

Evaluation of Pharmaceutical Residues in Wastewater

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Abstract

The presence of bio active pharmaceutical residues in the aquatic environment is majorly due to incomplete removal at wastewater treatment plants. This study evaluated the concentrations of various pharmaceutical compounds in influents and effluents from six selected pharmaceutical industries and assessed their percentage removal after treatment at wastewater treatment plants (WWTPs). Many pharmaceutical industries, do not comply with environmental standards before discharging their effluents into the receiving water body. The results revealed the levels of various pharmaceutical residues in the wastewater treatment plants effluents and the receiving water body. The target analytes include, ibuprofen, diclofenac, acetaminophen, amoxicillin, caffeine, metronidazole, ofloxacin, ciprofloxacin, pyrimethamine and sulfadoxin. Solid phase extraction (SPE) and High-Performance Liquid Chromatography (HPLC) techniques were employed for this work. OASIS HLB cartridges C18 were used for preconcentration of the analytes. The order of concentrations of the pharmaceutical residues in the WWTPs effluents were ibuprofen > acetaminophen > amoxicillin > diclofenac > ofloxacin > ciprofloxacin. Percentage removal at WWTPs ranged between 31% - 100%. This further suggests that the current wastewater treatment technology employed in the various locations were not efficient in completely removing all pharmaceutical residues present in the wastewater. Additional procedure for their total removal is necessary.

Key Words: Effluents, Influent, Wastewater treatment plant, Pollution, Pharmaceutical compounds and Cartridges,

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I. Introduction

Active pharmaceutical compounds in the aquatic environment have been considered to be a group of emerging contaminants over the decades [1]. The increase in the use of human and veterinary medicines and improvement in analytical techniques in the proper detection of these compounds have increased the growing interest in the awareness of the presence of these bioactive pharmaceutical residues (PRs) in the biota. These active pharmaceutical compounds include a wide range of chemicals that were previously not recognized but are now under serious investigation because their negative effects on aquatic organisms are presently being felt globally as a result of continuous discharge into the aquatic environment and are considered to be pseudo persistent [2,3]. Many studies have exposed their presence in trace amounts ranging from ng / L to µg / L [4,5]. Several investigations have also shown that their presence is partially due to insufficient removal from wastewater treatment plants (WWTPs) which, as a result, is the cause of 70-80% of their presence in the aquatic environment. The remaining 20-30% may be due to improper disposal of unused or expired drugs, agricultural wastes, etc [6]. When they are released into the receiving waters, they usually tend to partition themselves into different compartments such as surface water, groundwater, soil, sediment, and living organisms depending on their physical and chemical characteristics [7]. A threshold value of 10ng / L in surface water has been suggested recently in Europe for some classes of pharmaceutical compounds [8,9]. However, this value has been greatly exceeded in many European rivers [10,11]. Another study has also revealed that the influx of pharmaceutical residues from municipal sewage treatment plants (STPs) is an important source of chemical pollution in the surface, ground, and even bottled water. [12,13,14]. For instance, an investigation conducted by the US Geological survey in 1999 to ascertain the presence of pharmaceuticals and personal care products (PPCPs) such as steroids, antibiotics, analgesics, hormones, and other pharmaceutical compounds in the surface and groundwater confirmed the presence of at least one pharmaceutical at low concentrations in more than two-thirds of the samples analyzed [15]. Although the concentrations of the individual pharmaceutical reported were low and may not cause harm to human health, chronic exposure to various mixtures may however disturb the balance in the human body and also promote antibiotic resistance thereby posing a threat to human health and that of the living organisms within that environment [16,17]. There are some reported effects of pharmaceuticals on living organisms such as delayed development in fish and frogs, delayed metamorphosis in frogs, increased feminization of male fish, and also altered behaviour in fish [18]. This study aimed at evaluating the levels of

concentrations of some pharmaceutical residues in the influents and effluents from six pharmaceutical industries' treatment plants and establish the percentage removal of the individual analyte. The pharmaceutical compounds analyzed include some over-the-counter drugs such as ibuprofen, diclofenac, acetaminophen, caffeine, and metronidazole. The samples were filtered with 0.45 μm glass filter, pre-treated with sodium EDTA and subjected to Solid-phase extraction. High performance liquid chromatographic analysis was carried out on each sample. Ultraviolet (UV) detector was used as the detector instrument. Acetaminophen (N-acetyl-p-aminophenol) is a widely used over-the-counter analgesic and antipyretic drug in Nigeria. Caffeine (1,3,7-trimethylpurine-2,6-dione) on the other hand is a purine methylxanthine alkaloid and a central nervous system stimulant. It is however one of the world's most consumed psychoactive drugs. Some common products that contain caffeine are coffee, tea, soft drinks, energy drinks, and chocolate derived from cocoa beans.

II. Materials and methods

2.1 Sample Collection and pre-treatment

One liter of both influent and effluent wastewater was collected in duplicates from six pharmaceutical companies located in industrial areas of Isolo and Amuwo Odofin local government areas of Lagos, Nigeria. The sampling was carried out bi-monthly for a period of twenty-four months. They were collected with pre-cleaned glass bottles wrapped with aluminium foil. The bottles were previously washed with detergent and soaked with chromic acid overnight after which they were rinsed with distilled water and wrapped in aluminium foil. After water sample collection, the bottles with their contents were subsequently placed in a cooler packed with ice, maintained at 4^oc, and transported to the laboratory for the analysis of various pharmaceutical compounds which include ibuprofen, diclofenac, amoxicillin, metronidazole, caffeine, sulfadoxin, ofloxacin, ciprofloxacin pyrimethamine, and acetaminophen. The procedure described by Batt et al, 2008 was employed for this work [19]. The samples arrived at the laboratory within 36 hours of collection. Immediately upon arrival at the laboratory, 500 ml of the wastewater were filtered through a 0.45- μm glass filter. The clear filtrates obtained were subsequently subjected to solid-phase extraction after treatment with Na₂EDTA to remove any metal present.

2.2 Solid-phase Extraction.

The solid-phase extraction procedure was used to preconcentrate the solutions. 500ml of wastewater that has been pretreated with Na₂EDTA was filtered with a 0.45 μm glass filter. Pharmaceutical compounds were extracted in one step by solid phase extraction using a Baker vacuum system and Oasis HLB cartridges C18 (10g sorbent with 12 mL capacity) previously conditioned at neutral pH with 6 mL methanol and acetone (HPLC grade) [20]. Elution was performed with 10 mL methanol and acetone respectively at a flow rate of 5-10 mL min⁻¹ in the ratio of 1:1 (v/v) at room temperature and pressure. The extracts were evaporated under a gentle stream of nitrogen and reconstituted to 1 mL with methanol [21].

2.3 Chemicals and reagents

The six analytes are Ibuprofen, diclofenac, acetaminophen, caffeine and metronidazole. All chemicals were purchased from Sigma Aldrich Chemicals Germany. Trifluoroacetic acid (TFA) (99%), Caffeine (99%), diclofenac (99%), metronidazole (99%), ibuprofen (98%), acetaminophen (99%), Ofloxacin (99%), Ciprofloxacin (99%), Amoxicillin (99%), Sulfadoxin (99%), Pyrimethamine (99%), Acetonitrile, methanol and distilled water

2.4 Stock solutions and linearity:

The stock solutions were prepared by dissolving 10mg of individual standard in 10ml of acetonitrile and stored in the refrigerator at 4^oC. However, working solutions were prepared periodically from the stock solution by mixing appropriate aliquots of the stock solutions diluted with acetonitrile and water. (45/45, v/v) and stored at 4^oC. Various concentrations for all the pharmaceutical compounds analyzed were tested for linearity. The calibration curves were linear. The linearity of an analytical procedure is its ability (within a given range) to obtain test results that are directly proportional to the concentration of the analyte in a given sample. Blank solutions were also analyzed.

2.5 HPLC Analysis

In this study, wastewater samples were analyzed with Liquid chromatographic equipment (HPLC 1290 series, Agilent Technology USA) connected to an Ultra Violet detector [22]. A sun fire column C18 (100 cm, 4.6 mm, 4 μm) preceded by a guard column (Sun Fire, C18, 2.1 \times 10mm, 3.5 μm , Waters, Milford MA USA) was used at a temperature of 40^oC. A mobile phase consisting of a mixture of 1:1 acetonitrile and water with 0.1%

TFA at a flow rate of 1 mL/min was used. Elution was done at a constant rate of 1.0ml/min. The different compounds were identified in the chromatogram by comparing the retention time of the various peaks with that of the corresponding compound in the standard solution. Peak areas were used for quantitative analysis.

2.6 Accuracy

The accuracy of the method was evaluated by analyzing two extracts from the samples with concentrations of 20µg and 30µg. They were injected twice and the average values were obtained.

2.7 Statistical analysis

Statistical analysis was performed with the statistical package for social sciences (SPSS) version 26. Concentrations of detected emerging contaminants were compared using a repeated measure mixed-model ANOVA with the sampling day as a random factor. Significant differences were recorded as P < 0.05.

2.8 Method validation and instrument performance:

Detection and quantification of pharmaceutical residues were analytically validated as stipulated by the international conference on harmonization of procedures [22]. However, the selectivity, linearity, limit of detection (LOD), the limit of quantification (LOQ), accuracy, and precision for simultaneous determination of the listed pharmaceuticals in aqueous media were evaluated. Analysis was done in duplicates and the average concentrations were recorded. Blank samples were also analyzed for the various pharmaceutical residues but were not present in the blank sample.

III. Results and Discussions

3.1 Concentrations of pharmaceutical residues in the influents

The concentrations of the ten selected pharmaceuticals in the influents of the wastewater treatment plants (WWTPs) are shown in table 4.1. The wastewater analyzed contain varying degrees of drug pollutants with metronidazole, acetaminophen, and pyrimethamine having the highest levels in the influents. Maximum metronidazole concentration was found to be 100.4± 0.4ng / L in site 5, with an average concentration of 32.8±0.3 ng / L. Acetaminophen had the second highest concentration in the wastewater treatment plants(WWTPs) influents ranging between 3.6±0.1 ng / L and 39.0±0.04 ng / L with an average of 15.1±0.3 ng / L. These were followed by pyrimethamine ranging between <LOD and 29.1±0.1 ng / L with an average concentration of 6.44±0.1 ng / L. High concentrations of metronidazole and acetaminophen reflect the popular usage of the drugs in Nigeria. Ciprofloxacin showed the lowest concentration in the influents ranging between 0.002±0.1 and 3.17±0.1 ng / L. In all the sites, over 60% of acetaminophen and diclofenac were found in the influents at different concentrations. The concentration of diclofenac ranged between 0.41±0.1 ng/L and 13.5±0.6 ng / L in the influents. The results showed that the average concentrations of the pharmaceutical residues in the influents were higher than those in the effluents. Wastewater usually originates from point sources such as industrial effluents, households, hospitals, etc. Inputs from surrounding contaminated areas such as effluent discharge ponds can be some of the causes of groundwater pollution. The levels of concentration depend on the source of contamination. Various amounts of drug residues were detected in the influent at different sites.

Table 3.1: Concentrations of pharmaceutical residues in the influents

Drug ID	S1	S 2	S3	S 4	S5	S6	mean concentration
Ibuprofen	2.77±0.8	14.9 ±0.8	<LOD	<LOD	<LOD	<LOD	2.93±0.3
Diclofenac	0.53 ±0.2	<LOD	0.41±0.1	<LOD	13.5±0.6	12.9±0.6	4.54±0.3
Caffeine	3.70 ±0.1	<LOD	<LOD	20.1±0.3	<LOD	<LOD	3.96±0.1
Acetaminophen	4.12±0.04	39.0±0.04	21.4 ±0.4	<LOD	3.64 ±0.1	22.3±1.1	15.1±0.3
Metronidazole	<LOD	<LOD	<LOD	96.1 ±1.1	100.4 ±0.4	<LOD	32.8±0.3
Amoxicillin	5.69±0.2	<LOD	<LOD	<LOD	<LOD	15.1±0.8	3.46±0.2
Ofloxacin	0.013±0.1	0.015±0.001	<LOD	2.58±0.4	<LOD	0.006±0.04	0.43±0.6
Ciprofloxacin	3.17±0.1	<LOD	<LOD	2.00±0.004	0.002±0.09	5.0±0.1	1.69±0.03
Sulfadoxin	1.61±0.8	<LOD	<LOD	8.06±0.2	<LOD	<LOD	1.61±0.2
Pyrimethamine	<LOD	<LOD	<LOD	9.60±0.7	29.1±0.1	<LOD	6.44±0.1

* S1-S6 :(Six different pharmaceutical industries where wastewater samples were collected.)

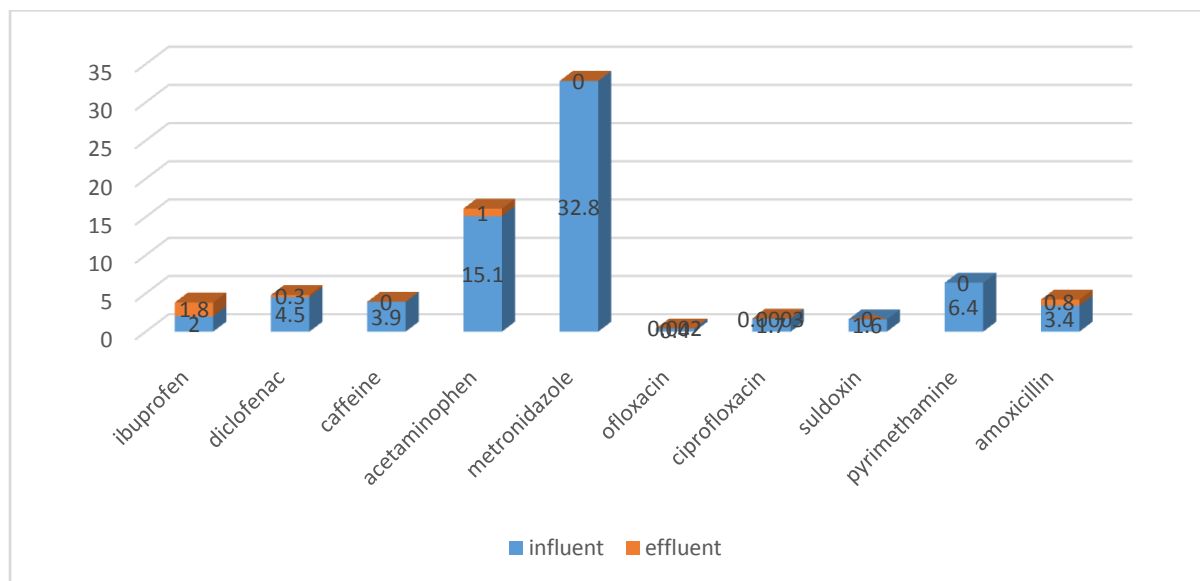


FIG3.1 Concentrations of pharmaceutical residues (ng/ L) in the WWYTPs influents and effluents.

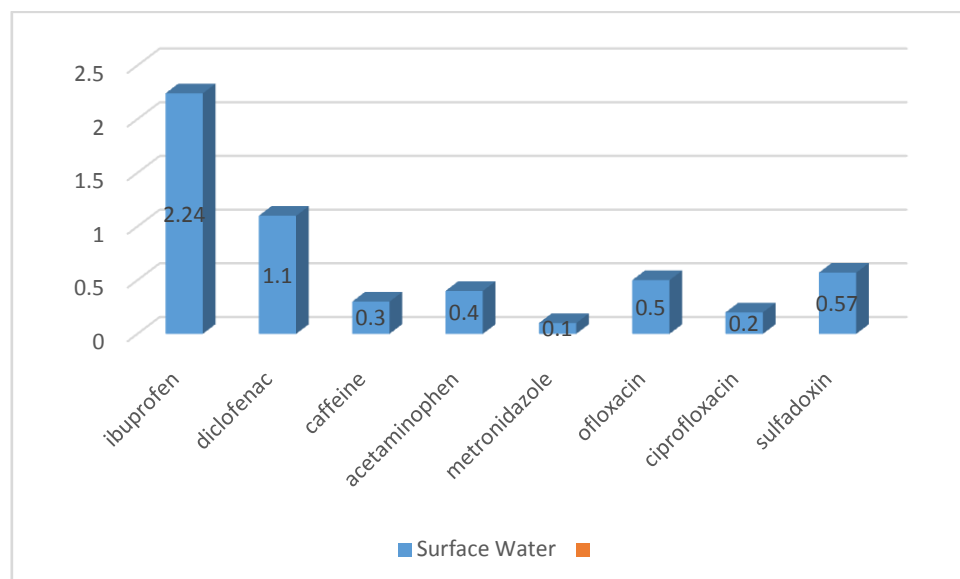


FIG 3.2: Concentrations of pharmaceutical residues (ng/L) in the surface water

The level of residues depends on the source of contamination. However, it is not very clear the extent of their cumulative physiological effects on humans and other organisms at low concentrations when discharged into the aquatic environment.

3.2 Concentrations of pharmaceutical residues in the effluents of WWTPs

The effluents from the selected wastewater treatment plants contained various drug residues as shown in table 3.2. In the effluents, ibuprofen had the highest levels and ranged between < LOD and 11.2 ± 0.8 with an average concentration of 1.86 ± 0.1 ng / L. This was followed by acetaminophen which ranged between < LOD and 5.95 ± 0.4 ng / L having an average concentration of 0.99 ± 0.6 ng / L. Ciprofloxacin had the lowest average concentration of 0.003 ± 0.1 ng / L in the effluent. It was however observed that the concentrations of the test pharmaceutical residues in the WWTPs effluents were generally lower than those in the influents. The concentrations of ofloxacin and sulfadoxin in the WWTPs effluents significantly decreased (98% for ofloxacin removal and 93% for sulfadoxin removal) compared with the influents. Also, metronidazole, pyrimethamine, and caffeine were not detected in the WWTPs effluents. This observation is an indication that the conventional wastewater treatment methods used in the treatment plants could remove metronidazole, pyrimethamine, and caffeine effectively. Effluents of urban wastewater and receiving waters in other countries were reported also to contain many pharmaceuticals at low concentrations [23,24]. These indicate that most of the current wastewater treatment practices are inefficient in completely removing such contaminants. For instance, five pharmaceuticals

(propranolol, sulfamethoxazole, carbamazepine, indomethacin, and diclofenac) were found in all wastewater and the receiving surface water samples in England with carbamazepine having the highest levels (2.336 ng mL⁻¹). The reported removal efficiencies for these compounds from the wastewater were in the range of 43–92%.[25]. In another study, five out of six drugs (diclofenac, ibuprofen, ketoprofen, naproxen, carbamazepine, and caffeine) have been detected in both influent and effluent from four STPs in Seville–Spain in the ng mL⁻¹ concentration range. The reported removal rates for these drugs were between 6% and 98% [24]. In the present study, not all the pharmaceutical compounds were able to be removed during wastewater treatment processes. The percentage removal from influents was between 36% and 100 %. The concentrations of detected pharmaceuticals in effluents were lower than the influents. There were significant differences in the concentrations of some residues at various treatment plants during the wet and dry seasons as observed in figures 3.3 to 3.8.

Table 3.2: Concentrations of pharmaceutical residues in the effluents of WWTPs

Drug ID	S1	S 2	S3	S 4	S5	S6	mean concentration
Ibuprofen	<LOD	11.2±0.8	<LOD	<LOD	<LOD	<LOD	1.86±0.1
Diclofenac	<LOD	<LOD	<LOD	<LOD	<LOD	2.37±0.2	0.39±0.03
Caffeine	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
Acetaminophen	<LOD	5.95±0.4	<LOD	<LOD	<LOD	<LOD	0.99±0.6
Metronidazole	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
Amoxicillin	<LOD	<LOD	<LOD	<LOD	<LOD	5.00±0.4	0.83±0.06
Ofloxacin	<LOD	0.013±0.01	<LOD	<LOD	<LOD	0.004±0.1	0.002±0.01
Ciprofloxacin	0.002±0.09	<LOD	<LOD	<LOD	<LOD	<LOD	0.0003±0.1
Sulfadoxin	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
Pyrimethamine	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD

* S1-S6 : Site 1- 6, LOD : Limit of detection

Table.3:3Percentage removal of the analytes at the wastewater treatment plants.

Drug ID	INFLUENT EFFLUENT REMOVAL		
	ng/l	ng/l	EFICIENCY (%)
IBUPROFEN	8.812	5.602	36
DICLOFENAC	6.824	2.617	61
AMOXICILLIN	10.387	5.004	51
SULFADOXIN	4.835	0.294	93
OFLOXACIN	0.653	0.009	98
CIPROFLOXACIN	2.501	1.724	31
CAFFEINE	11.890	NILL	100
ACETAMINOPHEN	21.826	9.997	54
METRONIDAZOLE	98.259	NILL	100
PYRIMETHAMINE	19.337	NILL	100

S1

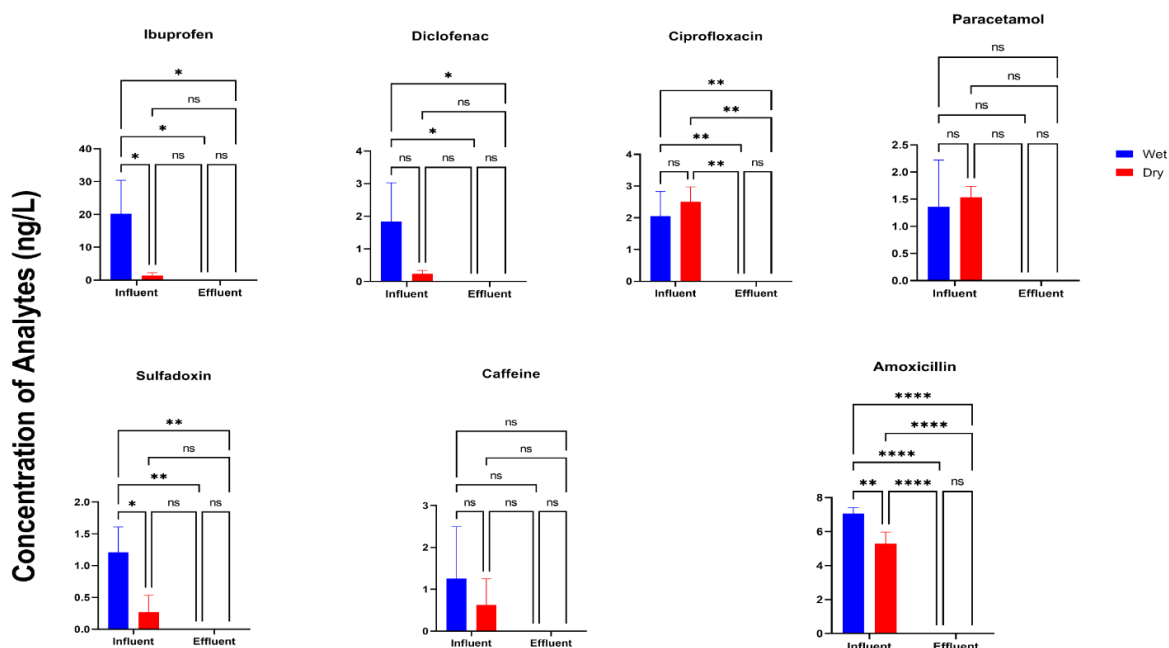


FIG.3.3: Seasonal variations of pharmaceutical residues in influents and effluents from site 1. Each bar represents the mean \pm SEM, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$ compared to their counterparts. April to October (otherwise called Raining season), November to March (otherwise called Dry season).

S2

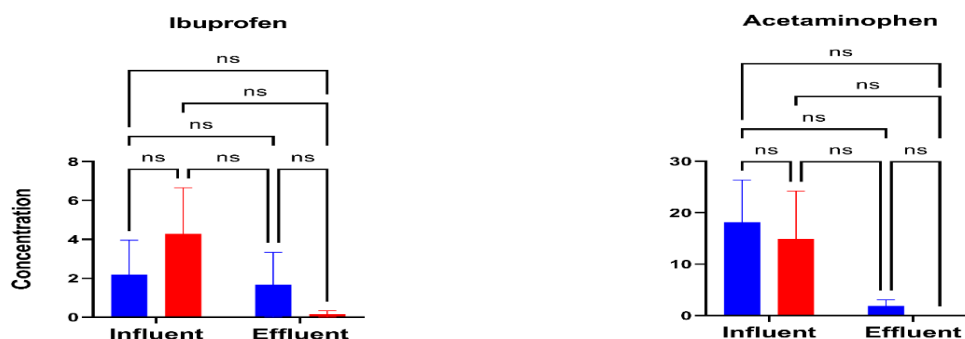


FIG. 3.4: Concentrations of analytes in influent and effluent of S2 during the dry and wet seasons. Each bar represents the mean \pm SEM, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$ compared to their counterparts

S3

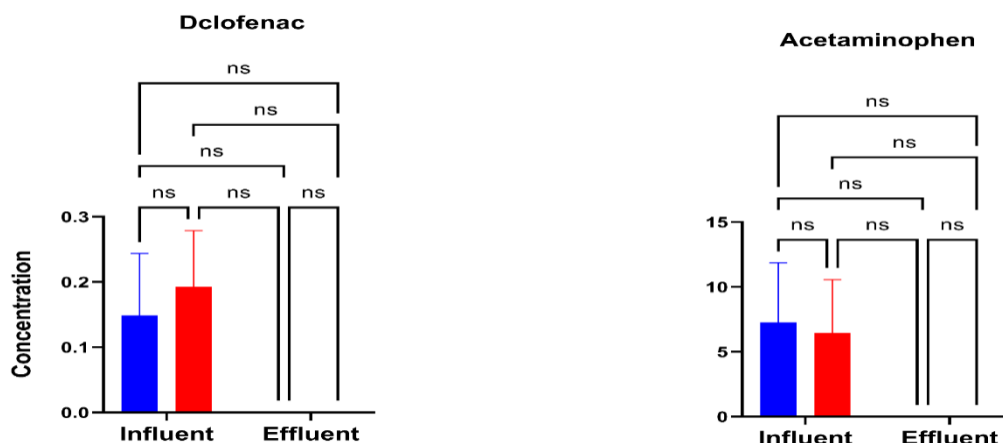


FIG 3.5: Concentrations of pharmaceutical residues in S3 during the wet and dry seasons

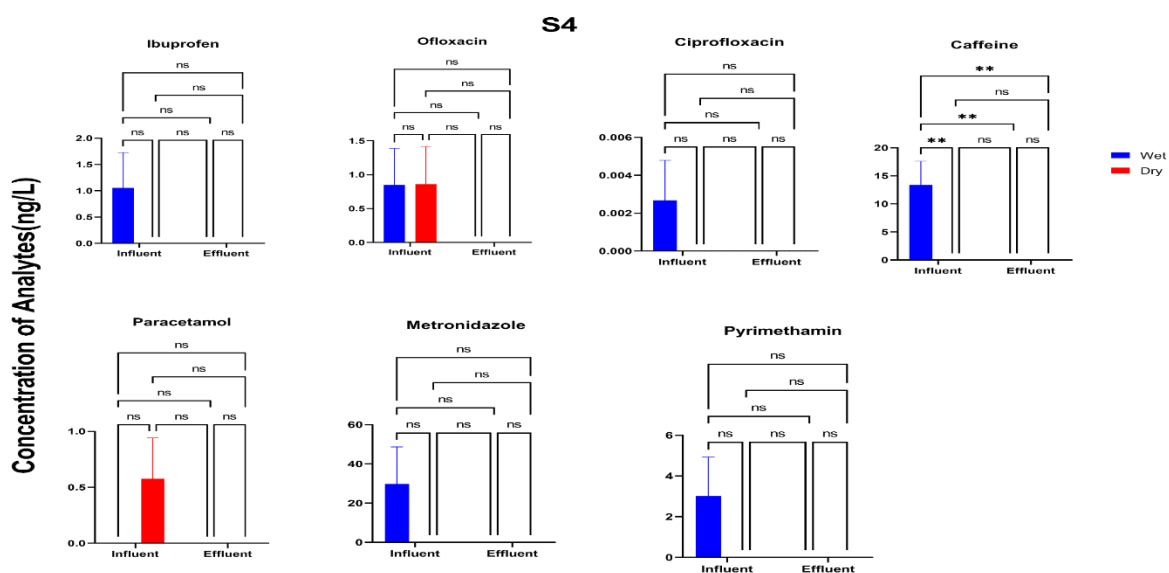


FIG 3.6: Concentrations of pharmaceutical residues in S4 during the wet and dry seasons.

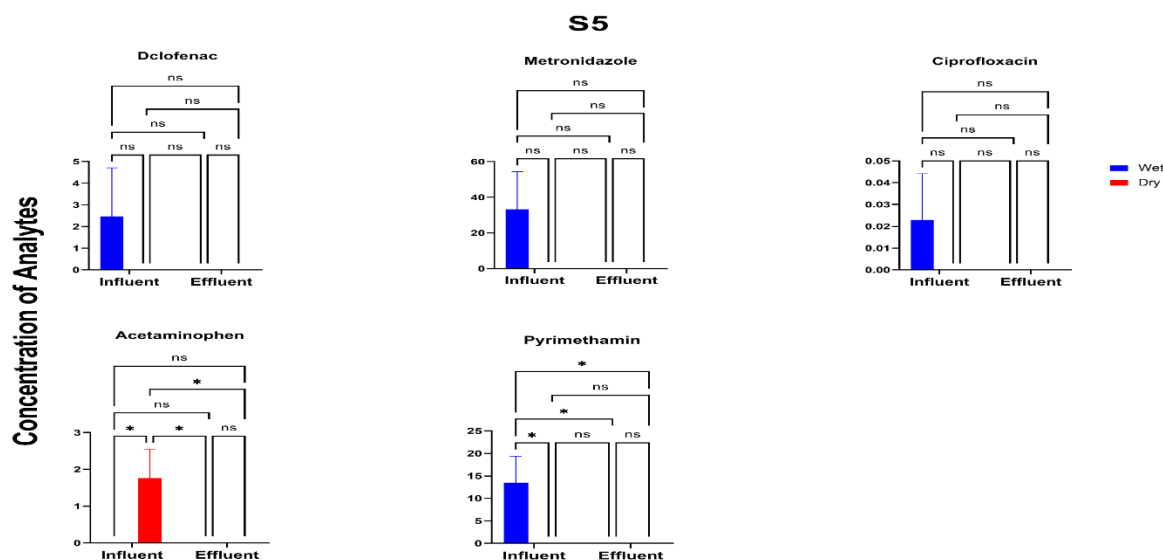


FIG 3.7: Concentrations of pharmaceutical residues in S5 during the wet and dry seasons.

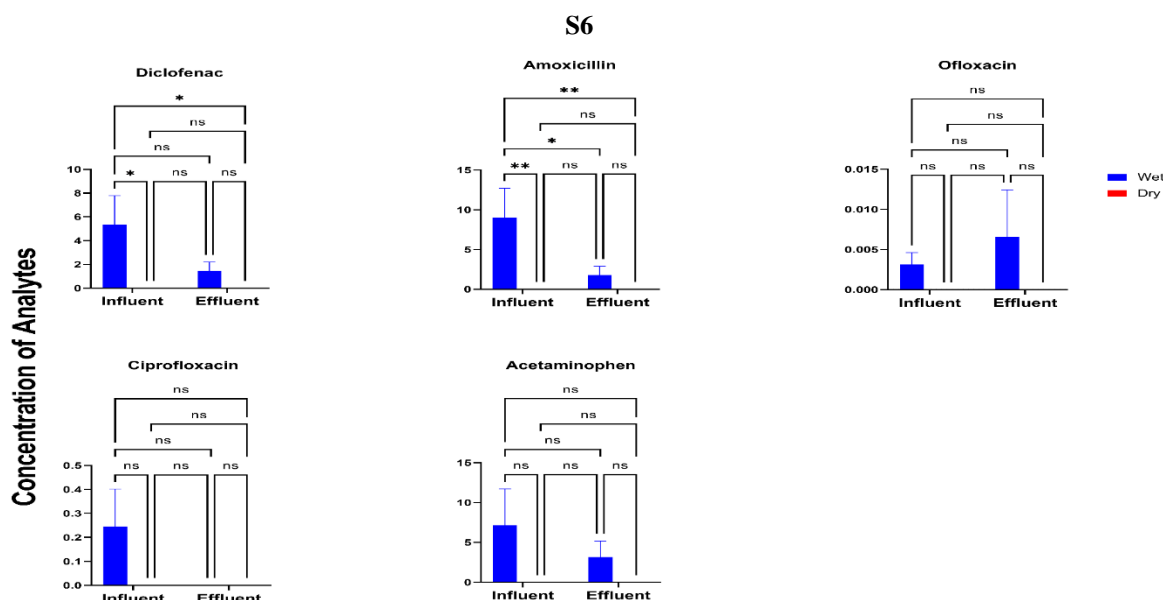


FIG 3.8: Concentrations of pharmaceutical residues in S6 during the wet and dry seasons.

3.3 Risk assessment of pharmaceutical residues in effluents

The risk quotient (RQ) is the basic principle that is internationally accepted in developing an environmental risk assessment guideline. The assessment of whether a substance presents a risk to other organisms is based on the comparison of the predicted effect concentration (PEC) or measured environmental concentrations (MEC) to its predicted no effect concentration (PNEC) to organisms in the ecosystem. The environmental effects of drug residues have been characterized by extrapolating PNEC based on mean ecotoxicological concentration (EC50) or LC50 values obtained from a set data of acute toxicity tests. A standard assessment factor of 1000 has been introduced to account for extrapolations from intra – as well as inter-species variability in sensitivity. The PNEC of the water compartment has been determined using equation (1)

$$PNEC_{\text{water}} = \frac{EC50 \text{ or } LC50}{1000} \text{Eq1 [26]}$$

If $RQ < 0.01$, it denotes negligible risk, $RQ < 1$ means low risk, $0.1 < RQ < 1$, It means medium risk and if $RQ > 1$, it represents high risk. [27]. High risk was calculated for acetaminophen and amoxicillin in the effluents which could be due to the high demand for the drugs.

Table 3.4: Risk assessments of pharmaceutical residues in WWTPs effluents

The risk Quotient method (RQ) was applied as a novel approach to estimate the environmental risk of pharmaceutical residues that are most frequently detected in wastewater effluents

Therapeutic group	Chemical Compound	Molecular formular	CAS number	Risk assessment of the Effluent
Analgesics	Ibuprofen	C ₁₃ H ₁₈ O ₂	15687-27-1	-
	Diclofenac	C ₁₄ H ₁₁ Cl ₂ NO ₂	15307-79-6	Low risk
	Acetaminophen	C ₈ H ₉ NO ₂	103-93	High risk
Anti biotics	Metronidazole	C ₆ H ₉ N ₃ O ₃	443-48-1	-
	Ofloxacin	C ₁₈ H ₂₀ FN ₃ O ₄	82419-36-1	Low risk
	Ciprofloxacin	C ₁₇ H ₁₈ FN ₃ O ₃	85721-33-1	Medium risk
	Amoxicillin	C ₁₆ H ₁₉ N ₃ O ₅ S	26787-78-0	High risk
Anti malaria	Sulfadoxin	C ₁₂ H ₁₄ N ₄ O ₄ S	2447-57-6	-
	Pyrimethamine	C ₁₂ H ₁₄ Cl ₂ N ₄	58-14-0	-
Stimulant	Caffeine	C ₈ H ₁₀ N ₄ O ₂	58-08-2	-

3.4 Concentrations of pharmaceutical residues (PRs) in the surface water

Many pharmaceutical residues (PRs) were detected in the surface water as shown in table 5. Ibuprofen had a maximum concentration of 3.33±0.6 ng/L with an average of 2.20±0.4 ng/ L. Ibuprofen is an analgesic that is used to relieve pain. It is also used as an anti-inflammatory drug for the reduction of inflammations and swellings. Ibuprofen and diclofenac are some of the most commonly used analgesics and anti-inflammatory drugs in Nigeria. Others include acetaminophen (paracetamol), naproxen, and aspirin [28]. The highest concentration of ibuprofen detected in the surface water was 5.04 ng / L in sw6. A similar study conducted in a river in Ogun State, Nigeria reported the presence of acetaminophen, diclofenac, ibuprofen, and ciprofloxacin in the mg/ml range [29]. Chronic exposure to diclofenac can negatively affect renal functions in fish. The kidney has also been found to be one of the target organs for diclofenac toxicity in many animals such as birds, mice, and humans [30,31,32]. The concentration of metronidazole ranged between 0.03±0.9 ng/L and 0.60±0.1 ng /L with an average concentration of 0.10±0.1 ng / L. Ibuprofen, diclofenac, and acetaminophen were detected in over 60% of all the samples. Diclofenac had the second highest concentration which ranged between 0.48±0.1 ng/L and 2.37±0.1 ng / L with a mean value of 1.10±0.08 ng / L as shown in table 3.5. Amoxicillin and pyrimethamine were not detected in the surface water. In Sw5, most of the PRs were below the detection limit except ofloxacin with a value of 1.45±0.4 ng / L.

Table 3.5: Concentrations of pharmaceutical residues (ng / L) in the surface water

Drug ID	SW1	SW2	SW3	SW4	SW5	SW6	Mean
Ibuprofen	3.23±0.6	1.26±0.5	3.90±0.2	<LOD	<LOD	5.04±0.4	2.24 ± 0.4
diclofenac	1.67±0.3	0.98±0.02	1.27±0.1	0.48±0.01	<LOD	2.37±0.1	1.1 ±0.08
Amoxicillin	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
Sulfadoxin	<LOD	<LOD	<LOD	<LOD	<LOD	3.46±0.7	0.57 ±0.1
Ofloxacin	<LOD	3.44±0.5	0.98±0.3	<LOD	1.45±0.4	<LOD	0.5 ±0.1

Ciprofloxacin	0.71±0.4	0.59±0.2	<LOD	<LOD	<LOD	<LOD	0.2 ±0.1
Caffeine	0.49±0.5	0.19±0.01	<LOD	1.23±0.1	<LOD	<LOD	0.3 ±0.1
Acetaminophen	1.33±0.5	0.57±0.4	0.52±0.2	0.40±0.3	<LOD	<LOD	0.4 ±0.2
Metronidazole	<LOD	<LOD	<LOD	0.60±0.1	<LOD	0.03±0.9	0.1 ±0.1
pyrimethamine	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD

* SW: Surface water

Pharmaceutical residues were detected in the surface water at various concentrations. They include ibuprofen, diclofenac, sulfadoxin ofloxacin, ciprofloxacin, caffeine, acetaminophen, and metronidazole. Ciprofloxacin concentrations ranged from <LOD -0.706 ng/L. Amoxicillin was not detected in any of the samples. Antibiotics are important components of modern medicine and are vital lines of defence against pathogenic bacteria and fungi. [33,34]. The unregulated use of antibiotics and discharged wastewater from pharmaceutical industries, household effluents, and agricultural farms are sources of antibiotics and their residues in the aquatic environment. The findings of this study are consistent with those of many other researchers reported in the literature in which low concentrations of pharmaceuticals were found in effluents of urban wastewater and receiving waters [35,36,37]. It is also in agreement with the study done by Rosal et al in 2010, where pharmaceutical compounds were detected at low concentrations in municipal wastewater with some compounds in the ng / mL⁻¹ range such as caffeine, acetaminophen, and paraxanthine while others were in ng / L⁻¹ range [38].

IV. Conclusions

Various concentrations of pharmaceutical compounds were detected at various in the influents and effluents of the six selected WWTPs and also in the receiving water body near the effluent discharge point. The concentrations of these drugs were in ng / L range with the effluent having a slightly lower concentration. Many of the PRs were detected in the influents, effluents, and surface water at different concentrations. The results indicate that WWTPs could not effectively eliminate all the pharmaceutical residues. The results from this study supported a similar work by Escher et al in 2011 which revealed the presence of some pharmaceutical compounds in effluents from hospital wastewater [16]. It is also consistent with other works found in the literature which revealed that many drugs, their metabolites, and transformation products are not efficiently removed during wastewater treatment processes. The results however further suggest that the conventional wastewater treatment technologies used in these areas are not efficient in removing all pharmaceutical pollutants from wastewater thereby encouraging the entrance of bioactive pollutants into the aquatic environment and contamination of the drinking water sources of the people living within the area. However, there is a need to encourage more research to optimize water treatment technology. Also, manufacturers, regulators, pharmacists, veterinary doctors, and consumers have to agree on various ways to reduce the discharge of pharmaceutical substances into rivers and streams. The result from this study will also assist in identifying the knowledge gap and research needs on pharmaceutical residues in the aquatic environment in Lagos, Nigeria. It may however contribute to the development of a national plan on pharmaceuticals. More research is needed to learn more about their fate and degradation pathways to ensure the safety of man and the environment.

Conflict of interest: I wish to state that, there is no conflict of interest.

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References

- [1]. Baker, D.R., Kasprzyk-Hordern, B . 2011. Critical evaluation of methodology commonly used in sample collection, storage, and preparation for the analysis of pharmaceuticals and illicit drugs in surface water and wastewater by solid-phase extraction and liquid chromatography-mass spectrometry. *J. Chromatogram*. 1218:7901–7913.
- [2]. Melana, L.H., Yelena, S., Paul, P et al. 2012. Pharmaceuticals and personal care products (PPCPs) in treated wastewater are discharged into Charleston Harbor, South Carolina. *Science of the Total Environment*. 437.
- [3]. Shahram, T., Paul, Y., Xiaoming, Z. 2010. Occurrence and removal of PPCPs and EDCs in the Detroit River Watershed, *Water practice, and technology*. 5
- [4]. Schreiber, A and Kern, R. 2010. Quantitation and identification of pharmaceuticals and personal care products (PPCP) in water samples, food, and environment.
- [5]. Jimoh, O.T., Ojo, O.F and Lesile, F.P. 2013. A review of pharmaceuticals and endocrine-disrupting compounds: sources, effects, removal, and detections, *Water, Air, and Soil pollution*. 224.
- [6]. Fent, K., Weston, A.A., Caminada, D. 2006. Review ecotoxicology of human pharmaceuticals. *Aquat. Toxicol.* 76: 122–159.
- [7]. Bottoni, P., Caroli, S., Barra Caracciolo, A. 2010. Pharmaceuticals as priority water contaminants, *Toxicol. Environ. Chem.* 92: 549–565.

- [8]. Pomati, P., Castiglioni, S., Zuccato, E. 2006. Effects of a complex mixture of therapeutic drugs at environmental levels on human embryonic cells, *Environ. Sci. Technol.* 40 (2006) 2442–2447.
- [9]. European Medicines Agency/Committee for Medicinal Products for Human Use (EMA/CHMP), Guideline on the environmental risk assessment of medicinal products for human use, EMA, London, UK, 2006 EMA/CHMP/SWP/4447/00.
- [10]. Loos, R., Gawlik, B. M., Locoro, G et al. 2009. EU-wide survey of polar organic persistent pollutants in European river waters, *Environ. Pollut.* 157:561–568.
- [11]. Alonso, S., Català, M., Maroto, R. R et al. 2010. Pollution by psychoactive pharmaceuticals in the Rivers of Madrid metropolitan area (Spain), *Environ. Int.* 36: 195–201.
- [12]. Chang, H., Hu, J.Y., Shao, B. 2007. Occurrence of natural and synthetic glucocorticoids in sewage treatment plants and receiving river waters. *Environ. Sci. Technol.* 41 (10), 3462–3468.
- [13]. Rosal, R., Rodriguez, A., Perdign, M., et al. 2010. Occurrence of emerging pollutants in urban wastewater and their removal through biological treatment followed by ozonation. *Water Res.* 44 (2), 578–588.
- [14]. Khan, S.J and Ongert, J.E. 2002. Estimation of pharmaceutical residues in primary and secondary sewage sludge based on quantities of use and fugacity modeling. *Water Sci. Technol.* 46 (3): 105–113.
- [15]. Kolpin, D.W., Furlong, E.T., Meyer, M.T et al. 2002. Pharmaceuticals, hormones, and other organic wastewater contaminants in U.S. streams, 1999–2000, a national reconnaissance. *Environ. Sci. Technol.* 36 (6): 1202–1211. 2002.
- [16]. Escher, B.I., Baumgartner, R., Koller, M et al. 2011. Environmental toxicology and risk assessment of pharmaceuticals from hospital wastewater, *Water Res.* 45 (1):75–92.
- [17]. Schriks, M., Heringa, M.B., Van der Kooij, M.M.E et al. 2010. Toxicological relevance of emerging contaminants for drinking water quality, *Water Res.* 44 (2), 461–476.
- [18]. Hernando, M.D., Mezcua, M., Fernandez-Alba, A. Ret al. 2006. Environmental risk assessment of pharmaceutical residues in wastewater effluents, surface waters, and sediments. *Talanta* 69: 334–342.
- [19]. Zhou, L.J., Ying, G.G., Zho, J.L et al. 2011. Trends in the occurrence of human and veterinary antibiotics in the sediments of the Yellow River, Hai River, and Liao River in northern China. *Environ. Pollut.* 159 pp 1877–1885. DOI: 10.1016/j.envpol.2011.03.034
- [20]. Ewandowska, J.L., Putschew, A., Schwesig, D. et al. 2011. The fate of organic micropollutants in the hyporheic zone of a eutrophic lowland stream: results of a preliminary field study”, *Sci. Total Environ.* 409: 1824–1835.
- [21]. Environmental Protection Agency of the United States of America method 1694: 2009. Analysis of pharmaceuticals and personal care products in water, soil, sediment, and biosolids by HPLC / ms. EPA-821-r-08-002. Retrieved from www.unitejchem.com
- [22]. International Conference on Harmonization of Chemical Procedures (ICH), Q2 (R1). 2005. Validation of analytical procedure: Text and methodology.
- [23]. Lacey, C., McMahon, G., Bones, J. 2008. An LC-MS method for the determination of pharmaceutical compounds in wastewater treatment plant influent and effluent samples. *Talanta* 75 (4): 1089–1097.
- [24]. Santos, J.L., Aparicio, I., Alonso, E. 2007. Occurrence and risk assessment of pharmaceutically active compounds in wastewater treatment plants. A case study: Seville city 4 (Spain). *Environ. Int.* 33 (4), 596–601.
- [25]. Zhou, J.L., Zhang, Z.L., Banks, E. 2009. Jiang. Pharmaceutical residues in wastewater treatment work effluents and their impact on receiving river water. *J. Hazard. Mater.* 166 (2– 3): 655–661.
- [26]. Bejarano, AC, Farr JK, Jenne P et al. (2016). The chemical aquatic fate and effects database (CAFÉ), is a tool that supports assessments of chemical spills in aquatic environments. *Environ Toxicol Chem* 35:1576-1586. <https://doi.org/10.1002/etc.3289>.
- [27]. EU Commission. (2003). Technical guidance on risk assessment in support of Commission Directive 93/67/EEC on risk assessment on new notified substances and Commission Regulation (EC) No 1488/94 on risk assessment for existing substances – part 11 EUR 20418EN.
- [28]. Madikizela, L.M., Ncube, S., Chimuka, L. (2019). Analysis, occurrence, and removal of pharmaceuticals in African water resources: A current status. *J Environ Manage.* 2020;253:109741. <https://doi.org/10.1016/j.jenvman.2019.109741>
- [29]. Olaitan, O.J., Anyakora, C., Bamiro, T., Tella, T.A. (2014). Determination of Pharmaceutical Compounds in Water By Solid Phase Extraction- Liquid Chromatography. *Journal of Environmental Chemistry and Ecotoxicity.* Feb 06.6(3):20-26.
- [30]. Oaks, J.L., Gilbert, M., Virani, M.Z., Watson, R.T., Meteyer, C.U., Rideout, B.A., Shivaprasad, H.L., Ahmed, S., Chaudhry, M.J., Arshad, M., Mahmood, S. (2004). Diclofenac residues as the cause of vulture population decline in Pakistan. *Nature.* 2004 Feb 12;427(6975):630-3.
- [31]. Hickey, E.J., Raje, R.R., Reid, V.E., Gross, S.M., Ray, S.D. (2001). Diclofenac-induced in vivo nephrotoxicity may involve oxidative stress-mediated massive genomic DNA fragmentation and apoptotic cell death. *Free Radical Biology and Medicine.* Jul 15.31(2):139-52.
- [32]. Lim, H.Y., Vincent, A.S., Halliwell, B., Wong, K.P. (2017). Nephrotoxicity of Diclofenac. *AJPSP*; Volume 5, Issue 1
- [33]. Madikizela, L.M., Chimuka, L. (2017). Occurrence of naproxen, ibuprofen, and diclofenac residues in wastewater and river water of KwaZulu-Natal Province in South Africa. *Environ Monit Assess.* 189(7):348. <https://doi.org/10.1007/s10661-017-6069-1>
- [34]. Rehman, M., Rashid, N., Ashfaq, M., Saif, A., Ahmad, N., Han J. (2015). Global risk of pharmaceutical contamination from highly populated developing countries. *Chemosphere.* 2015;138:1045– 1055. <https://doi.org/10.1016/j.chemosphere.2015.138.1045>
- [35]. Bartelt-Hunt, S.L., Snow, D.D., Damon, T. 2009. The occurrence of illicit and therapeutic pharmaceuticals in wastewater effluent and surface waters in Nebraska. *Environ. Pollut.* 157 (3), 786–791.
- [36]. Joss, A., Siegrist, H and Ternes, T.A. 2008. Are we about to upgrade wastewater treatment for removing organic micropollutants”, *sci. Technol.* 57 (2): 251–255.
- [37]. Radjenovic, J., Petrovic, M and Barcel, D. 2009. Fate and distribution of pharmaceuticals in wastewater and sewage sludge of the conventional activated sludge (CAS) and advanced membrane bioreactor (MBR) treatment. *Water Res.* 43 (3): 831–841.
- [38]. Gracia-Lor, E., Sancho, J.V and Hernandez, J.V. 2010. Simultaneous determination of acidic, neutral, and basic pharmaceuticals in urban wastewater by ultra-high-pressure liquid chromatography-tandem mass spectrometry. *J. Chromatogr.* 1217 (5), 622–632.

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