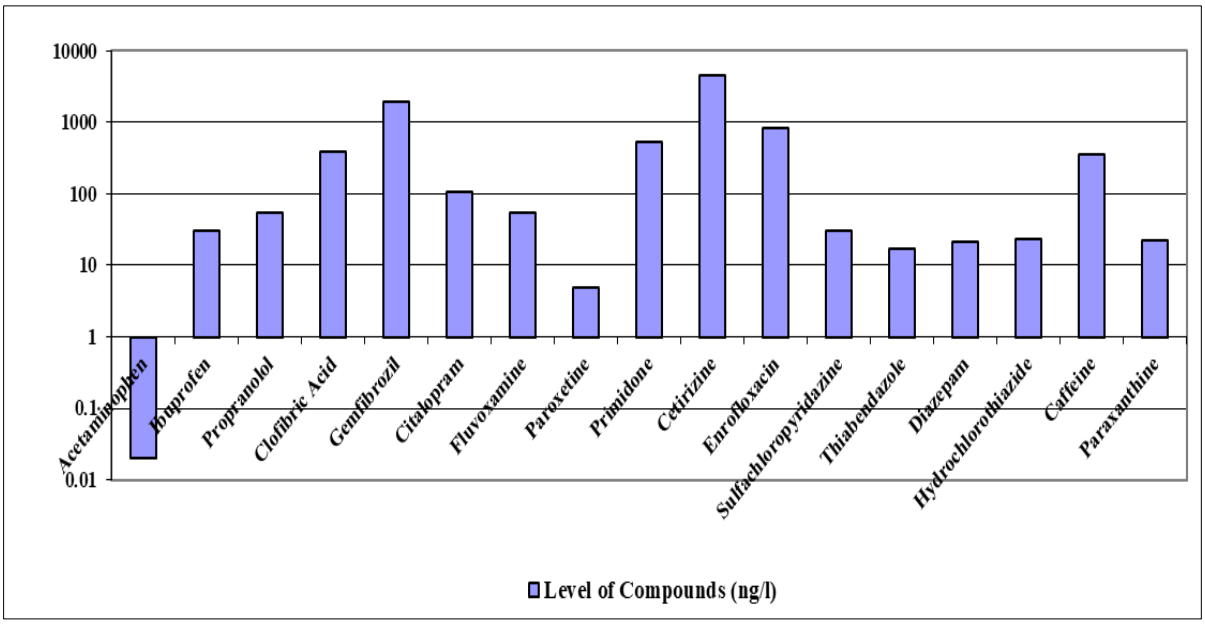

Figure 2 Analysis of pharmaceuticals residue in the Tigris River water, Wasit Governorate, Iraq (Oct. 2023 to Jul. 2024)

Carmona et al. 2014; conducted a study examining the environmental effects of clofibrate (CA) on aquatic ecosystems, with a particular emphasis on zebrafish (Danio rerio). Their findings indicated that continuous exposure to the clofibrate metabolite leads to a significant decrease in the growth of the affected fish, as well as a reduction in muscle triglyceride content. While earlier research by Owen et al. and Dutta et al. 2014; could not definitively ascertain the impact of CA on fish growth, their conclusions were deemed inconclusive. Notably, even minimal exposure to CA (10 mg/g group) resulted in decreased fecundity and notable embryo deformities in zebrafish. Despite various wastewater treatment initiatives, CA is only partially removed. DWI et al. reported that CA concentrations remain stable in Swiss lakes and are found in elevated levels in German rivers. Specifically, the concentrations of CA in surface water and effluents from sewage treatment plants are recorded at 0.551 µg/L and 1.6 µg/L for Swiss lakes and German rivers, respectively, while the North Sea, Greece, and the USA exhibit concentrations of 1 ng/L, 5 ng/L, and 0.8–2 µg/L in their water bodies [17,18,19].

Gemfibrozil (GEM), a lipid-regulating medication, is utilized globally for its efficacy in managing elevated triglycerides and cholesterol levels in the bloodstream, exhibiting a solubility of approximately 11 mgL^{-1}. It is classified as a

"hazardous substance" based on PNEC values due to its prolonged impact on aquatic ecosystems. Additionally, PNEC has identified various exposure pathways in children, including: (i) Fish (3.9 × 107 ngL^{-1}), (ii) Drinking water, and (iii) Combined ingestion of Drinking Water and Fish (7.9 × 10^5 ngL^{-1}). Research indicates that Gemfibrozil accumulates plasma androgen in Carassius auratus when exposed to concentrations of 1.5 μgL^{-1} over a two-week period. It has also been detected in the liver of Cyprinus carpio and Catostomus commersonii at concentrations of 0.09 μgL^{-1} and 0.0273 μgL^{-1}, respectively. Furthermore, Gemfibrozil is known to interfere with endocrine functions; its exposure in Carassius auratus has been linked to decreased testosterone levels. A study conducted in Mexico has reported elevated gemfibrozil concentrations (605 ngL^{-1}) in wastewater [31,33].

Godoy (2015) identified a concentration of 2991 ngL^{-1} of gemfibrozil in the Yamuna River, while the Pearl River in China exhibited a level of 19.8 ngL^{-1}, and the Madrid River in Spain recorded 4130 ngL^{-1}. Gemfibrozil is known to have detrimental effects on reproductive parameters and can disrupt spermatogenesis in male organisms. Prior research has indicated that Gemfibrozil is a persistent compound, with half-lives in surface water ranging from 119 to 288 days. Various physicochemical methods, such as advanced UV photo-oxidation and direct UV irradiation, have been successfully employed to degrade lipid-regulating pharmaceuticals, demonstrating higher removal efficiencies; however, these methods are not economically feasible. The biological removal of lipid-regulating drugs has emerged as a promising advanced technology. This biodegradation process involves the breakdown of complex pharmaceutical structures into simpler forms through enzymes produced by microorganisms. Some researchers have investigated the biodegradation of different lipid regulators, including lovastatin and simvastatin. Numerous abiotic and biotic factors, such as pH, molecular characteristics, redox potential, physicochemical properties, microbial diversity, temperature, and the toxicity of pharmaceutical contaminants, influence the efficiency of biodegradation. Additionally, the potential gemfibrozil-degrading organisms have not been thoroughly investigated, highlighting a significant research gap that warrants attention from the scientific community [22].

A limited number of investigations have examined the occurrence of psychiatric medications in aquatic ecosystems. Recent advancements in analytical techniques have facilitated the identification of antidepressants in various water bodies, including wastewater, surface water, groundwater, and even drinking water. Antidepressants are not completely metabolized by the human body and are excreted through urine and feces. Their primary components, along with metabolites or conjugates, eventually make their way to wastewater treatment plants (WWTPs). These facilities are primarily designed to remove biodegradable carbon, phosphorus, nitrogen, and pathogens, rather than specifically addressing psychotropic compounds. As a result, it is probable that these medications are only partially eliminated during the treatment process, with residual quantities being released into the environment through effluent or sludge. Retaining their pharmacological effects, the remaining psychotropic drugs can inhibit serotonin reuptake. The accumulation of these substances in the tissues of aquatic organisms, such as fish, may result in physiological and behavioral changes. Therefore, it is crucial to acknowledge the presence of psychotropic medications in the environment to comprehend their potential health and ecological implications [26,29].

The presence of pharmaceuticals in surface and groundwater sources used for drinking water treatment poses a considerable risk of these substances contaminating water intended for human consumption. The adoption of advanced water purification methods is anticipated to facilitate the complete removal of pharmaceutical contaminants. However, an analysis of the treated water reveals a potential risk of exposure to the effects of antidepressants for individuals consuming this water. In Warsaw, Poland, citalopram has been detected at a concentration of 1.5 ng/l, while venlafaxine has been found at levels ranging from 0.5 to 1.9 ng/l in tap water. In the United States, risperidone was identified at a concentration of 0.34 ng/l in treated water, and fluoxetine and norfluoxetine were measured at 0.64 ng/l and 0.77 ng/l, respectively, in tap water. In France, amitriptyline was recorded at 1.4 ng/l, and in Spain, venlafaxine was noted at 9 ng/l, both in tap water [23,29].

Primidone, an anticonvulsant introduced in the 1950s, undergoes metabolism in both humans and animals, resulting in the formation of two main pharmacologically active metabolites: phenobarbital and phenylethylmalonamide. Although phenylethylmalonamide does not have any recognized medical applications, phenobarbital is widely prescribed as an anticonvulsant and is among the most frequently used antiepileptic drugs worldwide. Historically, phenobarbital served primarily as a sedative and hypnotic. Since its introduction in 1912, it has been largely supplanted in Germany by benzodiazepines during the 1960s for these indications, primarily due to concerns regarding its potential for addiction and its narrow therapeutic window [13,15].

Since the 1960s, the benzodiazepine derivatives oxazepam and diazepam have been extensively utilized as tranquilizers for the treatment of anxiety and insomnia. Additionally, oxazepam functions as an active metabolite for various benzodiazepines, including diazepam. The anxiolytic drug meprobamate, which was launched in 1955, was rapidly eclipsed by benzodiazepines during the 1960s. While meprobamate is categorized as a non-prescribable narcotic in

Germany, it continues to be available in other European countries and the United States. Pyrithyldione, a sedative-hypnotic medication, was introduced in 1949 [9,17].

3.1.1. Pharmaceutical residue risk analysis

The hazard quotient (HQ) for the pharmaceuticals under examination was calculated in accordance with the US EPA Human Health Risk Assessment, with minor modifications [22]. Hazard refers to the potential for an entity to inflict harm, which can be classified as either acute or chronic. Acute hazards are those that present immediate and evident risks, while chronic hazards may not be readily observable and can lead to more insidious problems, often manifesting only after extended durations. In this study, the HQ will be utilized. Regulatory bodies, including environmental protection agencies (EPA) in various nations, employ HQ to categorize the risk associated with a chemical substance. The HQ is defined as the ratio of potential exposure to a substance compared to the threshold at which no adverse effects are anticipated. It is computed using the following relationship:

HQ = Average daily dose / Reference dose

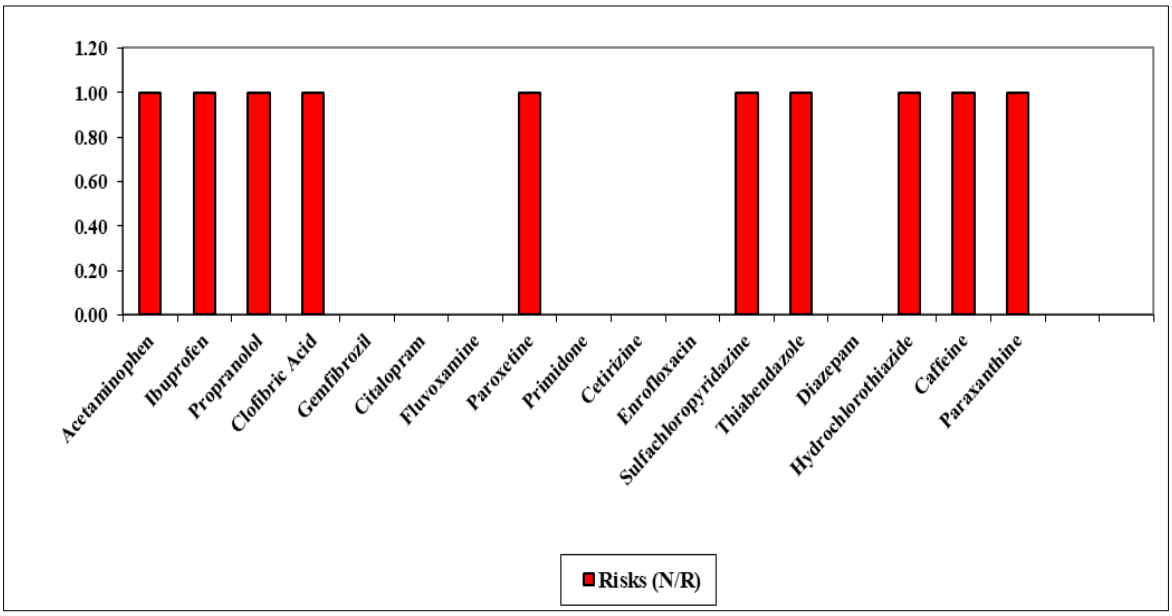

Figure 3 Risks of pharmaceuticals residue in the Tigris River water, Wasit Governorate, Iraq (Oct. 2023 to Jul. 2024)

A hazard quotient (HQ) of 1 or lower suggests that the likelihood of adverse effects is minimal, indicating a negligible level of hazard. Conversely, HQs exceeding 1 do not represent statistical probabilities of harm; rather, they serve as a straight forward indication of the extent to which an exposure concentration surpasses the reference concentration (RFC).

4. Conclusion

In light of the critical issue of pharmaceutical contamination in the aquatic environment, particularly concerning the water of the Tigris River in Wasit Governorate, Iraq, this study sought to evaluate the prevalence and associated risks of pharmaceuticals in the river's surface waters. A total of 17 different pharmaceuticals were identified in the surface water samples. Among these, several were classified as posing a high risk (HQ ≥ 1.0), including acetaminophen (an analgesic), caffeine (a stimulant), ibuprofen, clofibric acid, sulfachloropyridazine, thiabendazole, hydrochlorothiazide, paraxanthine, and paroxetine. Due to the significant ecological risks associated with these substances, it is imperative to conduct thorough assessments, which necessitate ongoing monitoring of their concentrations in surface waters. Additionally, the potential impacts on aquatic organisms must be meticulously analyzed for both chronic and acute toxicity. Strategies for the removal of these pharmaceuticals from surface waters and sustainable management practices should also be investigated. The study advocates for rigorous monitoring of pharmaceutical pollutants in wastewater from pharmaceutical manufacturing facilities and hospitals, investment in the production of environmentally friendly pharmaceuticals that degrade effectively after use, careful assessment of wastewater treatment plants (WWTPs) for their effectiveness in eliminating pharmaceutical contaminants, regulation of biosolid applications as fertilizers or soil

conditioners, oversight of treated wastewater for recreational purposes, and further research into the long-term effects of pharmaceuticals and their metabolites on aquatic life.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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