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ANALYSIS OF EFFLUENTS FROM PHARMACEUTICAL INDUSTRIES MANUFACTURING PARACETAMOL PRODUCTS LOCATED WITHIN KANO METROPOLIS, NIGERIA

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ABSTRACT

The presence of heavy metals, active pharmaceutical ingredients (especially antibiotics) and other contaminants in pharmaceutical effluents poses a great threat to aquatic and human life either directly or indirectly. The aim of the research is to assess the quality of the effluents from three pharmaceutical manufacturing companies located within Kano metropolis. Twenty-seven samples were collected using standard procedures and stored in a refrigerator. The samples (50 ml) were digested using Nitric acid(10 ml) and then analysed for the presence of Cadmium, Chromium, Nickel, Lead, and Copper using the Atomic Absorption Spectrophotometric method. The pH, Turbidity, Total Dissolved Solids (TDS), Electrical Conductivity (EC), Total Suspended Solids (TSS), and Chemical Oxygen Demand (COD) of the samples were also determined using standard procedures. The samples were screened for the presence of paracetamol using an adopted UV Spectroscopic method after validation. Some of the samples (22.22%) contained Lead above Federal Environmental Protection Agency (FEPA) official limit (<1 ppm) while Nickel, Copper, Cadmium and Chromium were within the FEPA official limits. Many of the samples (48.15%) had pH values outside the FEPA official limit (6-9) while 78.07% of samples were found to have Turbidity values above the FEPA limit (<5 NTU). All the samples had TDS values within the FEPA official limit (<2,000 mg/L) while EC was found to be above the FEPA official limit (<1000 µS/cm) in 33.33% of the samples. The TSS value of 70.37% of the samples was found to be above the FEPA official limit (<30 mg/L). COD was found to be above the official FEPA limit (<1000 mg/L) in 55.56% of the samples. Paracetamol was found in 25.92% of the samples within a concentration range of 0.16-1.64 mg/mL. The samples are therefore, not safe for disposal into the public water drainage system.

Keywords: Heavy metals, pharmaceutical effluent, physicochemical parameters, paracetamol, Kano

INTRODUCTION

Industrial waste water has been one of the major causes of environmental deterioration resulting to varieties of catastrophic environmental impacts and human calamities (Sridhar *et al*., 2000). Bakare *et al.,* (2003) and Adebisi *et al*., (2007), reported that the hazardous compounds present in the effluents from pharmaceutical industries pose a biohazard to humans and other aquatic living species. Contamination of water bodies with pharmaceutical by-products has been on the increase in recent years due to globalization and industrialization (Maya, 2021). In developing countries, such as Nigeria, industrial effluents are mostly dumped into water bodies without undergoing treatment (Osaigbovo and Orhue, 2006; Graham *et al.*, 2021). These bodies of water, serving as sources of irrigation and consumption to humans and animals, eventually cause deleterious effects on humans due to bioaccumulation of the harmful organic and inorganic constituents of the industrial

effluents (Ayodele *et al*., 1996; Ethan *et al*., 2003).

Most pharmaceutical effluents are known to contain varying concentrations of organic compounds (e.g**.,** phenolic compounds), inorganic compounds, biological materials, drug residues (e.g. antibiotics), heavy metals (e.g., Lead, Mercury, Cadmium), total solids and other toxic organic chemicals. These effluents which are discharged from pharmaceutical industries are known to affect the surfaces and bodies of water (Ericson and Foess, 1980; Olorunfemi and Gabriel*,* 2018). Some of the chemicals found in pharmaceutical effluents have mutagenic and carcinogenic properties and are linked to the causes of kidney failure, cancer, anaemia, hepatotoxicity, neurotoxicity, mental retardation, and immunological abnormalities (Olagunju *et al.,* 2020; Nnaneme, 2021). The presence of antibiotic residues in municipal and other water sources has been linked to the promotion of the development of pathogenic resistance organisms among others (Momodu and Anyakora, 2010). A lot of attention has been paid to heavy metals, and other contaminants from pharmaceutical effluents, since exposures to them has both direct and indirect effects on humans and aquatic organisms. This study aims to assess the quality of effluents discharged from some pharmaceutical industries located within the Kano metropolis, Nigeria.

METHODS

The Study Areas

The study was conducted within Kano metropolis, Kano state, Nigeria. The metropolis comprises of six-core urban local government areas (Dala, Fage, Gwale, Kano Municipal, Nasarawa, and Tarauni) and two peri-urban local governments (Kumbotso and Ungogo).

Sample Collection

Samples (1 L) were collected in a plastic container from three pharmaceutical industries, whose names were coded S, A, and P, within the Kano metropolis, Kano, Nigeria. At the sampling sites, samples were collected from the surface, middle and bottom of the water for three consecutive days. Samples collected in the morning from each of the three pharmaceutical industries were coded SM, AM, and PM, while those collected in the afternoon and evening were coded SA, AA, PA, and SE, AE, and PE respectively. The collected samples were transported to the laboratory in ice packs and then stored in a refrigerator prior to pre-treatment and analysis.

Elemental Analysis of the Samples

Samples were digested according to Association of Official Analytical Chemist (AOAC) (1990) procedure; portions (50 ml) were transferred into a beaker and 70 % HNO_3 (10 ml) was added and then heated gently until a clear solution was obtained. This was then filtered into a 50 ml volumetric flask and made up to mark with distilled water. The digested samples were then analyzed for the presence of Lead, Cadmium, Copper, Nickel, and Chromium against a blank using an Atomic Absorption Spectrophotometer (Model 6800 Shimadzu Japan, 2016). Measurements were taken and the concentrations (ppm) of the metals were extrapolated from their calibration curves (Table 1).

Physicochemical Parameters

The pH meter (PH-260-HANNA, 2016) electrode was calibrated using distilled water and a buffer of pH 7.4 after which the pH values of the samples were recorded. The Turbidimeter (WG2-B Turbidimeter Shanghai Xinrii China ,2016) electrode was

calibrated by elevating it using pure water and cleaning it with tissue paper prior to logging the readings for every sample. The Total Suspended Solids (TSS) enunciator indicator on the digital conductivity meter was activated, and the probe was inserted into the samples, agitated vertically and allowed to equilibrate before recording. The digital conductivity meter (DDS-307-DDS METER. UK ,2017), electrode was cleaned, rinsed, and wiped before being inserted into a sample, agitated vertically, and equilibrated before recording. The Total Dissolved Solid (TDS) and Chemical Oxygen Demand (COD) (Gallenhamp AMPS13/40, 1999), were also determined using the method reported by APHA, (1998).

Detection of Paracetamol in the Samples

Preparation of solutions

Stock solution (1 mg/mL) was prepared by dissolving paracetamol (10 mg) in a quantity of distilled water (5 ml) inside a volumetric flask (10 ml) and then making up to mark with distilled water. Working solutions within the range of 2-10 µg/mL were then prepared from the stock solution.

Analytical method for estimation of paracetamol

The UV-spectrophotometric method for the determination of paracetamol developed by Behera *et al.* (2012) was adopted and validated with respect to its λ_{max}, linearity, precision, and accuracy according to ICH (1996) guidelines. A five-point calibration curve within the concentration of (2-10 µg/mL) was constructed using Microsoft Excel, 2016.

Samples analysis

Each sample was analysed for paracetamol at 243 nm using the validated method and the absorbance obtained was used to extrapolate the concentration from the calibration curve.

RESULTS

The calibration curve and sensitivity parameter of the method for elemental analysis are presented in Table 1. The concentrations of the metals in the effluents from pharmaceutical industries are presented in Figure 1. The pH, Turbidity, Total Dissolve Solid (TDS), Electric Conductivity (EC), Total Suspended Solids (TSS), and Chemical Oxygen Demand (COD) of the samples are presented in Tables 2-7. The results were compared with limits set by the Nigerian Federal Environmental Protection Agency (FEPA, 1991). Precision and accuracy of the adopted UV method for the analysis of paracetamol are presented in Table 8, while the concentration of paracetamol in the samples are presented in Tablet 9.

Table 1: Calibration and Sensitivity Parameters of the Method for Elemental Analysis

Metal	Linear equation	LOD (µg/mL)	LOQ (µg/mL)	Correlation Coefficient (r)
Cd	Y= 0.3006x + 0.1050	0.3006	0.9109	0.9989
Cr	Y= 0.0045x + 0.0059	2.46408	7.4667	0.9988
Ni	Y= 0.0570x + 0.2143	3.2739	9.9208	0.9987
Pb	Y= 0.0265x + 0.0230	1.3191	3.9973	0.9964
Cu	Y= 0.1446x - 0.0403	0.5528	1.6739	0.9985

LOD = Limit of detection
LOQ = Limit of quantification

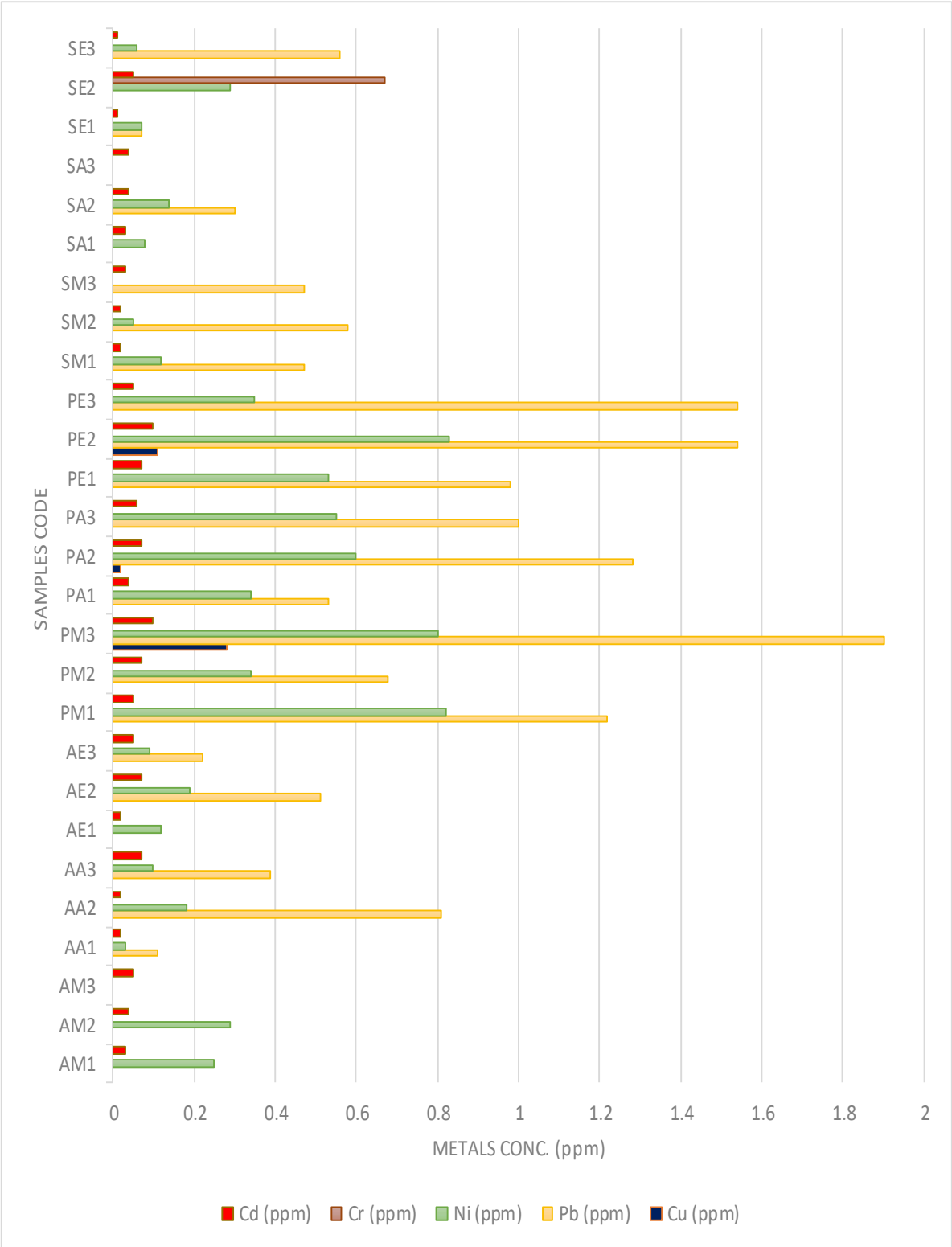
SAMPLES CODE
SE3
SE2
SE1
SA3
SA2
SA1
SM3
SM2
SM1
PE3
PE2
PE1
PA3
PA2
PA1
PM3
PM2
PM1
AE3
AE2
AE1
AA3
AA2
AA1
AM3
AM2
AM1
0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6
1.8
2
METALS CONC. (ppm)
Cd (ppm)
Cr (ppm)
Ni (ppm)
Pb (ppm)
Cu (ppm)

Table 2: pH Values of the Pharmaceutical Effluents

S/No.	Code	pH ± SEM
1	AM1	7.02±0.01
2	AM2	7.00±0.01
3	AM3	6.91±0.01
4	AA1	6.88±0.01
5	AA2	7.09±0.02
6	AA3	7.22±0.01
7	AE1	6.95±0.01
8	AE2	6.92±001
9	AE3	6.91±0.00
10	PM1	6.02±0.01
11	PM2	5.59±0.04*
12	PM3	6.65±0.01
13	PA1	5.81±0.01*
14	PA2	5.75±0.00*
15	PA3	6.07±0.01
16	PE1	6.19±0.01
17	PE2	6.01±0.01
18	PE3	5.98±0.01*
19	SM1	5.75±0.00*
20	SM2	5.81±0.01*
21	SM3	5.92±0.01*
22	SA1	5.75±0.01*
23	SA2	5.81±0.01*
24	SA3	5.84±0.01*
25	SE1	5.82±0.01*
26	SE2	5.82±0.01*
27	SE3	5.91±0.01*

* Outside 6-9 Federal Environment Protection Agency limit (FEPA, 1991)

Table 3: Turbidity values of the pharmaceutical effluents

S/No.	Code	TUTURBIDITY (NTU) ± SEM
1	AM1	4.10±0.06
2	AM2	2.00±0.06
3	AM3	19.53±0.18*
4	AA1	5.53±0.09*
5	AA2	6.40±0.12*
6	AA3	26.70±0.12*
7	AE1	2.60±0.06
8	AE2	2.50±0.06
9	AE3	4.80±0.06
10	PM1	181.23±0.15*
11	PM2	132.53±0.57*
12	PM3	990.67±2.19*
13	PA1	92.37±0.12*
14	PA2	237.67±0.88*
15	PA3	26.53±0.09*
16	PE1	36.27±0.07*
17	PE2	220.33±0.33*
18	PE3	247.00±1.15*
19	SM1	731.00±0.58*
20	SM2	20.10±0.06*
21	SM3	4.97±0.04
22	SA1	411.67±0.88*
23	SA2	17.10±0.06*
24	SA3	4.77±0.03
25	SE1	665.00±1.15*
26	SE2	471.00±0.58*
27	SE3	37.73±0.09*

* Above the ≤5.00 NTU Federal Environment Protection Agency limit (FEPA, 1991)

Table 4: Total dissolve solid (TDS) values of the pharmaceutical effluents

S/No.	Code	TDS (mg/L) ± SEM
1	AM1	513.00±0.58
2	AM2	437.00±0.58
3	AM3	512.00±0.58
4	AA1	444.67±0.88
5	AA2	960.33±5.24
6	AA3	643.33±1.45
7	AE1	471.00±0.58
8	AE2	460.00±0.58
9	AE3	493.00±0.58
10	PM1	468.00±0.58
11	PM2	362.33±0.88
12	PM3	543.00±1.15
13	PA1	269.67±0.33
14	PA2	495.33±0.67
15	PA3	507.67±0.33
16	PE1	461.33±0.67
17	PE2	564.67±0.67
18	PE3	594.67±0.88
19	SM1	412.33±0.33
20	SM2	114.50±0.00
21	SM3	114.50±0.00
22	SA1	461.67±0.67
23	SA2	228.67±0.33
24	SA3	245.33±0.33
25	SE1	595.67±0.33
26	SE2	261.33±0.88
27	SE3	195.40±0.06

Federal Environment Protection Agency limit (FEPA, 1991) ≤2000.00 mg/L

Table 5: Electric Conductivity (E.C) Values of the Pharmaceutical Effluents

S/No.	Code	E.C (uS/cm) ± SEM
1	AM1	1031.67±0.88*
2	AM2	864.67±1.45
3	AM3	1032.33±0.88*
4	AA1	803.67±1.86
5	AA2	1955.33±1.76*
6	AA3	1285.00±1.15*
7	AE1	935.33±0.88
8	AE2	922.33±1.20
9	AE3	984.00±0.58
10	PM1	896.33±1.20
11	PM2	721.00±1.00
12	PM3	1095.67±0.88*
13	PA1	543.33±0.67
14	PA2	992.00±0.58
15	PA3	1055.00±33.51*
16	PE1	921.33±0.67
17	PE2	1136.67±0.33*
18	PE3	1185.67±1.20*
19	SM1	823.00±0.58
20	SM2	228.00±0.00
21	SM3	229.67±0.33
22	SA1	930.67±0.33
23	SA2	458.67±0.33
24	SA3	490.33±0.33
25	SE1	1127.33±0.67*
26	SE2	525.00±0.58
27	SE3	390.33±0.33

* Above the ≤1000.00 uS/cm Federal Environment Protection Agency limit (FEPA, 1991)

Table 6: Total Suspended Solid (TSS) Values of the Pharmaceutical Effluents

S/No.	Code	TSS (mg/L) ± SEM
1	AM1	26.67±3.33
2	AM2	20.00±0.00
3	AM3	19.67±0.33
4	AA1	26.67±3.33
5	AA2	256.00±3.06*
6	AA3	97.33±3.71*
7	AE1	26.67±3.33
8	AE2	10.00±0.00
9	AE3	210.00±0.00*
10	PM1	616.67±3.33*
11	PM2	326.67±3.33*
12	PM3	1026.67±3.33*
13	PA1	33.33±3.33*
14	PA2	1160.00±5.77*
15	PA3	1149.33±0.67*
16	PE1	823.33±3.33*
17	PE2	1066.67±3.33*
18	PE3	1633.33±3.33*
19	SM1	2158.33±0.88*
20	SM2	29.33±0.33
21	SM3	39.67±0.33*
22	SA1	1723.33±3.33*
23	SA2	119.67±0.33*
24	SA3	161.00±0.58*
25	SE1	1751.00±5.8*
26	SE2	1039.33±0.67*
27	SE3	10.00±0.00

* Above the ≤30.00 mg/L Federal Environment Protection Agency limit (FEPA, 1991)

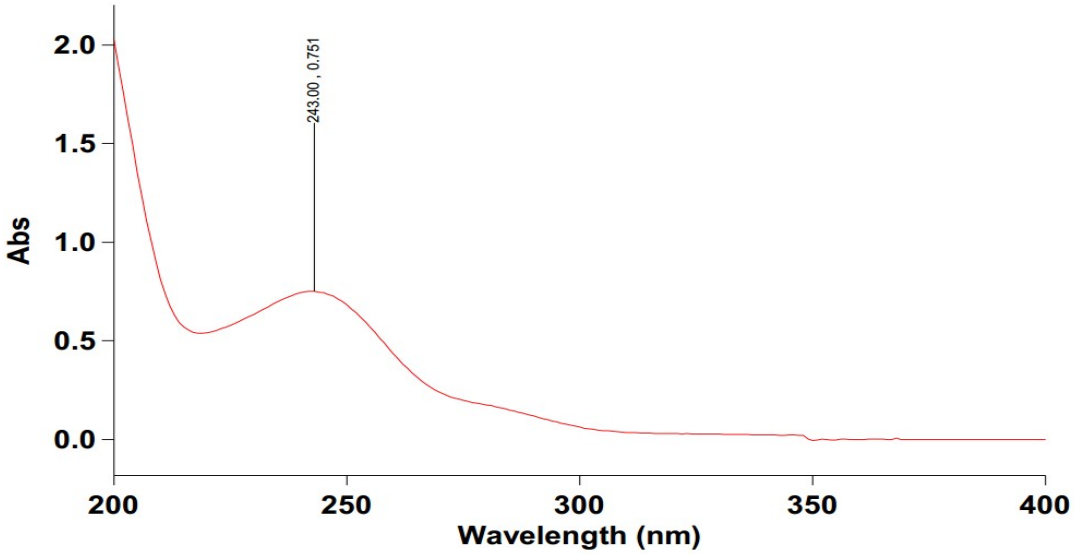

Figure 2: UV Spectrum of Paracetamol Standard Powder (10 µg/mL) in Distilled Water

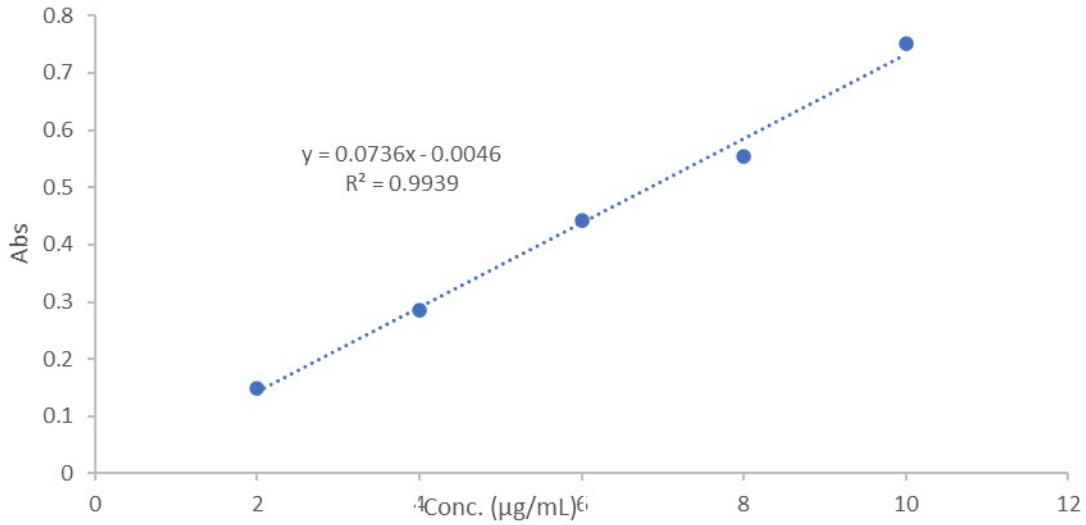

Figure 3: Calibration curve of Paracetamol standard powder (2-10 µg/mL) in distilled water at 243 nm

Table 7: Chemical Oxygen Demand (COD) Values of the Pharmaceutical Effluents

S/No.	Code	COD (mg/L) ± SEM
1	AM1	606.67±3.33
2	AM2	503.33±3.33
3	AM3	510.00±5.77
4	AA1	300.00±0.00
5	AA2	1200.00±0.00*
6	AA3	693.33±3.33
7	AE1	503.33±3.33
8	AE2	803.33±3.33
9	AE3	806.67±3.33
10	PM1	1033.33±33.33*
11	PM2	1100.00±0.00*
12	PM3	1766.67±33.33*
13	PA1	1000.00±0.00
14	PA2	1300.00±0.00*
15	PA3	1033.33±33.33*
16	PE1	1333.33±33.33*
17	PE2	1866.67±33.33*
18	PE3	2200.00±0.00*
19	SM1	3266.67±33.33*
20	SM2	406.67±3.33
21	SM3	500.00±0.00
22	SA1	5033.33±33.33*
23	SA2	1366.67±33.33*
24	SA3	2066.67±33.33*
25	SE1	1033.33±33.33*
26	SE2	1400.00±0.00*
27	SE3	2366.67±33.33*

* Above the ≤1000.00 mg/L Federal Environment Protection Agency limit (FEPA, 1991)

Table 8: Precision and Accuracy of the Developed Method

Parameters	Value	
Precision:	Intra-day **(%**RSD)	Inter-day **(%**RSD**)**
	0.98	1.08
Accuracy:	**% Recovery**	
	114.88	
	113.30	
	106.75	

%RSD = percentage Relative Standard deviation

Table 9: Concentration (mg/mL) of Paracetamol in the Pharmaceutical Effluents

Sample Code	Concentration (mg/mL)
SM1	1.64
SA1	0.95
SA2	0.16
SA3	0.36
SE1	0.89
SE2	0.25
SE3	0.31

DISCUSSION

Lead (Pb) was found to be above the FEPA official limit (<1 ppm) in 22.22% of the samples figure 1. The possible sources of lead from pharmaceutical industries could be from the raw material, processing equipment, packaging material, water, solvents amongst others. Lead is a nonferrous metal that is primarily absorbed through drinking water, airborne Lead-containing particulates, and Lead-based paints. Inorganic forms of Lead affect various systems, while organic Lead toxicities primarily affect the central nervous system (U.S. EPA, 1986). Children absorb Lead more efficiently than adults, and ingested Lead is more readily absorbed in fasting individuals (Elhe and Mckee, 1990). High concentrations of Lead can cause irreversible brain damage, seizures, coma, and death if not treated immediately. Moderate levels of Lead can cause neurological impairment, including fatigue, irritability, memory problems, and decision-making impairment (Deepa, 2018). Lead can also cause anaemia, high blood pressure, and increased risk for cardiovascular disease, myocardial infarction, and stroke. Kidney disease, both acute and chronic, is a characteristic of Lead toxicity (Goyer, 1988).

Copper, Nickel, Cadmium and Chromium were found to be within the FEPA official limits in all the samples figure 1. Nickel is associated with decreased body weight, heart and liver damage and skin irritation (Moore, 1991). Copper is an essential trace element however, it could bioaccumulate to cause anaemia, liver and kidney damage, and stomach and intestinal irritation (ATSDR, 1990). Cu poisoning is particularly severe in sheep even at low concentrations **(**Lenntech, 1998). Chromium (VI) toxicity targets the respiratory tract, causing symptoms like shortness of breath, coughing, and wheezing in acute cases, and perforations, ulcerations, bronchitis, decreased pulmonary function, and pneumonia in chronic cases (US. IRIS, 1999). A similar study conducted in Lagos, Nigeria revealed the concentration of heavy metals; Chromium, Cadmium, Lead, and Nickel above the permissible limit (Olorunfemi and Gabriel, 2018).

The pH (48.14%) of the samples was found to be outside the FEPA official range of (6-9) table 2. The acidic nature of the effluent samples is capable of stemming the pH of the receiving water bodies thereby, destabilizing fundamental properties such as alkalinity, metal solubility and hardness of water (Wang *et al,* 2016). Aquatic animals in contact with these effluents could be faced with metabolic imbalance leading to their death due to deleterious chemical reactions and metal toxicity. A similar study conducted in Nigeria reported that 42.30%

of the effluent samples had pH outside the official ranges (Chemezie *et al.*, 2017). High turbidity was observed in (78.07%) of the samples table 3. This could affect the penetration of sunlight, into the water bodies, required for plant photosynthesis and other biological processes. The majority of the samples (70.37%) had TSS levels above the FEPA official limit (<30 mg/L) table 6, which further supported the turbidity results. This could affect the respiration and reproduction of the animals and plants in contact with these effluents. A similar study reported 70.81% of the samples analyzed with TSS above the official limit, (Singare *et al.,* 2011). The TDS of all the samples were found to be within the FEPA official limit (<2,000 mg/L) table 4. TDS measures salinity in form of carbonates, bicarbonates, chlorides, sulphates, phosphates, and nitrates of calcium, magnesium, sodium, potassium, iron and manganese. At concentrations above the official limit, TDS affects water density, osmoregulation, and gas solubility. The electric conductivity (EC) in 33.33% of the samples was found to be above the FEPA official limit (<1000 µS/cm) table 5. The EC is a measure of purity, which reflects the safety of the water to aquatic animals and humans. A similar study reported 35.50% of effluent samples analyzed with electric conductivity above the official limit (Witjes *et al*., 2021). COD was found to be above the official FEPA limit (<1000 mg/L) in 55.56% of the samples table 7. This value is crucial for determining toxic conditions and the presence of biologically resistant substances. The COD measures the relative oxygen-depletion effect of waste contaminants, which is essential for waste treatment control.

The paracetamol calibration curve was found to be suitable for the studies as it's coefficient of determination ($r^2 = 0.9939$) is close to unity (Figure 3). Also, the method was found to be very sensitive as it can accurately quantify paracetamol as low as 0.16 µg/mL. Some of the samples (25.93%) were found to contain paracetamol within the concentration range of 0.16- 1.64 µg/mL (Table 9). Ingestion of paracetamol from the bodies of water contaminated with these effluents could lead to paracetamol acute liver damage, especially in children. Acute paracetamol toxicity was reported in the Western world, as the leading cause of liver failure and is responsible for the majority of drug overdoses in the US, UK, Australia, and New Zealand (Daly *et al*., 2008).

CONCLUSION

All the analyzed pharmaceutical effluent samples were found not to be safe for disposal into bodies of water as none of them passed the quality assessment. Hence there is a need for proper treatment of all industrial effluent before discharge into bodies of water. The relevant agencies, such as FEPA, should ensure that all industries comply with standard effluent treatment procedures before discharge into the environment.

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