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ASSESSMENT OF PHARMACEUTICAL RESIDUES IN SELECTED SURFACE WATERS IN IJEBU-ODE, NIGERIA USING SOLID PHASE EXTRACTION-HIGH PERFORMANCE LIQUID CHROMATOGRAPHY (SPE-HPLC)

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Abstract

The presence of pharmaceutical compounds (PCs) in the environment, especially in developed countries, has not only been ascertained, but their adverse impacts have been investigated and reported even at trace levels. However, there is a paucity of information on the occurrence patterns of these compounds in selected African environments like Nigeria. Hence, this study focused on the investigation of seven PCs in some surface waters within Ijebu-Ode, Ogun State, Nigeria, in five major rivers, namely Rivers Ona, Erinwe, Imagbon, Iweni, and Adamegi. These compounds include antibiotics- trimethoprim (TMP), sulfamethoxazole (SMZ), and ciprofloxacin (CIP); analgesics- paracetamol (PCM), diclofenac (DCF), and ibuprofen (IBU) and an antidiabetic- metformin (MET). The analyte PCs were monitored using a solid phase extraction- high-performance liquid chromatographic method (SPE-HPLC) which was developed and validated according to the International Conference on Harmonization guidelines. The highest levels of PCM (2.13 ± 0.28 µg/mL) and CIP (0.50 ± 0.07 µg/mL) were detected in the Erinwe River, while the highest concentrations of SMZ (2.25 ± 0.30 µg/mL) and TMP (0.35 ± 0.05 µg/mL) were detected in River Ona. Generally, the Σ PCs (µg/mL) in the rivers sampled are in the order SMZ (4.09) > PCM (3.01) > CIP (0.78) > DCF (0.56) > TMP (0.46) except for MET and IBU, which were not detectable in any of the rivers. Generally, the results obtained in this study are relatively high; hence, policies must be put in place to commence their removal from the environment.

Keywords: Pharmaceutical compounds, Surface waters, SPE-HPLC method, Environment, Nigeria.

Introduction

The contamination of the environment has been traced to the presence of specific compounds, such as polycyclic aromatic hydrocarbons (PAHs) (Finch and Stubblefield, 2019), pharmaceuticals, and personal care products (PPCPs) (Kümmerer, 2009; Omotola and Olatunji, 2020; Omotola et al., 2022), brominated flame retardants (BFRs) (Nakayama et al., 2019), poly- and per-fluoroalkyl substances (PFASs), microplastics (Prata et al., 2018; Zhang, 2017) and other persistent organic pollutants (Prata et al., 2018; Zhang, 2017).

Among these contaminants, the most prominent are the PPCPs. The presence of these compounds in the environment, especially in developed countries, has not only been ascertained, but their adverse impacts have been investigated and reported even at trace levels (Fu et al., 2017; Hernández Martínez et al., 2017; Omotola et al., 2021; Robson et al., 2017). Precisely, human health and other biotic components become threatened once the environment is polluted with these compounds. Pharmaceutical contamination is usually high in environmental matrices such as air, water, soil, and sediments because they are natural sinks or endpoints for pharmaceutical residues. Subsequently, the release of domestic sewage-containing pharmaceutical compound (PC) residues mainly causes water pollution (Huang et al., 2022; Ji et al., 2022; Zhou et al., 2021). Generally, waste treatment plants (WTPs) have been documented as the primary known point source of PC residues in the environment. In contrast, non-point sources, such as run-offs from diverse dumpsites and inappropriate disposal of refuse, are sometimes not traceable. These substances, unfortunately, find their paths into drinking water and aquatic biota.

Consequently, the WTP effluents are channeled into large water bodies since it is assumed the effluents are crystal clear from pollutants. However, the remediation processes involved in wastewater treatment are not designed to remove specific contaminants before the release of the 'clean water.' Of all the media in which PPCPs are investigated, the water ecosystem is the most explored with respect to the monitoring and detection of pharmaceutical contamination (Wilkinson et al., 2022). Wilkinson and co-authors embarked on a global study on pharmaceutical contamination, investigating 61 pharmaceutical compound residues in 258 rivers of the world. The assessment of these rivers is equivalent to the contamination influence of pharmaceuticals on 471.4 million people, cutting across 137 of the world's geographic regions. The continents with the highest levels of pollution, as shown in Figure 1, were Africa (sub-Saharan), Asia (South Asia), and South America (Wilkinson et al., 2022).

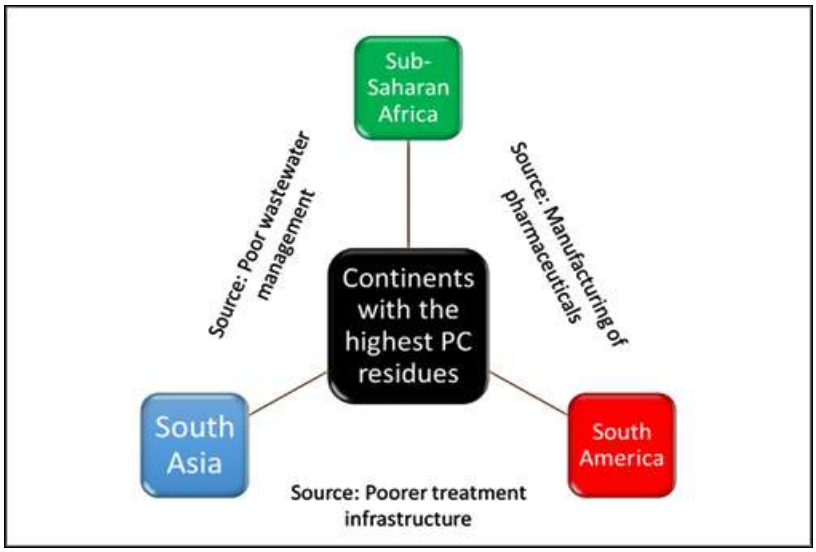

Figure 1: Most pharmaceutical-contaminated continents

These reports are at par with the results earlier reported by Omotola et al. (2022 with respect to the South African environment. The increased contamination level was associated chiefly with poor to inefficient waste management systems (Omotola et al., 2022; Wilkinson et al., 2022). According to Wilkinson et al. (2022, the most frequently detected residues of pharmaceuticals were metformin, caffeine, and carbamazepine. These pharmaceutical drugs were detected at over 50 % of the investigated sites. Since pharmaceuticals are biologically active compounds targeted at interacting with biochemical components, there is a high possibility that the combination of these compounds in the water ecosystem is highly deleterious to living entities. Unfortunately, most of these waters are used for recreational purposes, irrigation, and sometimes for direct drinking by animals or indirect use by humans. Hence, pharmaceutical contamination biomagnifies or accumulates in the food web (Richmond et al., 2018). As a result, the water ecosystem becomes a threat to lives.

Nevertheless, the detection of PC residues remains a challenge in Africa, with a specific focus on Nigeria, where relatively few studies are available regarding the PC contamination status of its ecosystem, unlike South Africa. The lack of substantial information on the subject matter in Nigeria could be due to scarcity or unavailability of instruments as a result of their high cost. Furthermore, the lack of technical know-how could also be a challenge with respect to the paucity of information on instruments' usage for pharmaceutical contamination studies in Nigeria. Chromatography is usually employed for this purpose, of which high-performance liquid chromatography (HPLC) is mostly used. Another technique is hyphenated, where chromatographic and spectrometric methods are coupled, such as liquid chromatography-mass spectrometry (LC-MS). Nowadays, a more sensitive method like the LC-tandem MS is mostly used to monitor PC residues. All these aforementioned instruments are still scarce and scanty in Nigeria to date. However, HPLC, which was used in this study, is still rarely available in commercial laboratories in Nigeria but is expensive. The present study, thus, focuses on the detection and quantitation of the residues of commonly prescribed pharmaceutical drugs in five major rivers, namely Rivers Ona, Erinwe, Imagbon, Iweni, and Adamegi within Ijebu-Ode, Ogun State, Nigeria. These PCs include antibiotics-trimethoprim (TMP), sulfamethoxazole (SMZ), ciprofloxacin (CIP); analgesics- paracetamol (PCM), diclofenac (DCF), and ibuprofen (IBU) and an antidiabetic- metformin (MET). The present study becomes one of the few studies carried out within Nigeria, precisely Ogun State, making it an eye-opener to future research works on the same subject. More so, this study adds to the pool of information on pharmaceutical contamination within Nigeria.

Materials and methods

Pharmaceutical standards of trimethoprim (99.8%), sulfamethoxazole (99.8%), paracetamol (99.8%), metronidazole (99.8%), diclofenac (99.8%), ibuprofen (99.3%) and ciprofloxacin hydrochloride (99.6%) were purchased from Merck, USA. Disodium ethylenediaminetetraacetic acid (98%), trifluoroacetic acid (TFA, >99.0%), HPLC grade methanol and acetonitrile - 99.9% were also purchased from Merck, USA. Waters Oasis hydrophilic-lipophilic balance (HLB) soli-phase extraction (SPE) Cartridges, 6cc, 200 mg, were used for the extraction procedure. SciFinder provides the structural details, systemic names, applications, and chemical information of the PCs under

investigation in this study. An HPLC system consisting of a binary pump, an auto liquid sampler (ALS) injector, a thermostatic column compartment, and a variable wavelength detector (VWD), capable of a gradient wavelength timetable with an online degasser was used in the reversed-phase mode. All experiments were carried out at the Labwox Laboratory, Ikeja, Lagos, Nigeria.

Method validation

The data obtained from instrument calibration and analyte recovery were subjected to the International Conference on Harmonization guideline for validation of the method developed. This procedure was to ascertain that the method meets acceptable specifications for its use (International Conference on Harmonisation, 2005). The parameters considered for validation in the present study included specificity, linearity and linear range, limit of detection (LoD), limit of quantitation (LoQ), and analytes recovery evaluations on stock solutions. All the samples collected were analyzed under the optimum chromatographic performance conditions to ascertain the peak areas of the analytes. Regarding the SPE method developed, the cartridges were conditioned sequentially using 6 mL of acetone, 6 mL of methanol, and 6 mL of buffered water (pH = 3). Afterward, the cartridges were loaded with 500 mL of water sample at 3-5 mL/min flow rate. The SPE columns were then dried, ensuring the removal of residual water by spinning cartridges in a centrifuge at 4000 rpm for 5 mins. After the cartridges were dried, the analytes were eluted with (3 × 2 mL) methanol. Preconcentration of the eluates was carried out with a stream of nitrogen gas to dry off methanol. This concentrate was then analysed on the HPLC using the developed and validated method. The % recovery of the seven PCs ranged from 93% for IBU to 106% for TMP. All samples were extracted and cleaned up within 72 hrs of arrival at the laboratory. The data obtained were interpreted using Excel Software Package 2016 for parametric analyses.

Sampling sites and sample collection

Water samples were collected from five sampling points, as shown on the map in Figure 2, including Adamegi River (3°53'26.98"E and 6°46'32.01"N), River Iweni (3°52'50.32"E and 6°46'17.87"N), Ona River (3°54'20.66"E and 6°47'45.33"N), Erinwe River (3° 53'4.16"E and 6° 46'33.37"N) and River Imagbon (3°58'10.46"E and 6°45'25.16"N). The sampling map was generated employing sampling point coordinates with the Google Earth Pro, 2023 application. Composite sampling was conducted, where samples were collected from upstream, midstream and downstream. These samples were composited, from which a representative sample was collected for each river. The Erinwe River has been reportedly subjected to flooding, which affected 150 ponds, amounting to the loss of fishes (https://fcwc-fish.org/other-news/ogun-fish-farmers-lose-n300m-to-flooding). Like River Ona, the Imagbon River is one of the Rivers within Ogun State where some community inhabitants swim or bathe. The Iweni and Adamegi Rivers are used for washing and fishing, respectively. These five rivers form part of the major rivers within Ijebu-Ode, and as such, people interact with them a great deal. Hence, this study is interested in monitoring the occurrence pattern of PC residues in them.

Figure 2: Map of sampling sites

Results and discussion

Development and validation of instrumental method

Analytical method validation is key before a previously developed method is acceptable. For this study, the optimum instrumental parameters employed in the analysis of MET, TMP, SMZ, PCM, CIP, DCF, and IBU were injection volume of 20 µL, and mobile phase compositions of 0.1%v/v TFA in water (A) and acetonitrile (B). The optimum instrumental parameter for the detection and separation of the analytes is given in Table 1.

The gradient started with 88 % A from 0 to 6 mins, followed by a linear decrease of mobile phase A to 40 % for 6 to 15 mins and this was maintained for another 10 mins. Ultimately, the composition of phase A was increased to 88% for 25 to 25.2 mins, and maintained until 30 mins, to reach the initial condition for the next injection. The total run time was 30 mins per injection, achieved with an optimum column temperature kept constant at 40 ◦C, a 1.0 mL/min constant flow rate and a sample injection volume set at 20 µL (Table 1). A sample chromatogram of the analytes is given in Figure 3.

One validation parameter ascertained was the specificity of the developed method, which is based solely on the retention times of the analytes. This was done by injecting into the chromatographic column under optimum conditions, varying concentrations of the mixture of the 7-PCs ranging from 0.2 µg/mL to 10.0 µg/mL. The analytes' retention times were 4.301, 5.012, 11.651, 12.561, 13.423, 20.064, and 20.561 for MET, PCM, TMP, CIP, SMZ, DCF and IBU, respectively (Table 2). Another important criterion for acceptable analytical results is the quality of the calibration curve.

Table 1: Optimum parameters employed in the HPLC analysis of targeted PCs

HPLC system and parameters optimized			
Column type and temperature	Phenomenex C18 (250 x 4.6 mm) 5µm particle size; 40 °C		
Injection volume	20 µL		
Elution solvent system	Mobile Phase A - 0.1%v/v TFA in water Mobile Phase B - HPLC Grade acetonitrile		
Flow rate	1.0 mL/min		
Wavelength of detection	230 nm		
Pressure	~112 Bar		
Gradient program	Time (mins)	A (%)	B (%)
	0	88	12
	6	88	12
	15	40	60
	25	40	60
	25.2	88	12
	30	88	12

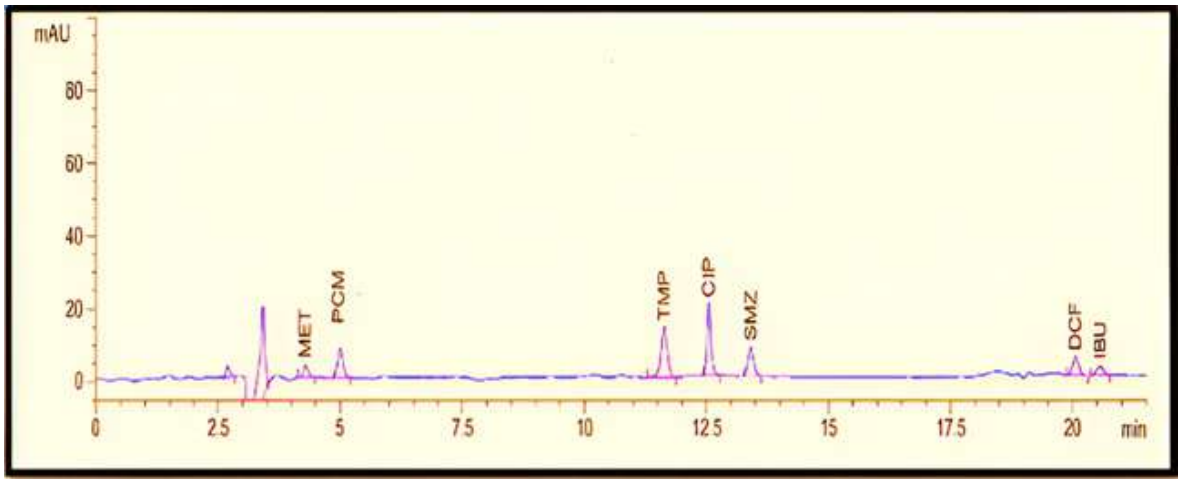

Figure 3: Sample chromatogram of targeted pharmaceuticals

Five to six different concentrations of the PC mixture were prepared and analysed on the HPLC to prepare the calibration curves for each analyte, as shown in Supplementary Information 1.

The correlation coefficients (R^2) were 0.99936, 0.99997, 0.99994, 0.99985, 0.99996, 0.99995, and 0.99985 for MET, PCM, TMP, CIP, SMZ, DCF and IBU, respectively. For the best-fit curve of each analyte, the equation of regression is shown in Table 2. The correlation coefficient values were greater than 0.90 ; this validates the method developed. Furthermore, among the germane validation parameters investigated in this study are the LoD and LoQ, which were obtained following the formula recently stated by —. Omotola et al (2004). The instrument's LoDs (µg/mL) for MET, PCM, TMP, CIP, SMZ,DCF and IBU were 0.321, 0.052, 0.076, 0.122, 0.065, 0.065, and 0.136, while the instrument's LoQs (µg/mL) were 1.072, 0.174, 0.255, 0.406, 0.217, 0.217, and 0.545, respectively (Table 2).

Table 2: Validation results for the selected pharmaceuticals

Analyte PCs	Retention time (mins)	Best fit equation	Slope	Regression coefficient (R^2)	LoD (µg/mL)	LoQ (µg/mL)
MET	4.301	$y = 23.037x - 2.101$	23.037	0.99936	0.321	1.072
PCM	5.012	$y = 56.756x + 1.539$	56.756	0.99997	0.052	0.174
TMP	11.651	$y = 115.668x + 4.155$	115.668	0.99994	0.076	0.255
CIP	12.561	$y = 122.883x - 5.429$	122.883	0.99985	0.122	0.406
SMZ	13.423	$y = 62.077x - 0.597$	62.077	0.99996	0.065	0.217
DCF	20.064	$y = 40.726x + 1.289$	40.726	0.99995	0.065	0.217
IBU	20.561	$y = 24.436x + 0.715$	24.436	0.99985	0.163	0.545

Analysis of surface water samples and comparison with previous studies

The method developed and validated was used in the analysis of water samples collected from five major sites within Ijebu-Ode, Ogun State, Nigeria. Water samples were obtained from different points within these rivers and put into pre-cleaned bottles. The water samples were extracted at ambient temperature and processed for the recovery of the aforementioned analytes using the validated method of extraction earlier mentioned and thereafter detected and quantified using the optimum method on the HPLC. The extractable PC residue concentrations in the water samples are presented in Table 3 and Figure 4. The highest levels of PCM (2.13 ± 0.28 µg/mL) and CIP (0.50 ± 0.07 µg/mL) were detected in the Erinwe River, while the highest concentrations of SMZ (2.25 ± 0.30 µg/mL) and TMP (0.35 ± 0.05 µg/mL) were detected in River Ona (Table 3). Diclofenac was not detected in all the sampling sites except the Ona River (Figure 4), with a concentration of 0.56 ± 0.07 µg/mL (Table 3). Generally, the ΣPCs (µg/mL) in the Rivers sampled are in the order SMZ (4.09) > PCM (3.01) > CIP (0.78) > DCF (0.56) > TMP (0.46) MET and IBU (not detected, ND) (Table 3). The high concentrations of SMZ in the Rivers can be easily traced to its significant usage in humans and veterinary medicine , either for prophylactic or therapeutic purposes. Similarly, the relatively high level of PCM was not surprising at all, as this PC is one of the most widely used over-the-counter analgesics. However, its usage is not at par with the analgesic DCF (Figure 4). This could be due to the controversies surrounding the consumption of the PC , hence its relatively lower level (0.56 µg/mL) reported in this study.Unlike SMZ, TMP is rarely administered as a stand-alone PC but mostly in combination with SMZ for synergistic effects;hence, its relatively lower amount

Table 3: Levels (µg/mL) of pharmaceutical residues in sampled surface waters (n=15)

Pharmaceuticals Compounds	Adamegi		Erinwe		Imagbon		Iweni		Ona		$\sum$ PCs
	Mean	Std. Dev.	Mean	Std. Dev.	Mean	Std. Dev.	Mean	Std. Dev.	Mean	Std. Dev.	
Metformin	< LOD	_	< LOD	_	< LOD	_	< LOD	_	< LOD	_	_
Paracetamol	< LOD	_	2.13	0.28	0.23	0.03	0.65	0.09	< LOD	_	3.01
Trimethoprim	< LOD	_	< LOD	_	< LOD	_	0.11	0.02	0.35	0.05	0.46

Pharmaceuticals Compounds	Adamegi		Erinwe		Imagbon		Iweni		Ona		$\sum PCs$
	Mean	Std. Dev.	Mean	Std. Dev.	Mean	Std. Dev.	Mean	Std. Dev.	Mean	Std. Dev.	
Ciprofloxacin	< LOD	_	0.50	0.07	< LOD	_	< LOD	_	0.28	0.04	0.78
Sulfamethoxazole	< LOD	_	1.24	0.17	0.31	0.04	0.29	0.04	2.25	0.30	4.09
Diclofenac	< LOD	_	< LOD	_	< LOD	_	< LOD	_	0.56	0.07	0.56
Ibuprofen	< LOD	_	< LOD	_	< LOD	_	< LOD	_	< LOD	_	_
$\sum PCs$		_	3.87	_	0.54	_	1.05	_	3.44	_	8.90

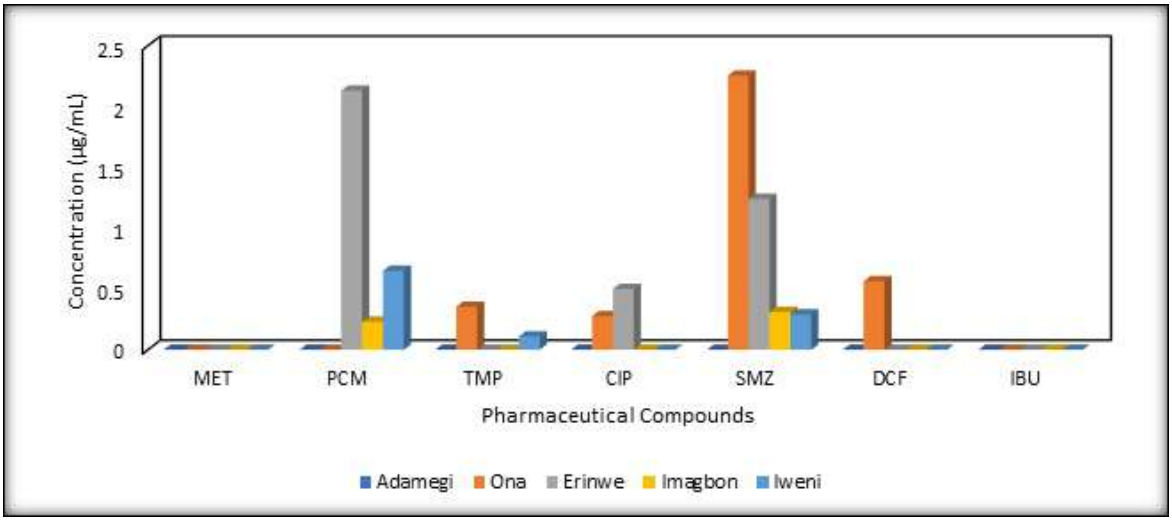

Figure 4: Graphical presentation of the levels (µg/mL) of PC residues in sampled rivers

detected when compared with SMZ. Of all the Rivers sampled in this study, the Erinwe River had the highest levels of analyte PCs (3.87 µg/mL), followed by River Ona (3.44 µg/mL), River Iweni (1.05 µg/mL) and finally, River Imagbon (0.54 µg/mL). It is worthy of mentioning that none of the analyte PCs was detectable in River Adamegi (Figure 4). However due to the limitations of HPLC with respect to its sensivity, it might not be safely concluded that these PC residues are not present in the Adamegi River. Perhaps if a more sensitive instrument, such as the LCMS or the LC-tandem MS is used for the same purpose, the status of these PCs in this river might be ascertained.

The level of CIP (0.50 µg/mL) detected in this study is above those reported in the Ghanian river water and effluent (1.17E-03 and 2.62E-04 µg/mL) by Azanu et al. (2018; Kenyan river water (5.09E-04 µg/mL) by Ngumba et al. (2016 and South Africa surface waters (1.43E-02 µg/mL) by –Agunbiade and Moodley (2016 (Table 4). Similarly, this study's CIP concentration is higher than reported (4.40E-04 µg/mL) in tap water in Nigeria (Olaitan et al., 2017). The relatively lower CIP value reported in the tap water is not surprising, as most tap water in Nigeria is supposedly potable. However, there is a paucity of information regarding the

permissible limits of PCs in the environment, unlike other pollutants like heavy metals. Previous studies on SMZ in water show relatively lower levels when compared to the present study (Table 4). Reports by Abou-Elwafa Abdallah et al. (2019 and K'oreje et al. (2016 indicated SMZ levels of 1.90E-05 µg/mL and 3.90E-02 µg/mL in Egypt's effluent and Kenyan river water, respectively.

These values are lower than the 2.25 µg/mL SM reported in this study. From these results, there is a feasibility that the Egypt's and Kenya's treatment plants are more functional, making it a wake-up call to the Nigerian governing bodies with respect to the provision of efficient treatment plants. Comparing the SMZ data obtained by Ebele and team members in the Nigerian surface water in 2020 , this study's SMZ reported is much higher. This corroborates the lack of efficient treatment plants in Nigeria. Furthermore, the data obtained for PCM, DCF and TMP in this study are also higher than those reported in the Ugandan lake water ; South Africa's surface water and Egypt's surface water , respectively (Table 4). Unlike other previous studies within Africa where MET and IBU were detected , these PCs were not detectable in the studied surface waters or were below the instrument's detection limit. The use of HPLC in the analysis of the samples is noteworthy, as compared to previous similar works where more sensitive instruments like the LC-tandem MS were used. Generally, the reports from this study are alarming and must be taken with utmost priority by stakeholders concerning removing PC residues from the Nigerian environment. Unfortunately, these compounds are toxic to biotic components even at environmentally relevant concentrations , hence the earnest commencement of green remediation strategies to eliminate them from the environment.

Table 4: Comparison of the PC levels (µg/mL) in this study with previous studies in Africa

Analyte PC	Country detected	Sample matrix	Conc. Reported (µg/mL)	References
Ciprofloxacin	Ghana	River water and effluent	1.17E-03 and 2.62E-04	(Azanu et al., 2018)
	Nigeria	Tap water	4.40E-04	(Olaitan et al., 2017
	Uganda	Lake water	4.10E-05	(Nantaba et al., 2020)
	Kenya	River water	5.09E-04	(Ngumba et al., 2016)
	South Africa	Surface water	1.43E-02	(Agunbiade and Moodley, 2016)
	This study	Surface water	<LOD – 0.50	
Sulfamethoxazole	Egypt	Effluent	1.90E-05	(Abou-Elwafa Abdallah et al., 2019)
	Nigeria	Surface water	3.18E-03	(Ebele et al., 2020)
	Kenya	River water	3.90E-02	(K'oreje et al., 2016
	South Africa	Surface water	5.32E-03	(Matongo et al., 2015)
	Kenya	River water	1.38E-02	(Ngumba et al., 2016)
	This study	Surface water	<LOD – 2.25	

Paracetamol	Nigeria	Tap water	3.10E-04	(Olaitan et al., 2017
	Nigeria	Surface water	1.24E-02	(Ebele et al., 2020)
	Kenya	River water	1.07E-01	(K'oreje et al., 2016
	Uganda	Lake water	2.70E-05	(Nantaba et al., 2020)
	South Africa	Surface water	1.05E-03	(Fatoki et al., 2018)
	This study	Surface water	<LOD – 2.13	
Diclofenac	Nigeria	Tap water	1.38E-04	(Olaitan et al., 2017
	Nigeria	Surface water	2.00E-04	(Ebele et al., 2020)
	Egypt	surface water	3.61E-03	(Abou-Elwafa Abdallah et al., 2019)
	Uganda	Lake water	1.60E-04	(Nantaba et al., 2020)
	South Africa	Surface water	3.67E-03	(Fatoki et al., 2018)
	This study	Surface water	<LOD – 0.56	
Trimethoprim	Nigeria	Water (Surface water or effluent)	2.00E-03	(Ogunbanwo et al., 2022)
	South Africa	Wastewater effluent (point of exit)	6.18E-05	(Ncube et al., 2021)
	Kenya	River water	2.65E-03	(Ngumba et al., 2016)
	Egypt	Effluent	2.74E-03	(Abou-Elwafa Abdallah et al., 2019)
	Egypt	Surface water	2.30E-04	(Abou-Elwafa Abdallah et al., 2019)
	This study	Surface water	<LOD – 0.35	
Metformin	Nigeria	Water (Surface water or effluent)	1.00E-02	(Ogunbanwo et al., 2022)
	Nigeria	Surface water	<5.00E-07 - 1.76E-03	(Ebele et al., 2020)
	Egypt	Effluent	5.61E-03	(Abou-Elwafa Abdallah et al., 2019; Waleng and Nomngongo, 2022)
	Nigeria	Groundwater	<5.00E-07 - 3.49E-04	(Ebele et al., 2020)
	Egypt	Surface water	6.30E-05	(Abou-Elwafa Abdallah et al., 2019)

	This study	Surface water	<LOD	
Ibuprofen	Nigeria	Wastewater	3.80E-02	(Lan et al., 2019)
	South Africa	Effluent	1.03E-03	(Mhuka et al., 2020
	Egypt	Effluent	6.70E-03	(Abou-Elwafa Abdallah et al., 2019)
	South Africa	River water	5.87E-02	(Waleng and Nomngongo, 2022)
	South Africa	Sea water	1.70E-04	(Ngubane et al., 2019)
	This study	Surface water	<LOD	

Limitations of the Study

The analytical method employed in this study, namely Solid Phase Extraction coupled with High Performance Liquid Chromatography (SPE-HPLC), although effective and validated for the target compounds, is less sensitive compared to advanced techniques such as liquid chromatography-mass spectrometry (LC-MS) or LC tandem MS (LC-MS/MS). This limitation may have contributed to the non-detection of certain compounds such as metformin and ibuprofen, especially in low-concentration samples like those from River Adamegi. The possibility that these compounds were present at levels below the HPLC detection threshold cannot be ruled out. Furthermore, the study focused on a limited number of pharmaceutical compounds, excluding many other commonly used drugs and their transformation products or metabolites, which may also pose significant environmental risks. This constraint potentially underrepresents the full scope of pharmaceutical contamination in the study area. Also, the present study did not assess ecological or human health risks associated with the detected pharmaceutical residues. Although the levels of certain compounds were comparatively high, their actual toxicological implications remain unexplored. Quantitative risk assessments, such as hazard quotients or risk characterization ratios, would provide valuable context to the environmental significance of the measured concentrations. Additionally, while comparisons were made with previous studies across Africa, differences in analytical techniques, sample matrices, and reporting formats may influence the comparability of results. Therefore, future research should adopt more sensitive analytical instrumentation, expand the range of target analytes, and integrate risk assessment models to generate a more holistic understanding of pharmaceutical contamination in surface waters.

Conclusion

The present study investigated the presence of seven PC residues in some Nigerian surface waters using an HPLC method which was developed and validated according to the ICH guidelines. The PCs included MET, PCM, TMP, CIP, SMZ, DCF and IBU, with retention times (mins) of 4.301, 5.012, 11.651, 12.561, 13.423, 20.064, and 20.561, respectively. The results of the validation procedures ascertained that the method was suitable for the purpose for which it was developed. The highest levels of PCM (2.13 ± 0.28 µg/mL) and CIP (0.50 ± 0.07 µg/mL) were detected in the Erinwe River, while the highest concentrations of SMZ (2.25 ± 0.30 µg/mL) and TMP (0.35 ± 0.05 µg/mL) were detected in River Ona. Diclofenac was not detected in all

the sampling sites except the Ona River, with a concentration of 0.56 ± 0.07 µg/mL. Generally, ΣPCs (µg/mL) in the Rivers sampled are in the order SMZ (4.09) > PCM (3.01) > CIP (0.78) > DCF (0.56) > TMP (0.46) with the exception of MET and IBU, which were not detectable in any of the rivers. Notably, there is still a lack of a compromise method using either HPLC or LCMS to monitor the presence of PCs in environmental matrices, making monitoring studies tedious. Researchers should focus more on developing a uniform method or a standard operating procedure for sets of pharmaceuticals to make these studies much easier and faster**.** Also, the fate and behavior of these compounds in the environment have not been wholly explored. This will help proffer appropriate remediation strategies for environmental removal and transformation by-products. Although reports of the ecotoxicological effects of pharmaceuticals are helpful in establishing the public's state of health, ecotoxicity studies have not focused on ascertaining the mechanisms by which they produce their effect at detected/monitored concentrations. Hence, future research should investigate these mechanisms, and these procedures/processes are encouraged to be fundamentally included in the water management policies for a practical assessment.

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