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PHYSICOCHEMICAL AND BACTERIOLOGICAL PROPERTIES OF PHARMACEUTICAL WASTEWATER IN OSUN STATE

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ABSTRACT

Background: The pharmaceutical industry bears much responsibility for environmental pollution. **Objective:** This study was carried out to determine the physicochemical and bacteriological analysis of the pharmaceutical effluents, in Osun State, Nigeria. **Methods:** Five wastewater samples from different locations were analyzed using standard chemical and bacteriological methods. The results obtained were compared with WHO and NESREA recommended limits. **Results:** The ranges of values obtained for physicochemical parameters analyzed were from 25.9°C to 27.5°C temperature, 5.2 to 5.4 pH, 159.68 to 1542.80 true colour, 284.53 to 1769.92 Pt-Co apparent colour, 16.37 to 51.34 NTU turbidity, 1483.14 to 1528.75 mg/L total suspended solids (TSS), 43.01 to 128.50 mg/L total dissolved solids (TDS), 0.08 to 0.27 µS/cm conductivity, 268.75 to 540.51 mg/L $CaCO_3$ acidity, 1.30 to 5.70 mg/L dissolved oxygen, 4.75 to 16.00 mg/L biological oxygen demand in (BOD), 12.13 to 17.63 mg/L chemical oxygen demand (COD), 15.25 to 15.80 mg/L sulphate, 0.48 to 2.14 mg/L Nitrate, 0.18 to 1.05 mg/L Nitrite, 107.31 to 234.98 mg/L chloride, 0.31 to 0.32 mg/L phosphate, 1.24 to 202.50 mg/L magnesium, 21.82 to 73.25 mg/L calcium. The total bacteria count and coliform count of the wastewaters samples ranged from 5.1×10^6 to 6.5×10^6 CFU/Ml and 2.2×10^6 to 4.5×10^6 CFU/mL with the highest coliform count observed at the point of discharge. Four different bacteria were isolated with *Escherichia coli* predominating followed by *Klebsiella aerogenes*, *Bacillus cereus* and *Enterobacter aerogenes*. **Conclusion:** The results of this study confirmed high levels of pollutants in pharmaceutical effluent samples and this could hamper the ecosystem. Thus, a more effective treatment approach is recommended for pharmaceutical industrial effluents in the interest of public health.

KEYWORDS: physicochemical, bacteriological, pharmaceutical wastewater, environment, treatment, public health.

INTRODUCTION

Pharmaceutical wastewater contains a variety of poisonous and dangerous chemicals, the most of which are harmful to human health and because of their acute toxicity, including genotoxicity and mutagenesis potential, the consequences of pharmaceutical compounds on public health and the environment are essential. (Nadal *et al*., 2004, Akintonwa *et al*., 2009; Bakare *et al*., 2009; Adeoye *et al*., 2015). Most pharmaceuticals are discharged to the environment; toxicants in wastewater accumulate in aquatic bodies, soil, and other biological systems, and frequently surpass critical threshold levels (Cleuvers, 2003; Hernandoa *et al.*, 2006; Larsson *et al*., 2007).

Pharmaceutical and personal care product effluents (PPCPs) are the wastewater produced by these companies throughout the drug production process. Their environmental impact is immense. The growing demand for healthy living has led to the establishment of additional pharmaceutical and PPCP manufacturing enterprises in Nigeria. The dangers of toxic substances in pharmaceutical effluent cannot be overstated, as they endanger fish (feminization of male fish), frogs, wildlife, and increase antibiotic resistance in microorganisms because most antibiotics end up in the environment through excretion, dumping, equipment washing, or wash off discharges, though the danger is reported to be lower in man due to the very low concentrations of these contaminants (Johnson and Sumpter, 2001, Bhatnagar *et al*., 2002 and Ibegbulam-Njoku *et al.*, 2013). Level of wastewater pollution varies from industry depending on the type of process and capacity of the industry (Garcia *et al*., 1995).

With the rise in worldwide medicine demand, the pharmaceutical sector has become one of the top 26 polluters of solid waste and effluent into the environment (Anyakora *et al*., 2011). Approximately half of the global effluent from pharmaceutical industry is released without any recommended pretreatment, according to estimates (Anetor *et al*., 1999; Osaigbovo and Orhue, 2006). Several investigations have identified chemical components in pharmaceutical effluents and proved their toxicity to living creatures. As a result, in recent years, there has been a lot of interest in researching the effects of discharged pharmaceutical effluents on the ecosystem, its services, and human health (Daughton and Ternes, 1999; Jones *et al*., 2001; Larsson *et al*., 2007; Idris *et al*., 2013 and Kumari and Tripathi, 2019). Pharmaceuticals and personal care products (PPCPs) are becoming more contaminated, posing a major threat to the environment and human health. Their occurrences have been observed worldwide in a variety of aquatic and terrestrial settings, including sludge. (Balmer *et al*., 2005; Buser *et al.,*2006; Giokas *et al*., 2007; Calafat *et al.,*2008; Thomaidis *et al*., 2012).

In the view of the fate of pharmaceuticals wastewaters in the environment and the growing concerns over their biological effects because when discharged immediately into the environment without an adequate treatment causes pollution of land or water, this study aimed at analyzing the physicochemical and bacteriological parameters of effluents generated at the pharmaceutical industry, point of discharge, upstream, downstream and the surrounding stream.

2. 0. MATERIALS AND METHODS

2.1 Study Location

Osun State is a state in southwestern Nigeria; bounded to the east by Ekiti and Ondo states, to the north by Kwara State, to the south by Ogun State and to the west by Oyo State. Named for the River Osun—a vital river which flows through the state. The state was formed from the southeast of Oyo State on 27 August 1991 and has its capital as the city of Osogbo.

2.2 Sample collection

A sterile universal bottle was opened aseptically, then held at their bases and submerged to a depth of about 20 cm with their mouth facing upwards. Samples were taken by filling the bottle to the top to exclude air in case of a current (Chouhan, 2015).

2.3 Physicochemical Analysis of the wastewater and water samples

Temperature, pH, TDS and conductivity were determined in situ using portable pH/EC/TDS/Temperature meter. Dissolved oxygen (DO) was determined using Winkler methods while biochemical oxygen demand (BOD) was determined by dilution method (Golterman, *et. al*., 1978). Chemical oxygen demand (COD) was determined by dichromate digestion method, chloride by mercuric nitrate method (APHA, *et. al.*, 2012). The nitrate ion was analysed using brucine-sulphanlinic acid method while Nitrite was determined by diazotization method of APHA *et al*., (2012), the phosphate by the vanadomolybdo-phosphoric acid colorimetric method and the sulphate by the turbidimetric method (Ademoroti, 1996). Apparent colour was determined on unfiltered samples colorimetrically using Potassium Chloroplatinate-cobalt (Pt-Co.) solutions standards, while turbidity was determined nephelometrically by comparison with turbidity (NTU) standards (APHA, *et. al.*, 2012). The total suspended solids (TSS) of samples were determined gravimetrically after oven drying them to constant weight at 105 ± 2°C (USEPA, 1998). Total acidity, Total alkalinity, Magnesium, Calcium ions were determined by titrimetric methods (Golterman, *et. al*., 1978; Ademoroti, 1996; Okoya and Elufowoju, 2020).

2.4 Microbiological Sample Processing (Serial Dilution)

An aliquot (1mL) of the wastewater was transferred into 9mL of distilled water and diluted serially in ten folds (10^{-2} to 10^{-5}) according to the method described by Adesemoye *et al*. (2006). This was serial diluted to obtain a dilution of 10^{-2}, 10^{-3}, 10^{-4} and 10^{-5}. From the appropriate dilution, 1ml was placed on the sterile petri dishes and approximately 20mL sterile molten nutrients agar using poured plate techniques was added. MacConkey agar was used for coliform plate counts. The plates were allowed to set and incubated at 37°C. These were done in duplicate. Colony counts were done using illuminated colony counter (Gallenkamp England) from plates with less than 300 but more than 30 and results expressed as actual colony counts multiplied by dilution factor and was expressed as colony forming units (cfu/mL) of the sample.

$$\text{No. of cfu/mL} = \frac{\text{No.of colonies counted X Dilution factor}}{\text{Volume of sample taken}}$$

The colonies were repeatedly subcultured on fresh nutrient and Maconkey agar to obtain pure isolates**.**

2.5 Biochemical Characterizations

The bacteria isolates were identified and characterized using cultural, morphological and standard biochemical tests as described by Cheesbrough (2009). The following tests were used for the identification of the bacteria: Gram stain, catalase, motility, indole production, citrate, triple sugar ion agar (TSIA) reaction, oxidase and urease.

2.6 Antimicrobial Susceptibility Testing

The antimicrobial susceptibility testing was done using disc diffusion with Mueller- Hinton agar (Kirby Bauer's) method according to the clinical and laboratory standards institute (CLSI, 2020) guidelines using the following antimicrobial agents: Augmentin (10μg), Trimethoprim/ Sulfamethoxazole (25μg), Levofloxaacin (30μg), Cefepime (30μg), Ampicillin-Sulbactam (10μg), Ofloxacin (5μg), Cephalexin (30μg) and Pefloxacin (30μg) for all Bacterial isolates.

3. RESULTS

Table 1 shows the physicochemical analysis of the wastewater samples. The temperature ranged of 25.9 ± 0.14 °C to 27.5 ± 0.00 °C. The values of true colour, apparent colour and turbidity in the wastewater samples ranged from 241.12 ± 7.07 to 1542.80 ± 0.32, 284.53 ± 7.07 to 1769.92 ± 0.13 Pt-Co and 16.37 ± 0.00 to 51.34 ± 0.01 NTU respectively. The total suspended solids (TSS), total dissolved solids (TDS) and conductivity values ranged between 1483.14 ± 1.24 to 1528.75 ± 1.06 mg/L, 43.01 ± 0.04 to 128.50 ± 0.35mg/L and 0.08 ± 0.04 to 0.27 ± 7.07μ/scm respectively. The value of the acidity of the samples ranged from 268.75 ± 1.06 to 540.51 ± 0.74 mg/L $CaCO_3$. The dissolved oxygen (DO), biological oxygen demand in (BOD) and chemical oxygen demand (COD) of the wastewater samples ranged from 1.3 ± 0.14 to 5.7 ± 0.14 mg/L, 4.75 ± 0.07 to 16 ± 0.00 mg/L and 12.13 ± 0.18 to 17.63 ± 0.04 mg/L respectively.

Sulphate concentrations ranged from 15.25 ± 0.00 to 15.79 ± 7.07 mg/L, Nitrate concentrations ranged from 0.48 ± 0.10 to 2.14 ± 0.01 mg/L, Nitrite concentrations ranged from 0.18 ± 0.04 to 1.05 ± 0.00 mg/L. Chloride concentrations ranged from 107.31 ± 0.00 to 234.98 ± 0.36 mg/L and Phosphate concentrations ranged from 0.31 ± 0.00 to 0.32 ± 7.07 mg/L. The ranges of values of Magnesium and Calcium were 1.24 ± 0.03 to 202.50 ± 0.14 mg/L and 21.82 ± 0.34 to 73.25 ± 0.00 mg/L respectively. The organic matter (OM) and total organic carbon (TOC) were between the range of 34.56 ± 0.01 to 36.30 ± 7.07 mg/L and 20.08 ± 0.01 to 21.92 ± 0.41 mg/L.

Table 2 shows the total bacteria count and coliform count of wastewater effluents. The total bacteria count ranged between 5.1 X 10^6 cfu/mL and 6.5 X 10^6 cfu/mL. Total coliform counts of range between 2.2 X 10^6 cfu/mL and 4.5 X 10^6 cfu/mLTable 3 shows the Gram's reaction and biochemical characterization of bacteria isolated from wastewater. The predominant bacteria species isolated were identified as *Escherichia coli*, *Klebsiella aerogenes*, *Bacillus cereus* and *Enterobacter aerogenes* from Raw Pharmaceutical Wastewater, Point of Discharge, Upstream, Downstream and Surrounding Stream samples.

Table 4 shows the antibiotic resistance pattern of the bacteria isolated from the wastewater and water samples, *Klebsiella aerogenes* exhibited 100.0% resistance to both cephalexin and cefepime while augmentin, ofloxacin, levofloxacin, cotrimoxazole and pefloxacin showed 50.0% resistance rate, only ampicillin/sulbactam had no resistant to *Klebsiella aerogenes*. *Escherichia coli* exhibited 100 % resistant to cephalexin and 90.0 % to ampicillin/sulbactam and cefepime. Ofloxacin, levofloxacin and pefloxacin had no resistant rate. However, *Enterobacter aerogens* exhibited 100.0 % resistant to all the tested antibiotics except ampicillin/sulbactam and cefepime while *Bacillus cereus* exhibited 100.0 % resistant to all the antibiotics except cefepime.

Table 1: Physicochemical properties of wastewater and water samples.

PARAMETER	Raw Pharmaceutical Wastewater	Point of Discharge	Upstream	Downstream	Surrounding Stream	NESREA STANDARD	WHO	SAMPLE 2	SAMPLE 3	NESREA STANDARD
DO (mg	2.42 ± 0.00	5.7 ± 0.14	1.36 ± 0.14	1.38 ± 0.14	1.30 ± 0.14	3.00	4-7	5.7 ± 0.14	1.30 ± 0.14	3.00
BOD (mg/L)	16 ± 0.00	4.75 ± 0.07	8.20 ± 0.35	8.15 ± 0.35	8.25 ± 0.35	20.00	30.00	4.75 ± 0.07	8.25 ± 0.35	20.00
ALKALINITY (mg/L $CaCO_3$)	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00<BDL>	50.00	0 ± 0.00	0 ± 0.00	0.00<BDL>
ACIDITY (mg/L $CaCO_3$)	540.51 ± 0.74	268.75 ± 1.06	351.01 ± 0.04	350.01 ± 0.04	352.01 ± 0.04	0.00<BDL>	5.50	268.75 ± 1.06	352.01 ± 0.04	0.00<BDL>
CHLORIDE (mg/L)	234.98 ± 0.36	107.34 ± 0.04	106.31 ± 0.00	105.31 ± 0.00	107.31 ± 0.00	10.00	250-1000	107.34 ± 0.04	107.31 ± 0.00	10.00
NITRATE (mg/L)	0.66 ± 0.00	2.14 ± 0.01	0.49 ± 0.12	0.48 ± 0.15	0.48 ± 0.10	10.00	50.00	2.14 ± 0.01	0.48 ± 0.10	10.00
NITRITE (mg/L)	0.23 ± 7.07	1.05 ± 0.00	0.18 ± 0.04	0.18 ± 0.04	0.18 ± 0.04	0.00<BDL>	3.00	1.05 ± 0.00	0.18 ± 0.04	0.00<BDL>
SULPHATE (mg/L)	15.25 ± 0.00	15.29 ± 7.07	15.60 ± 7.07	15.70 ± 7.07	15.80 ± 7.07	0.00<BDL>	400.00	15.29 ± 7.07	15.80 ± 7.07	0.00<BDL>
APP. COLOUR (mg/L)	1769.92 ± 0.13	466.97 ± 0.01	290.53 ± 7.07	294.53 ± 7.07	284.53 ± 7.07	COLOURLESS		466.97 ± 0.01	284.53 ± 7.07	COLOURLESS
TRUE COLOUR	1542.80 ± 0.32	159.68 ± 0.00	241.12 ± 7.07	241.12 ± 7.07	241.12 ± 7.07	NA	15-50	159.68 ± 0.00	241.12 ± 7.07	NA
COD (mg/L)	17.63 ± 0.04	12.13 ± 0.18	13.60 ± 0.00	13.66 ± 0.00	13.60 ± 0.00	40.00	250.00	12.13 ± 0.18	13.60 ± 0.00	40.00
TURBIDITY (NTU)	51.34 ± 0.01	40.56 ± 0.01	18.35 ± 0.00	17.37 ± 0.00	16.37 ± 0.00	5.00	5.00	40.56 ± 0.01	16.37 ± 0.00	5.00
TSS (mg/L)	1528.75 ± 1.06	1774 ± 1.41	1483.14 ±1.24	1483.14 ±1.24	1483.14 ±1.24	10.00	100.00	1774 ± 1.41	1483.14 ±1.24	10.00
PHOSPHATE (mg/L)	0.31 ± 0.00	0.32 ± 7.07	0.31 ± 0.00	0.31 ± 0.00	0.31 ± 0.00	2.00		0.32 ± 7.07	0.31 ± 0.00	2.00
ORGANIC MATTER	36.30 ± 7.07	34.56 ± 0.01	35.54 ± 0.37	35.52 ± 0.37	35.51 ± 0.37	0.00<BDL>	10-30.00	34.56 ± 0.01	35.51 ± 0.37	0.00<BDL>
TOTAL ORGANIC CARBON	21.92 ± 0.41	20.08 ± 0.01	20.55 ± 0.00	20.48 ± 0.00	20.46 ± 0.00	0.00<BDL>	5.00	20.08 ± 0.01	20.46 ± 0.00	0.00<BDL>
HARDNESS (mg/L$CaCO_3$)	188.09 ± 0.00	966.84 ± 0.00	717.43 ± 0.04	717.43 ± 0.04	717.43 ± 0.04	0.00<BDL>	150.00	966.84 ± 0.00	717.43 ± 0.04	0.00<BDL>
MAGNESIUM (mg/L)	1.24 ± 0.03	202.5 ± 0.14	161.40 ± 0.57	161.40 ± 0.57	161.40 ± 0.57	0.00<BDL>		202.5 ± 0.14	161.40 ± 0.57	0.00<BDL>
CALCIUM (mg/L)	73.25 ± 0.00	54.83 ± 0.04	21.82 ± 0.34	21.82 ± 0.34	21.82 ± 0.34	0.00<BDL>		54.83 ± 0.04	21.82 ± 0.34	0.00<BDL>
Ph	5.40 ± 0.00	5.20 ± 0.00	5.30 ± 0.17	5.40 ± 0.18	5.40 ± 0.14	6.0-9.0		5.20 ± 0.00	5.4 ± 0.14	6.0-9.0
TEMPERATURE (°C)	25.9 ± 0.14	26.7 ± 0.00	26.5 ± 0.00	27.5 ± 0.00	27.5 ± 0.00	40.00		26.70 ± 0.00	27.5 ± 0.00	40.00
APPEARANCE	Pink	Pink	Grey	Grey	Grey	COLOURLESS		Pink	Grey	COLOURLESS
ELECTRICAL CONDUCTIVITY(µS/cm)	0.27 ± 7.07	0.20 ± 0.01	0.08 ± 0.04		0.10 ± 0.04	0.08 ± 0.04	1000.00 250.00	0.20 ± 0.01	0.08 ± 0.04	1000.00
TOTAL DISSOLVED SOLIDS (mg/L)	101.10 ± 0.35	128.50 ± 0.35	43.01 ± 0.04		43.01 ± 0.04	43.01 ± 0.04	500.00	128.50 ± 0.35	43.01 ± 0.04	500.00
							3.48 ± 0.30	4.91 ± 0.25		

Legend: BDL-Below Detection Limit

Table 2: Total bacteria and coliform plate count of wastewater and water samples.

Sample	ID Total bacteriacount 10^6	(cfu/mL) Coliform count (cfu/mL) 10^6
Raw Pharmaceutical		
Wastewater	5.1	3.8
Point of Discharge	6.5	4.5
Upstream	6.3	3.4
Downstream	6.0	3.0
Surrounding stream	5.6	2.2

LEGEND
Sample 1: Raw Pharmaceutical Wastewater
Sample 2: Point of Discharge
Sample 3: Upstream
Sample 4: Downstream
Sample 5: Surrounding Stream

Table 3: Gram reaction and Biochemical Characterization of Bacteria isolated from wastewater and water samples.

Sample ID	Gram Reaction	Catalase	Motility	Indole	Citrate	TSIA Reaction	Oxidase	Urease	Growth @ 50°C	Growth in 7% Nacl	Glucose	Presumptive Diagnosis
1a	GNB	+ve	-ve	-ve	+ve	Slant Y Butt Y No H_2S	-ve	+ve	ND	ND	ND	*Klebsiella aerogenes*
1b	GNB	+ve	+ve	+ve	-ve	Slant Y Butt YG No H_2S	-ve	-ve	ND	ND	ND	*Escherichia coli*
2a	GNB	+ve	+ve	+ve	-ve	Slant Y Butt YG No H_2S	-ve	-ve	ND	ND	ND	*Escherichia coli*
2b	GNB	+ve	-ve	-ve	+ve	Slant Y Butt YG No H_2S	-ve	+ve	ND	ND	ND	*Klebsiella aerogenes*
3	GNB	+ve	+ve	+ve	-ve	Slant Y Butt YG No H_2S	-ve	-ve	ND	ND	ND	*Escherichia coli*
4a	GNB	+ve	-ve	-ve	+ve	Slant Y Butt Y No H_2S	-ve	+ve	ND	ND	ND	*Klebsiella aerogenes*
4b	GNB	+ve	+ve	+ve	-ve	Slant Y Butt YG No H_2S	-ve	-ve	ND	ND	ND	*Escherichia coli*
5a	GPB	+ve	+ve		+ve	ND	ND	ND	-ve	+ve	+ve	*Bacillus cereus*
5b	GNB	+ve	+ve	-ve	+ve	Slant Y Butt YG No H_2S	-ve	-ve	ND	ND	ND	*Enterobacter aerogenes*
5c	GNB	+ve	+ve	+ve	-ve	Slant Y Butt YG No H_2S	-ve	-ve	ND	ND	ND	*Escherichia coli*

KEYS

GNB = Gram Negative Bacilli GPB = Gram Positive Bacilli TSIA = Triple Sugar Iron Agar +ve = Positive -ve = Negative G = Gas Y = Yellow ND = Not Detected

Table 4: Antibiogram of bacteria isolated from the wastewater and water sample.

Sample ID	Augmentin	Ampicillin/ Sulbactam	Cephalexin	Ofloxacin	Levofloxacin	Cotrimaxazole	Pefloxacin	Cefepime
1a	15mm (I)	24mm (S)	5mm (R)	0mm (R)	0mm (R)	0mm (R)	0mm (R)	0mm (R)
1b	17mm (S)	15mm (I)	10mm (R)	25mm (S)	26mm (S)	25mm (S)	23mm (S)	17mm (S)
2a	10mm (R)	11mm (R)	0mm (R)	17mm (S)	20mm (S)	20mm (S)	17mm (S)	0mm (R)
2b	11mm (R)	12mm (R)	8mm (R)	21mm (S)	25mm (S)	24mm (S)	19mm (S)	0mm (R)
3	9mm (R)	11mm (R)	8mm (R)	23mm (S)	27mm (S)	24mm (S)	17mm (S)	0mm (R)
4a	11mm (R)	8mm (R)	11mm (R)	26mm (S)	21mm (S)	20mm (S)	19mm (S)	0mm (R)
4b	12mm (R)	6mm (R)	8mm (R)	24mm (S)	20mm (S)	23mm (S)	19mm (S)	0mm (R)
5a	11mm (R)	0mm (R)	0mm (R)	0mm (R)	0mm (R)	0mm (R)	0mm (R)	20mm (S)
5b	11mm (R)	30mm (S)	0mm (R)	0mm (R)	0mm (R)	0mm (R)	0mm (R)	20mm (S)
5c	20mm (S)	0mm (R)	10mm (R)	25mm (S)	19mm (S)	0mm (R)	18mm (S)	0mm (R)

KEYS

R = Resistant I = Intermediate S = Sensitive

DISCUSSION

Temperature is a significant physicochemical parameter used to assess water quality for human consumption and influence various activities in water bodies such as chemical reaction rates, gas solubility's, and water taste and colour amplification (Olajire and Imeppeoria, 2001). The temperature values obtained in this investigation were below the NESREA permitted limit for wastewater release into the environment. For raw pharmaceutical wastewater, point of discharge, upstream, downstream and surrounding stream the average temperature was 25.9 °C ± 0.14, 26.7 °C ± 0.00, 26.5 °C ± 0.00, 27.5 °C ± 0.00 and 27.5 °C± 0.00, respectively (table 1). This is comparable to the findings of Obasi *et al*. (2014), who found a maximum temperature of 26.65 °C for microbiological and toxicological assessment of pharmaceutical wastewater from the Lagos Megacity, Nigeria.

The pH of the pharmaceutical wastewater samples ranged from 5.2 ± 0.00 to 5.4 ± 0.00 at the five sampling locations, with raw pharmaceutical wastewater having the highest value and point of discharge having the lowest. The pH was found to be acidic. Although the readings were lower than the pH values, they were still outside of NESREA's permitted limits. This demonstrates that the impact of final effluents on receiving water bodies would have a negative impact on their domestic recreational and aquatic ecosystem purposes, which is unacceptable because it could cause illnesses like acidosis, and pH is an indicator of the presence as it controls their activities (Prescott *et al*., 1999; Elemile *et al*., 2019).

According to Iwuozor and Emuobosu (2018), the high acidity of effluents could be due to a high concentration of hydrogen ion (H+) in the effluents, and when they reach the receiving water bodies, the acidic nature of the effluents is capable of destabilizing fundamental properties such as alkalinity, metal solubility, and hardness of water, and the low pH has synergistic effects on heavy metal toxicity (Olaitan *et al*., 2014, Adesakin *et al*., 2020). The pH value reported in surrounding stream might be connected to the prevalent soil type in the area's surface water body, or it could be attributable to organic material buildup from runoff. According to Adesakin *et al.* (2020), when organic materials decompose, carbon dioxide is produced and mixed with water to form the weak acid "Carbonic acid".

The wastewater and water samples of Nitrate, Phosphate, and Nitrite levels were within NESREA's permissible limits for wastewater and WHO guidelines for water quality, ranging from 0.48 ± 0.10 – 2.14 ± 0.01mg/L, 0.31 ± 0.00 – 0.32 ± 7.07 mg/L, and 0.18 ± 0.04 – 1.05 ± 0.00 mg/L, respectively. As of the time of the study, the levels of the three anions were below national and international standards, indicating that they pose no threat to human health. Diuresis, increased starch deposits, and spleen hemorrhage might all be symptoms of long-term exposure to nitrate and nitrite levels over the maximum permissible concentration (Reimann *et al.*, 2003; Adesakin *et al.*, 2020).

The total suspended solids measured in this investigation ranged from 1483.14 ± 1.24 mg/L to 1774.00 ± 1.41 mg/L. Point of discharge after treatment had the highest result, indicating that the TSS value was greater than raw pharmaceutical wastewater. TSS in the wastewater, which is filterable particles, had levels higher than the acceptable NESREA (10 mg/L). Pathogens can adhere to suspended debris and raise the danger of disease out breaks; therefore it also acts as an indicator of turbidity in the wastewater. This is in contrast to Rono (2017), who claimed that following sewage treatment, TSS levels at the outflow decreased and because suspended particles absorb heat from sunlight, high TSS can induce a rise in surface water temperature. Point of discharge had the greatest hardness value (966.84 ± 0.00 mg/L). The results for raw pharmaceutical wastewater (188.09 ± 0.00 mg/L) might be due to dissolved calcium and magnesium ions in the raw materials used in drug production. However, a significant concentration of hardness in Point of discharge might be the consequence of leaching from the company's machineries segment's effluents. Magnesium levels in the wastewaters ranged from 1.24 ± 0.03 mg/L to 202.50 ± 0.14 mg/L. Calcium and magnesium, as well as carbonates, sulphates, and chlorides, are thought to naturally provide temporary and permanent hardness. Water with 0-7 mg/L $CaCO_3$ is soft, 75-150 mg/L $CaCO_3$ is hard, and of 300 mg/L $CaCO_3$ are defined as sample with total hardness by Adeyeye and Abulude (2004). Hard water is not harmful to one's health, but it can be inconvenient when used for various home tasks such as washing and cleaning (Adesakin *et al.*, 2020).

The sample turbidity levels (16.37 ± 0.00 - 51.34 ± 0.01 NTU) were greater above the NESREA limits of 5 NTU. Raw pharmaceutical wastewater had the highest NTU value of 51.34 ± 0.00 NTU. This might be caused by the wastewater's nutritional level. The high turbidity reported in the surrounding stream did not meet NESREA and WHO turbidity guidelines. The turbidity of the surrounding stream is higher than WHO's standard of below 5.0 NTU, this could be as a result of suspended solid caused by soil particles and plankton (microscopic plants and animals) through the sediments bearing run off that enters the stream bank, erosion, palm oil processing and farming activities that goes on around the stream which agrees with what Antigha and Ogarekpe, 2019 reported. Continuous discharge into the environment, according to Liasu and Okoya (2015), might result in a rise in organic materials in the environment, posing health risks to both aquatic creatures and humans. High turbidity is a sign of pollution, since it may have a detrimental influence on the people of the research area's health. It's generally linked to a larger concentration of disease-causing organisms like bacteria and parasites. Turbid water has a history of creating health problems, including nausea, cramps, diarrhoea, and migraines.

When compared to NESREA, all five wastewater and water samples had low dissolved oxygen (DO) values, indicating that this company produced many organic compounds with high oxygen demand waste. Carbon, hydrogen, oxygen, nitrogen, and other elements are commonly found in organic molecules. Organisms can eat them and break them down. Even biodegradable products may pollute the environment and too much organic matter in wastewater might harm the receiving water, this is because organisms utilize dissolved oxygen in the water to break down pollutants, a large volume of biodegradable materials is hazardous to lakes, streams, and oceans. This can diminish or deplete the oxygen supply in the water required by aquatic life, resulting in fish death, stench, and overall water quality degradation (Okoya and Ogunkoya, 2009).

Surrounding stream (1.30 ± 0.14 mg/L) has a lower DO value than raw pharmaceutical wastewater, point of discharge, upstream and downstream (2.42 ± 0.00 mg/L, 1.36 ± 0.14 mg/L, 1.38 ± 0.14 mg/L and 5.70 ± 0.14 mg/L), which might be due to fertilizer runoff from farmlands and lawns, as well as a palm oil factory that processes palm nuts near the stream. DO, according to Olajire and Imepeoria (2001), may not pose a direct threat to people, but it may have an impact on other chemicals in the water and because the toxicity of some elements is heightened by low concentrations of dissolved oxygen, when paired with the presence of hazardous compounds, low concentrations of dissolved oxygen may trigger stress reactions in aquatic environments (Helmer and Hespanhol, 1997). According to the stipulation of WHO, 2011 the depletion of dissolved oxygen poses adverse effects such as discolouration of water among others.

The BOD of the effluents calculated from DO values were below the NESREA permitted limits, indicating that the organic matter in raw pharmaceutical wastewater and surrounding stream had low demand for oxygen and this is because aerobic bacteria must take up energy from the process organic matter in the presence of oxygen, it also meant that bacteria could survive inside the effluents (Sharma, 2004). This indicated that the majority of available oxygen was utilized for waste biodegradation, leaving just a minor quantity for biochemical processes. The findings are consistent with those of Chris-Otubor and Olorunfemi (2015) and Kumara *et al*. (2010), who also observed low dissolved oxygen levels. DO levels were also found to be low, suggesting that oxidation was performed during the treatment process of live organisms present in the effluent, resulting in a drop in dissolved oxygen levels (USEPA, 2012). It differs, however, from the findings of Iwuozor and Emuobosa (2018), who discovered that the physico-chemical characteristics of industrial effluents from a brewing company in Imo state, Nigeria, surpassed the NESREA allowed limit.

The total dissolved solid (TDS) result is less than the NESREA limit of 500 mg/L. TDS is not typically thought of as a main pollutant (i.e., it is not thought to have any health impacts), but it lowers light penetration, lowering algae's capacity to photosynthesise. TDS were over the legal limit, according to Amaku and Akani (2016), and the interaction of hydrographic forces leaves a huge number of materials in the effluents, causing some degree of population of organisms in the effluents.

The electrical conductivity values varied between 0.08 ± 0.04 to 0.27 ± 7.07 µS/cm. Raw pharmaceutical wastewater had the highest value (0.27 ± 7.07 µS /cm) while surrounding stream had the lowest (0.08 ± 0.04 µS /cm). It accords with Ewere *et al*. (2014) results. NESREA had established a limit of fewer than 1000 µS /cm, due to its presence assists in buffering the ions and the impact aids in regulating the pH, the Electrical Conductivity of water is a valuable and straightforward indication of its salinity or total salt content (Ewere *et al*., 2014). However, according to Iwuozor and Emuobosa (2018), the effluent conductivity of the industry was above the acceptable limit (Muhibbu-din *et al*., 2011, Syed, 2008, Iwuozor and Emuobosa, 2018).

The total bacteria count recorded in this study varied widely from 5.1 to 6.5 X 10^6 cfu/mL. The highest value 6.5 X 10^6 cfu/mL was recorded in point of discharge. The point of discharge (after treatment), showed that the count is higher compared to the raw pharmaceutical wastewater. This could be as a result of the type of the treatment used. This suggested that the treatment used did not kill or eliminate the microbial lives in the wastewater. Also the proliferation of the bacteria in this sample might be because of the present of some essential degradable nutrient which may be out-competed by other species. The total bacteria count in upstream, downstream and surrounding stream is lower compared to raw pharmaceutical wastewater and point of discharge; this could be as a result of the dilution effect of the increased water volume within water bodies during rainy season and also discharge from the environment. The index of the microbial load (10^6) is high and indicated dense population of bacteria in the wastewaters.

Four types of bacteria were identified during the period of the study, with *Escherichia coli* predominating followed by *Klebsiella aerogenes*, *Enterobacter aerogenes* and *Bacillus* *cereus*. This is supported by the study conducted by Anyamene and Ojiagu (2014) who reported that there is presence of *Escherichia coli*, *Klebsiella* and *Enterobacter* species in wastewater.

Among the Gram negative bacteria, *Escherichia coli* had the highest percentage of isolation. This work supports Andy and Okpo's (2018) findings that *E. coli* can resist competition from other indigenous microbes with a faster growth rate. Regardless, because the wastewater was collected before interaction with the external environment, the isolation of these pathogens from raw pharmaceutical wastewater is concerning. According to Lateef (2003) and Hatcher *et al*. (1992), it is not implausible to infer that these pathogens were introduced into the manufacturing process by human healthy carriers through handling, processing, and purifying methods, as well as unsanitary post-production handling. The continuous contamination of the process may be enhanced through the processing equipment, if wastewater without prior contact with external environment harbors potential human pathogens, the same may hold for the products in the factory.

The existence of these bacteria in point of discharge paints a bleak picture of the factory's wastewater treatment, as discharge from wastewater might have serious consequences for human health and the aquatic ecology. Another reason for high total bacteria and coliform counts could be due to insufficient treatment processes or a poorly operated treatment plant, which can result in the multiplication or survival of various microorganisms in already treated wastewater, potentially contaminating the environment (Anastasia *et al*., 2012). In the Eastern Cape South Africa, coliform has also been isolated from treated effluents in previous research (Dungeni *et al*., 2010). According to Chris-Otubor and Oluwafemi (2015), Akpor and Munchie (2011), and Adewoye *et al*. (2010), these wastewaters can be a source of infection in the communities where they are channeled, where they may seep into water bodies such as streams and wells, or where residents collect such water and use it for laundry and irrigation farming.

The antibiogram of the bacteria isolated from the waste water showed that *Escherichia coli* exhibited a least antibiotic resistant to the fluroquinolones group of antibiotics while augmetin was effective agansit *Klebsilella aerogenes*. Cefepime was effective against *Bacillus cerues* and *Enterobacter aerogenes.* However, the multiple antibiotic resistant recorded in this study pose a major threat to the community as this will contribute to the increase in the antibiotics resistance pattern in this study area.

CONCLUSION AND RECOMMENDATION

The pharmaceutical industry bears much responsibility for environmental pollution; therefore it is necessary to study the physical, chemical and bacteriological parameters. The results obtained from this research showed that most of the parameters are not within the standards. Such wastewaters should be adequately treated before being discharged into the environment. The high level of pollution from the industry could affect ecosystem and humans; therefore it is recommended that modern treatment should be used, proper precautions and strong monitoring so that the environment can be sustained. Creation and awareness of personal hygiene standards for workers is necessary. Proper handling facilities at point of use level should be adopted to minimize risk of cross contamination along the drug supply chain.

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