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# Ecological Risk Assessment of Pharmaceutical Residues in Surface Water

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**Abstract**
Pharmaceutical compounds have been frequently detected in the aquatic environment globally and are suspected to have some negative health consequences. The present study evaluates the sources, occurrences, spatiotemporal variabilities, concentrations, and potential risks of some pharmaceutical residues in surface water of Isolo and Amuwo Odofin areas of Lagos Nigeria. surface water samples were collected bi-monthly for a period of twenty-four months. The samples were filtered with 0.45µm glass fiber and analyzed using HPLC with a UV detector. Solid-phase extraction was achieved with OASIS HLB cartridges C18 for pre-concentration of 500ml of the sample. The target analytes were acetaminophen, ibuprofen, diclofenac, metronidazole, amoxicillin, sulfadoxin, pyrimethamin, ofloxacin, ciprofloxacin and caffeine. Levels of pharmaceutical residues (PRs) in the water samples ranged from 1.261-5.035ng / L for ibuprofen, 0.484 - 2.366ng / L for diclofenac, nd -3.57 ng / L for sulfadoxin, 0.976 - 3.440 for ofloxacin, 0.585 - 0.706 ng / L for ciprofloxacin, 0.187-1.228ng / L for caffeine, 0.395-1.329 ng / L for acetaminophen and 0.032 – 0.598 ng / L for metronidazole. Amoxicillin and pyrimethamine were not detected in all the samples. The order of concentration of the pollutants are Ibuprofen > diclofenac > ofloxacin > sulfadoxin > acetaminophen> caffeine > caffeine > ciprofloxacin > metronidazole. Measured sample concentrations were compared with the approved values in "European Committee on antimicrobial susceptibility (EAUCAST)" database and some of the detected pharmaceutical compounds were found to be of high concentrations. Ecological risk assessments of each pharmaceutical active ingredient was evaluated and Rist Quotients (RQ) > 1 were found for metronidazole, ofloxacin and ciprofloxacin, indicating high risk. The need for improved wastewater treatment technologies cannot be over emphasized. Continuous monitoring and better regulatory frameworks may be necessary.

**Keywords**: pharmaceutical residues, Solid-phase extraction, HPLC, Surface water, Aqueous samples.

## 1.1 Introduction

A contaminant is a potentially undesirable substance (physical, chemical, or biological) present in the environment [1]. The term "emerging contaminants" does not mean that these pollutants are just beginning to penetrate our environment, they have been there from time immemorial but at very negligible concentrations. The Earth system comprising the Earth and its atmosphere is an assemblage of atoms of the 92 natural elements. Almost all of these atoms have been present for over 4.5 billion years ago by a gravitational accretion of a cloud of gases and dust. However, over the years and with continuous industrialization as well as continuous discharge of wastewater into the environment, their concentrations are on the increase and as such are beginning to have noticeable negative impacts on humans, plants, and animals in general [2]. Historically, environmental monitoring programs have focused on organic chemicals, particularly those that are known to resist degradation, bioaccumulate in the fatty tissues of organisms, and have known adverse toxicological effects [3]. Pharmaceutical pollutants are a unique group of emerging contaminants as a result of their potential to induce physiological effects at very low concentrations. Their presence is of great concern due to the possible ecological impacts such as ( endocrine disruption) to biota within the environment[4]. several analytical techniques have been employed in analyzing these pharmaceuticals using liquid chromatographic-mass spectrometer, high-performance liquid

chromatography, gas chromatographic methods, and many others. The small organisms in the aquatic environment such as planktons are eaten by higher animals which are finally eaten by humans up the food chain thus transferring the pollutants to humans. Pollution is an ill wind that blows no living thing any good. Water pollution can be harmful to mankind and fish in general. Toxic chemicals can cause cancers, scale rot and fin rot in fish. Toxic chemicals can accumulate in fish making many fish too dangerous for human consumption[5].Some heavy metals and toxic chemicals that end up in the waterways cause cancer and birth defects in humans and others affect the reproductive system or damage the nervous system[6].Many pharmaceutical contaminants are not soluble. The human body is about 70 percent water, up to 50 – 60 percent of pharmaceuticals are known to be excreted from the human body[7].Locally the occurrence of pharmaceuticals in our treated water in Lagos state is not well understood, little or no research is carried out on this topic, and yet there is a continuous massive discharge of these pharmaceutical effluents into the environment. Another very important concern emanating from the presence of pharmaceuticals(PCs) in the environment is the creation of antibiotic-resistant bacteria strains in the natural bacteria populations and endocrine disruptors(ED). Wide use of antibiotics in human medicine and animal treatment is one of the major sources of the emergence and spread of antibiotic-resistant bacteria [8].These antibiotic-resistant bacteria may enter the food chain if the sludge is used as fertilizer on agricultural land [9]. Some studies have shown adverse effects on aquatic organisms including the toxicity of ciprofloxacin on green algae, and the toxicity of oxolinic acid ( a commonly used feed additive in field farms) to Daphnia Magna [10]. The pharmaceutical compounds of interest include over-the-counter therapeutic drugs used to prevent or treat human diseases [11], Such as acetaminophen(paracetamol), metronidazole, ibuprofen, caffeine, diclofenac, ciprofloxacin, ofloxacin, pyrimethamin , sulfadoxine, amoxicillin, and others. Over the past few years, there has been increasing awareness of the unintentional presence of these pharmaceuticals(PhCs) in various compartments of the aquatic environment such as water, sediment, and biota which are capable of causing some detrimental effects to the aquatic organisms [12]. After administration, the active substances of the medications are metabolized by the body but only to a certain extent. The unmetabolized portion is excreted largely in the urine and to a lesser extent in the feces, unchanged, as a mixture of metabolites. however, in some cases, they may be conjugated by the attachment of an inactivating compound.This makes sewage and treated wastewater the greatest source of human pharmaceuticals (PhCs) that reach the surface water whether after excretion or through inappropriate disposal. Additional sources of residues of active compounds in the environment are effluents from livestock farms (eg PhCs such as tylosin, and spiramycin are used as animal growth promoters ) and wastewater from pharmaceutical industries. The pharmaceuticals detected in high frequencies in surface waters are generally those administered in greater quantities, many exceptions occur. Some compounds such as antibiotics are consumed in large amounts but are not frequently detected in the effluents from wastewater treatment plants (WWTPs), their concentrations generally range from several ng/l with few exceptions. This has led to these contaminants being described as " micropollutants". The difficulties in the detection and monitoring of micropollutants are mainly due to the sophisticated analytical techniques and instrumentations required, the time-consuming methodologies and the high cost involved. The concentration of PhCs in wastewater and treated effluents in the environmental matrix does not necessarily mean that it is of concern or may cause harm, however, major concerns arising from the detection of chemicals that there is evidence that may cause adverse effects to aquatic life[13].

A wide range of pharmaceuticals have been repeatedly observed in the aqueous environment worldwide for the past decades. Among these are, inflammatory drugs, antibiotics, analgesics, stimulants, antimicrobials, steroids, disinfectants, fragrances, and many other chemicals that are widely used daily for various purposes[14]. This research is targeted at the pharmaceuticals only, due to their large consumption. Pharmaceutical products (PCPs) may enter the environment directly or indirectly through anthropogenic activities such as sewage discharge, livestock breeding, landfill leachate, and fertilizing, resulting in their presence in surface water and groundwater at concentration levels up to ng/L. It has been shown that continuous exposure to low subtoxic concentrations of certain (PCPs) can lead to unexpected consequences and unintended effects on non-target species and induce undesirable effects on humans and ecosystems at large [15]. Their presence in the environment may pose a threat to human health. Chang and others, in 2007 reported that, the flux of pharmaceuticals from municipal sewage treatment plants (STP) is a considerable source of chemical pollution in surface, ground, marine, and even tap or bottled waters [12]. Some of the reported effects on living organisms include delayed development in fish and frogs, increased feminization of fish population, delayed metamorphosis in frogs and so many other negative reactions including altered

behaviour and reproduction as reported by Hernando and others in 2006. Few are routinely monitored in the environment while many are unregulated because of insufficient knowledge in terms of their toxicity, impacts, and behaviors [16]. Current literature shows that pharmaceuticals are continuously released into the environment in extremely large quantities on regular basis through different ways such as human activities (via excretion and disposal of unwanted medications to sewers ), wastes from pharmaceutical industries residues and wastes from hospitals, use of illicit drugs (especially) antibiotics and steroids, and agro-products [17][18][19]. As a result of the fact that pharmaceuticals easily dissolve in aqueous media and also do not usually evaporate at normal temperature or pressure. They make their way into the soil and aquatic environment through sewage treated sewage sludge (biosolids), and irrigation with reclaimed water. However, some pharmaceuticals break down or degrade upon release into the environment. Most of them remain unchanged and eventually become persistent in the environment. It is a known fact that most of these chemicals remain bioactive even at extremely low concentrations after excretion from the body or after disposal to landfills and water bodies and have unpredictable biochemical interactions when mixed with a tendency to accumulate in the food chain together with their negative health impact on aquatic organisms and consumers [18]. As a result, pharmaceuticals, their metabolites and by-products are of great concern due to their potential ecological and environmental impacts. Recent literature indicates that the flux of pharmaceuticals from municipal sewage treatment plants is a considerable source of chemical pollution in surface and groundwater [20]. Most of the reviews concerning the occurrence and transformation of pharmaceutical compounds (PCs) in water matrices focus mainly on the surface water and wastewater of which some of the concentrations of PCs have been identified recently. Several studies made countrywide overviews of emerging organic contaminants (EOCs) including pharmaceutical compounds (PCs) in the groundwater of Italy [21], Spain [22] and the UK [23] and provided useful information on the presence, sources and potential risks to the environment in these countries. Lapworth and co-workers reviewed the occurrences and data of EOCs and PCs in groundwater worldwide published before 2011 and discussed their sources and pathways [16]. This paper principally talks about the occurrence of several groups of PCPs that are ubiquitous in pharmaceutical effluents due to their incomplete removal before discharge to the environment. These include antibiotics, anti-inflammatory, stimulants, anti-malaria, analgesics, anti microbial and many others with special focus on the literature published in the past few years. It summarizes the various concentrations detected in the environment, adsorption and degradation, also the dominant mechanisms in the transport of pharmaceutical pollutants.

## 2.0 **Materials and methods**

### 2.1 **Sample Collection**

One litter of Nine composite samples were collected from six different points along the canal through mile two river and Tincan Island Lagoon. The sampling was carried out bi - monthly for a period of 24 months, applying coherent protocols and procedures which enable collection of representative samples using standard depth and width techniques as used by Batt et al [24]. At each point of collection , composite surface water samples were collected from five vertical profiles through a stream cross section into pre cleaned glass bottles wrapped with aluminium foil . The bottles were previously washed with detergent, soaked with chromic acid and rinsed with distilled water. The samples were then transported to the laboratory in a cooler packed with ice and maintained at $4^0$C for the analysis of the above mentioned pharmaceutical compounds. The procedure described by Batt et al 2008 for the analysis of pharmaceuticals in waste and surface water was employed for this work [24]. . The pH, temperature, conductivity and total dissolved solid of the samples were measured in-situ using a Bellingham - Stanley multi parameter water quality meter (Germany) . The pH were found to be in the range of 5.5 - 7.8.

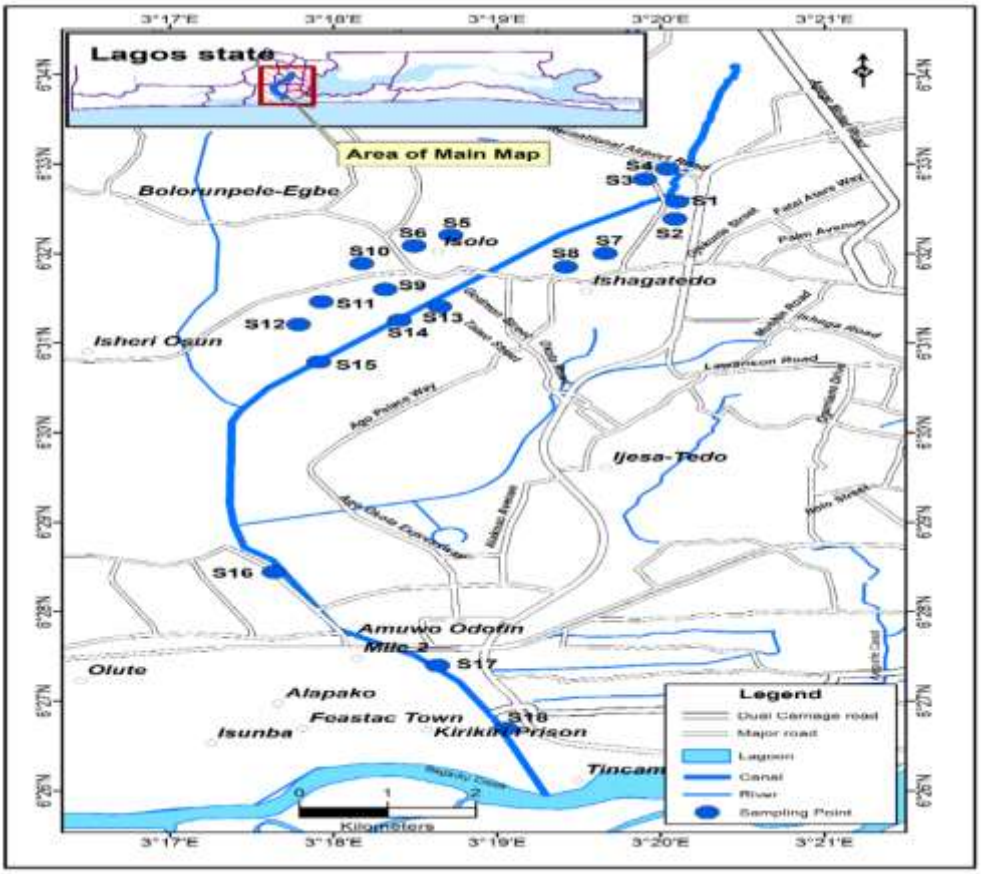


Fig .1: Routes of sample collection points

2.2 **Sample Preparation and Pre-treatment**

Wastewater samples were collected, in clean glass bottles wrapped with aluminium foil. The glass bottles were previously washed with detergents and soaked with chromic acid over night, after which they were pre-rinsed with distilled water. Immediately on arrival at the laboratory, 500 ml of samples were filtered through 0.45-µm glass fibre purchased from Whatman (UK). Each sample was however treated with 0.25g of $Na_2EDTA$ (Sodium ethylene diamine tetra acetic acid). Target analytes were extracted in one step by sold phase extraction [25], with the aid of a vacuum system (J.T. Baker, The Netherlands).

2.3 **Solid phase Extraction**. Application of solid phase extraction procedure was employed to extract the targeted analytes from aqueous samples. The extraction was done in batches with the aid of a vacuum manifold. The manifold accommodated maximum of twelve Oasis HLB cartridges C18 (10g sorbent with 12 ml capacity). Each cartridge was preconditioned with 6 ml methanol and 6ml distilled water at a flow rate of 6ml/min and thereafter loaded with 500ml of the filtered sample which have been pretreated with $Na_2EDTA$ . As the extraction was being carried out, the vacuum pump was adjusted so that the flow rate was approximately 5-10ml/min. Elution of the analytes was done slowly with 10ml methanol /aceton (1:1 v/v) .The extract was evaporated to near dryness at 40-50$^0$c under a gentle stream of nitrogen and reconstituted to 1ml with methanol and transferred for HPLC analysis as stipulated by Environmental protection agency of the United States of America (EPA method 1694) [26]

2.4 **Chemicals and Reagents**

All chemicals were purchased from "Sigma Aldrich" Chemicals ( Germany). Trifluoroacetic acid (TFA) (99%), caffeine (99%), diclofenac (99%), metronidazole (99%), ciprofloxacin (99%), ibuprofen (99%) , ofloxacin (99%) ,acetaminophen (99%), pyrimethamin (99%), sulfadoxin (99%) and diclofenac (99%), ethylenedieminetetracetic acid disodium salt dehydrate ($Na_2EDTA$, 99%), acetonitrile, methanol and miliqui water The reagents and standards used in this study were all analytical grade and supplied by sigma Aldrich chemicals Germany

2.5 **Preparation of stock solution :**
Stock solutions (1 mg / ml) of standard ibuprofen, diclofenac, acetaminophen, amoxicillin, ciprofloxacin, ofloxacin, sulfadoxin, pyrimethamine, metronidazole and caffeine were prepared in and working solutions of 10,20,30,40 and 50 µg / mL were prepared each by serial dilution. The test tubes containing the stock solutions were wrapped in aluminum foil and stored in a refrigerator at $4^0$c.

2.6 **HPLC Analysis**
Liquid chromatographic separations were performed using HPLC (1290 series, Agilent Technology USA) with UV detector . A sun fire column C18 ((100 cm, 4.6 mm, 4 µm) Waters, Milford MA USA) preceded by a guard column (Sun Fire, C18, 2.1 × 10mm ,3.5µm, Waters, Milford MA USA) was used at a temperature of 40 $^0$c with a mobile phase consisting of a mixture of 1:1 acetonitrile (water with 0.1% TFA at a flow rate of 1 mL/min) was used.

**Chromatographic conditions of the equipment**
Table 1

| DRUG SAMPLE | MP | FR | UvDW (nm) | IV | $R^2$ | RT |
|---|---|---|---|---|---|---|
| Ibuprofen | 0.1%TFA: CAN(40:60 | 1.0 | 248 | 20 | 0.9984 | 5.2 |
| Ciprofloxacin | 0.1%TFA: ACN (65:35) | 1.0 | 278 | 20 | 0.9974 | 4.6 |
| Diclofenac | MeOH 100% | 1.0 | 283 | 20 | 0.9968 | 4.6 |
| Ofloxacin | $KHPO_4$: MeOH(30:70) | 1.0 | 294 | 20 | 0.9992 | 4.2 |
| Acetaminophen | $NaH_2PO4$: ACN.(65:35) | 1.0 | 260 | 20 | 0.9891 | 2.8 |
| Sulfadoxin | 0.1%TFA: ACN.(70:30) | 1.0 | 278 | 20 | 0.9998 | 2.9 |
| Caffeine | $KHPO_4$:A CN:MeOH(40:40:20) | 1.0 | 254 | 20 | 0.9993 | 2.2 |
| Amoxicillin | 95% phos phate buffer(0.1mol/l) $PH_4$ and ACN | 1.0 | 229 | 20 | 0.9999 | 1.8 |
| Pyrimethamin | ACN:phos phate buffer (75:25) | 1.0 | 230 | 20 | 0.9999 | 2.36 |
| Metronidazole | KHO4:AC N(80:20 V/V) | 1.0 | 298 | 20 | 0.9983 | 3.5 |

Note : MP = Mobile Phase, FR= Flow Rate, UvDW= Ultra violet detector wavelength, IV= Injection Volume, $R^2$ = Correlation coefficient, RT = Retention Time.

Analysis of Data :
Concentrations of various drug pollutants were all expressed as mean ± standard deviation.

3.0 **Results**
The various water samples analysed contain different concentrations of pharmaceutical pollutants in the surface water of the studied area. In all the surface water samples analysed, amoxicillin and pyrimethamin were not detected. In SW1. Ibuprofen had the highest concentration of 3.227 ng / L. Diclofenac, ciprofloxacin, caffeine and acetaminophen were also detected in SW1. Ofloxacin had the highest concentration of 3.440 ng / L in SW2. The other pharmaceutical residues (PRs) were below the limit of detection. In Sw3, the order of concentration of PRs is ibuprofen> diclofenac > ofloxacin > acetaminophen. Other PRs were not detected. Sw4 has its order of concentration as caffeine > metronidazole > diclofenac >

acetaminophen. Others were not detected. In Sw5, the PRs were below the detection limit except ofloxacin with a value of 1.452 ng / L. The order of concentration in SW6 is ibuprofen > sulfadoxin > diclofenac > metronidazole. Others were not detected.. The concentrations of diclofenac and metronidazole detected was 2.66 and 0.032 ng /L in respectively in SW6. Ibuprofen ranged from 1.2613- 5.03ng / with an average concentration of 2.24ng / L. Diclofenac ranged from 0.48 2.36 -2.366 ng / L. Table 4 shows explicitly the various concentrations in ng / L of the drug analytes detected at various points along Isolo canal through Tin can Island lagoon, Lagos, Nigeria.
Note SW1-6: surface water samples from site 1 to site 6.

Table 2. Concentrations of detected drugs in (ng / l) at various surface along the surface water

| Chemical compound | SW 1 | SW 2 | SW 3 | SW 4 | SW 5 | SW 6 | Mean concentration |
|---|---|---|---|---|---|---|---|
| Ibuprofen | 3.277±0.6 | 1.261±0.5 | 3.901±0.2 | nd | nd | 5.035±0.4 | 2.20 |
| Diclofenac | 1.670±0.3 | 0.979±0.02 | 1.266±0.1 | 0.484±0.01 | nd | 2.366±0.1 | 1.10 |
| Amoxicillin | nd | nd | nd | nd | nd | nd | nd |
| Sulfadoxin | nd | nd | nd | nd | nd | 3.457±0.7 | 0.50 |
| Ofloxacin | nd | 3.441±0.5 | 0.976±0.3 | nd | 1.452±0.4 | nd | 0.50 |
| Ciprofloxacin | 0.706±0.4 | 0.585±0.2 | nd | nd | nd | nd | 0.20 |
| Caffeine | 0.487±0.5 | 0.187±0.01 | nd | 1.228±0.1 | nd | nd | 0.30 |
| Acetaminophen | 1.329±0.5 | 0.566±0.4 | 0.524±0.2 | 0.395±0.3 | nd | nd | 0.40 |
| Metronidazole | nd | nd | nd | 0.598±0.1 | nd | 0.032±0.9 | 0.10 |
| Pyrimethamin | nd | nd | nd | nd | nd | nd | nd |

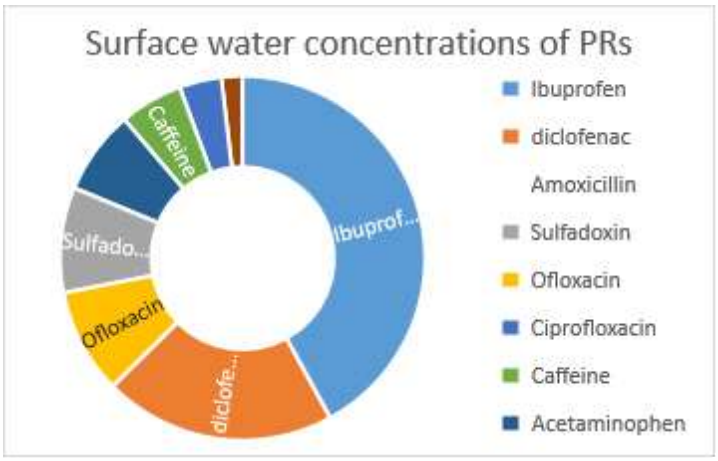


Fig.2: Concentrations of drug pollutants in the surface water (ng / l)

## 4.0 **Discussions**

Some drug pollutants were detected in the surface water at various concentrations. They include ibuprofen, diclofenac, sulfadoxin ofloxacin, ciprofloxacin, caffeine, acetaminophen and metronidazole. 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. Analgesics however have anti inflammatory and antipuretic properties [27]. 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 5.035ng / L in sw6. A similar study conducted in a river in Ogun State, Nigeria reported the presence of acetaminophen, diclofenac , ibuprofen and ciprofloxacin in mg/ml range [29]. Chronic exposure to diclofenac can impaire renal functions in fish. The kidney has also been found to be the target organ for diclofenac toxicity in many animals such as birds, mice and humans [30,31,32]. In another study in South Africa, Madikizela , in 2017 , reported the levels of concentrations of ibuprofen in Kwazulu - Natal at the point where a tributary Msunduzi joins the Umgeni river[33]. This study is also consistent with the reports of Banzhaf et al in 2017, who reported that, concentrations of pharmaceuticals in surface water ranged from nd-13ng / L for carbamazepine, nd- 17ng / L for ibuprofen and 1.0 – 12 ng / L for diclofenac [34] . Also detected in this study was ofloxacin ranging from 0.976 -3.40 ng / L. Ciprofloxacin concentrations ranged from 0.585-0.706 ng / L. Amoxicillin was not detected in any of the samples. Antibiotics are integral components of modern medicine and are also very vital lines of defence against pathogenic bacteria and fungi by stopping their growth [33.35]. The unregulated use of antibiotics and also discharged waste water from pharmaceutical industries , agricultural farms and household effluents are some major sources of antibiotics and their residues in the aquatic environment. Anti biotics can be present in the environment for a long period of time because of their biological and physico chemical properties. These, enhance their ability to contaminate the water resources [36]. There is also an increasing awareness about the presence of antibiotics in the aquatic environment globally. Many studies focused on waste water treatment plants' (WWTP) effluent discharges as the main source of contamination [37,38]. One of the major concerns about the presence of antibiotics in the environment over a long period, is the proliferation of antimicrobial resistant genes and anti microbial resistant bacterial [39]. Caffeine and metronidazole were also detected at average concentrations of 0.30 ng / L and 0.10ng / L respectively across all the sites. Metronidazole is used in the treatment of infections of the reproductive system, gastrointestinal track, skin, heart, bone, joint and nervous system. Metronidazole belongs to nitroimidazole class of antibiotics. It is also used in the treatment of sexually transmitted diseases and it is a commonly used antibiotics in Nigeria. The presence of pharmaceutical pollutants in surface water exposes the need to consider their potential environmental risks. Some conventional methods for environmental risk assessment in a given ecosystem include the use of acute and / or chronic toxicity data based on the most sensitive organism or a combination of organisms within the ecosystem in order to determine the predicted no effect concentration (PNEC) of an environmental pollutant. This value is then compared with the measured environmental concentration (MEC or PEC) respectively. However, in order to determine the risk quotient (RQ) for each compound , maximum values were obtained from European committee on antimicrobial susceptibility data base (EUCAST data base). The accepted range for RQ is where the low risk is below 0.1, medium risk is from 0.1 to 1.0 and high risk is greater than 1 [40,41]. Risk quotient is defined as the ratio of the maximum measured environmental concentration (MEC) to the predicted no effect concentration (PNEC). The ecosystem risk from pollutants can then be gauged [40] . However, calculation of this ratio is sometime challenging due to lack of information regarding the effects of pharmaceutical pollutants (PPs) in the environment and also difficulty in establishing PNEC. Recent researches have found that ecological risk is limited for many PPs because of dilution [42,43,44]. Moreover, some other studies have found PPs of high and medium risks in secondary effluents, rivers and small lakes [45,46,47,48]. Various concentrations of pharmaceutical pollutants were detected at both upstream and down stream with some analytes having relatively higher concentrations at upstream as shown in table 3 and figures 3 to 6. This may be as a result of discharges from numerous households, hospitals and pharmaceutical production facilities scattered in the area. However. unregulated and unmonitored sources of effluent may be discharging to the river channel, such as vacuum trucks collecting effluent in urban areas. Balakrishna et al. in 2017 reported in a study in India, that pharmaceutical production facilities are some of the key sources of pharmaceutical pollution in developing countries [49]. Some other drug pollutants were also detected down stream. This study also reveals the cold weather accumulation of pharmaceuticals as a result of decreased sunlight and temperature which directly reduce the biodegradability of organic compounds thereby causing increased concentrations

during the wet periods as shown in figures 3-6 [50] . Also increased concentrations of pharmaceutical residues during the wet period may be as a result of increased precipitation during wet seasons with its diluting effect on the analytes and increased consumption of medicaments against illness and flu. Previous studies had suggested a variety of reasons for variations across the year which include seasonal usage and changes in the environment ( e.g temperature and river flow) [51,52].

Table 3 Mean concentrations of detected pharmaceutical pollutants at upstream and down stream of the surface water [ng/l] [$X_{av}$ ±S.D].

| Pharmaceutical Compound | Upstream Average concentration(ng / l) | Down stream Average concentration (ng / l ) | Fold change |
|---|---|---|---|
| Ibuprofen | 2.295 ±1.0 | 5.035 ±4 | 2.194 |
| Diclofenac | 1.321 ±0.1 | 1.425 ±1.30 | 1.079 |
| Ofloxacin | 3.441 ±2.0 | 1.452 ±0.20 | 2.370 |
| Cafeine | 0.307 ±0.4 | 1.228 ±0.04 | 4.000 |
| Acetaminophen | 0.947 ±0.5 | 0.395 ±0.60 | 2.395 |
| Metronidazole | <LOD <LOD | 0.032 ±0.40 | <LOD |
| Sulfadoxin | <LOD <LOD | 3.457 ±0.20 | <LOD |
| Ciprofloxacin | <LOD <LOD | <LOD NILL | <LOD |

4.1 **Ecological Risk Assessment:**

The risk quotient (RQ) is the basic international principles adopted in developing an environmental risk assessment guideline (ERA) [ 53,54 ]. ERA is based on ecological threshold data from experiments on aquatic organisms (algae,Cladocera (usually, Daphnia sp.), and / or fish species). Moreover, E(L) C50 and No effect concentration (NOEC) values derived from acute and chronic tests respectively are also considered.

$$PNEC_{water} = \frac{E(L)C50 \text{ or } NOEC \text{ or } HC5}{AF} \quad \text{Eq 1} \quad [55]$$

Where EC50 is the concentration (or dose) effective in producing half of the maximal response. The magnitude of the assessment factor (AF) is dependent on the available toxicological information. The reliability of the results increases if toxicological data for aquatic organisms are available at several different trophic levels. The value of AF is decreased in cases where large and relevant datasets are available. For instance , if toxicity data is only available based on E(L)C50, an AF of 1000 is used , but, if NOEC (No effect concentration) is derived from experiments with single trophic levels ( eg fish), an AF of 100 is used . Also , if NOEC is available for two trophic levels, eg fish and Cladocera (Daphnia) , AF of 50 is applied and if NOEC is known for all three trophic levels, AF is equal to 10 [56]. However, in case of using at least five different species, (independent on trophic levels), with the same toxicological data, meaning HC5 value ( ie the concentration at which five percent of the species in the special sensitivity distribution exhibit an effect) is known, AF IS 5 [57]. If different toxicity data are available for each level then the lowest concentration limit results will be used to determine the PNEC because ERA is based on the most sensitive elements of the ecoststem so as to estimate the ecological hazard [58]. ERA is achieved after the measured environmental concentration (MEC) and the toxicological threshold values of the investigated pollutants are determined

since Risk Qotient (RQ) that is used to categorise harmful effects for the ecosystem is defined as the ratio of maximum (MEC) to the PNEC a shown in equation 2..

RQ = MEC / PNEC (Eq 2)

If RQ < 0.01 denotes a negligible risk, RQ < 0.1 means a low risk, 0. 1< RQ < 1, it represents a medium risk and RQ > 1 , represents a high risk to aquatic organisms [59,60]. Table 4 shows the potential ecological risk of the various drug pollutants calculated for three trophic levels ( Algae, Daphnia and Fish). In a vast majority of aquatic mixture toxicity studies, the toxicity of the mixture is usually assessed by concentration addition (CA) model and neglected the toxic models of actions of the toxic constituents. The CA models means that the contribution of the individual toxicants to the overall effects may be added in the form of toxic units (TU) and it is described in equation 3 [61].

$$TU = \sum_{i=1}^{n} \frac{MECi}{E\ (L)\ C50i\ or\ NOECi} \quad \text{(Eq 3)}$$

The environmental concentrations of pharmaceutical residues usually vary depending on their chemical stability, biodegradability, physicochemical characteristics, and the efficiency of the wastewater treatment technologies used [62] . Analgesics-anti inflammatories (eg ibuprofen , diclofenac, naproxen, ketoprofen etc) and anti epileptics (carbamazepine), are usually present in surface waters at high – medium ng / L concentrations especially for anti inflammatories . However , the risk of these drug residues is suspected to

| Therapeutic groups | Chemical Compound | Molecular formular | CAS number | RQ Iin surface water |
|---|---|---|---|---|
| Analgesics | Ibuprofen | $C_{13}H_{18}O_2$ | 15687-27-1 | - |
| | Diclofenac | $C_{14}H_{11}Cl_2NO_2$ | 15307-79-6 | Medium risk |
| | Acetaminophen | $C_8H_9NO_2$ | 103-93 | Medium risk |
| Anti biotics | Metronidazole | $C_6H_9N_3O_3$ | 443-48-1 | High |
| | Ofloxacin | $C_{18}H_{20}FN_3O_4$ | 82419-36-1 | High |
| | Ciprofloxacin | $C_{17}H_{18}FN_3O_3$ | 85721-33-1 | High |
| | Amoxicillin | $C_{16}H_{19}N_3O_5S$ | 26787-78-0 | - |
| Anti malaria | Sulfadoxin | $C_{12}H_{14}N_4O_4S$ | 2447-57-6 | - |
| | Pyrimethamin | $C_{12}H_{14}Cl_2N_4$ | 58-14-0 | - |
| Stimulant | Caffeine | $C_8H_{10}N_4O_2$ | 58-08-2 | - |

be high because of their high volumeof usage around the world. However, the pearson correlation table, as shown in table (7) shows a weak positive correlation between diclofenac, ibuprofen and pH . Also, weak positive correlation exists between caffeine and temperature .

Table. 4: Potential ecological risk (RQ) of different therapeutic groups in surface water.

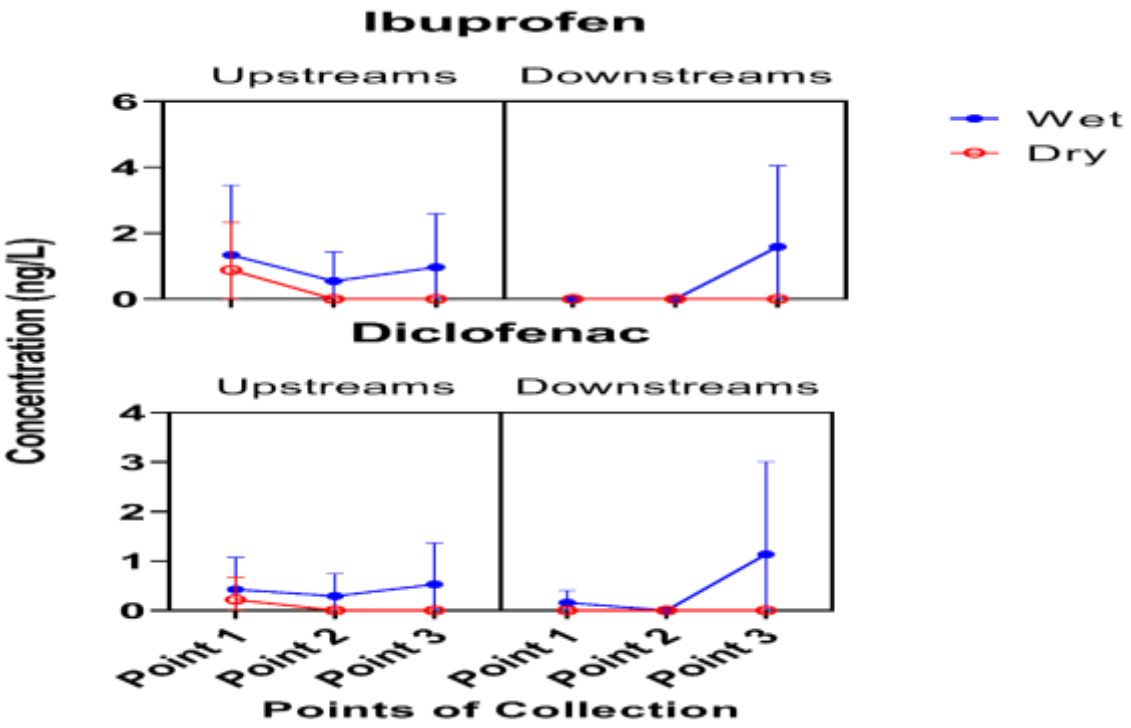


Fig:3:
Concentrations of Ibuprofen and Diclofenac in the Surface Water from both upstreams and downstreams collected at different points during dry and wet season. Each line represents the mean ± SEM.

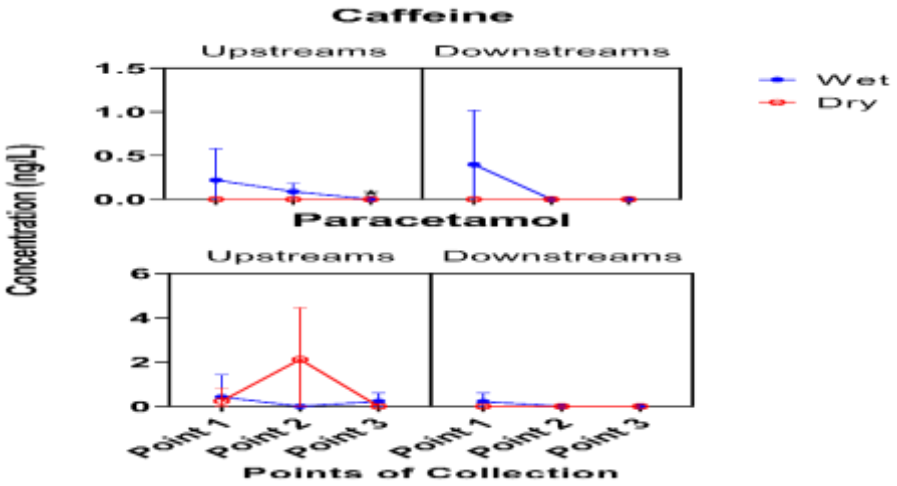


Fig.4: Concentrations of Caffeine and Paracetamol in the Surface water upstream and downstream during the dry and wet season. Each line represents the mean ± SEM. *p<0.05 compared to their counterparts**.**

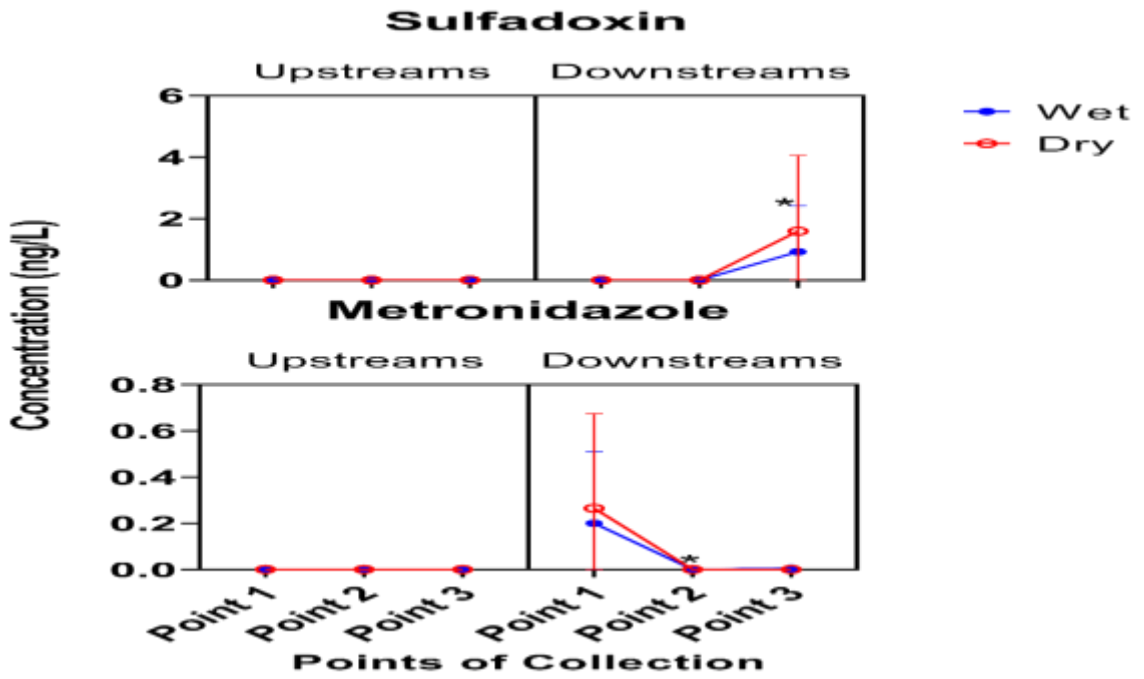


Fig.5: Concentrations of Sulfadoxin and metronidazole at upstream and down stream of the surface water during the wet and dry season. April to October (otherwise called Raining season) , November to March (otherwise called Dry season)

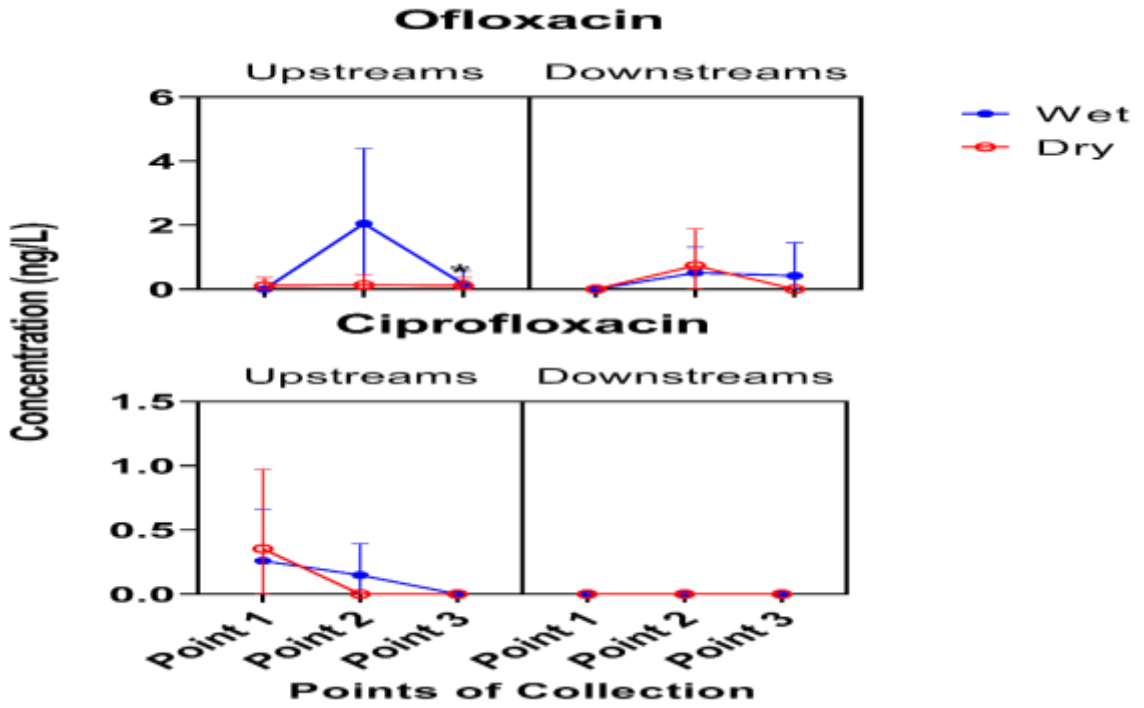


Fig.6: Concentrations of Ofloxacin and Ciprofloxacin at upstream and down stream during the wet and dry season

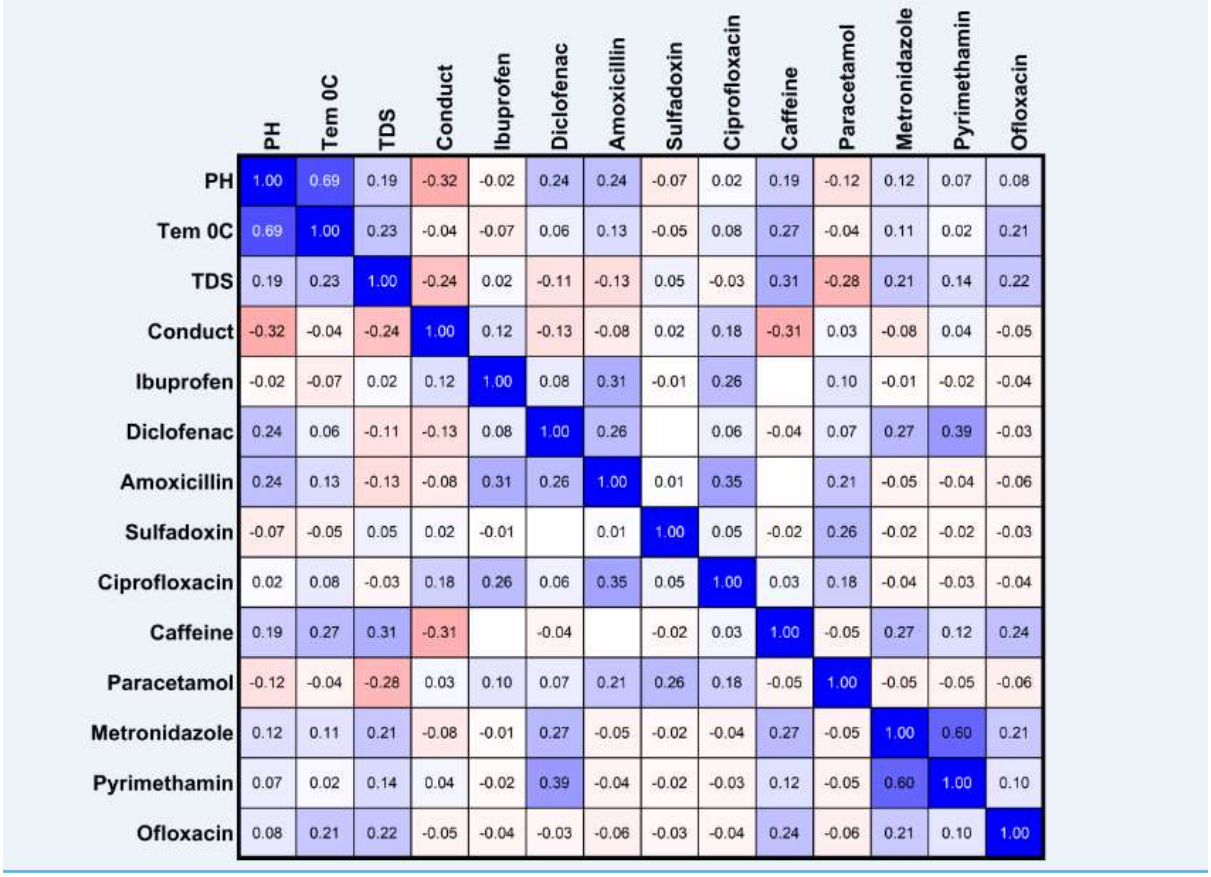


Fig.7 : Correlations among pH, Temperature, conductivity and total dissolved solids using pearson correlation model.

## 5.0 **Conclusion**

Pharmaceutical pollutants exist in our environment. Rapid increase in the number of pharmaceutical industries and the widespread availability of different types of therapeuticals and increased intake of drugs due to demand from illnesses may result in increased concentrations of pharmaceuticals in municipal waste water. Commonly applied methods for their removal at treatment plants do not ensure their total removal from waste water. Pharmaceuticals that are frequently detected in surface water include anti inflammatory drugs (NSAID), diclofenac and ibuprofen. Antibiotics in the environment can lead to drug resistance in microorganisms. The ecological risk assessment revealed that the concentrations of these pollutants especially diclofenac and acetaminophen are presently at medium risk while high risk was observed for ciprofloxacin, ofloxacin and metronidazole. There is need for improvement in the wastewater treatment technologies being used for wastewater purification. Also, continuous monitoring and better regulatory frameworks may be necessary to prevent further pollution of the area.

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