# Quantitative determination of active pharmaceutical ingredient and trace elements in ciprofloxacin tablets distributed in Lagos State, Nigeria

**[1*]Emeka C. Ogoko, [1]Henrietta I. Kelle and [2]Gana J. Babaman**

[1]Department of Chemistry, National Open University of Nigeria, Jabi Abuja.
[2]Central Drug Laboratory, Medical Compound. National Agency for Food and Drug Administration and Control, Yaba, Lagos, Nigeria.

**ABSTRACT**

***Background*:** Substandard ciprofloxacin with low or very high concentrations of the active ingredients are injurious to health and may be responsible for drug bacterial resistance and failure of therapeutic functions. This study attempt to assess the physicochemical quality and concentration of the active ingredient in some brands of Ciprofloxacin consumed in Lagos State, Nigeria.

***Methods*:** Analysis of weight uniformity, friability, hardness and disintegration were performed using standard methods. Determinations of the concentration of active pharmaceutical ingredient and heavy metals in ciprofloxacin tablets were done using high performance liquid chromatography techniques (HPLC) and atomic absorption spectrophotometer (AAS) respectively.

***Results*:** Results of content uniformity revealed that the weight of twenty samples of ciprofloxacin were within the compendia specification for content uniformity. The disintegration rate ranged from 3 to 6 minutes and was within the allowable limits of not more than 15 minutes. The mean hardness and friability of all the brands complied with the standard specification for hardness (not less than 20N) and friability (not more than 1%) respectively. The assay results of ciprofloxacin samples ranged from 96. 8% - 106.1% with a relative standard deviation of 0.2%. The concentration of ciprofloxacin in analyte samples were within the recommended specifications range of 90.0% - 110.0% and within the maximum allowable standard deviation of 1.5%. The heavy metals concentrations were within the permissible limit of not more 20 ppm in ciprofloxacin tablets.

***Conclusion*:** The results of this study revealed that the ten brands of ciprofloxacin complied with the standard recommended limits and were fit for their therapeutic functions.

***Keywords*:** Ciprofloxacin, concentration, disintegration, hardness, weight uniformity

## 1. INTRODUCTION

Most drug users generally belief that counterfeit drugs especially antibiotics have flooded over the markets in most cities and villages in Nigeria. This may be due to the attendance economic benefits by the importers and manufacturers of these sub-standard products, coupled with anticipated poor compliance to the drug regulations and weak quality control practices in Nigeria [1]. Substandard drugs with low concentrations of the active ingredients are detrimental to health and are responsible for resistance of antibiotics by bacterial, thereby making the eradication, treatment and control of infectious diseases ineffective [2-4]. The quality of pharmaceutical products must be reliable and reproducible, if consumer safety is to be assured. There is therefore need for quality control and assurance of drug products during manufacturing and after manufacturing [5]. Generic drug products which are chemically identical must contain the same active therapeutic ingredients in the same strength, concentration or dosage. Besides, the route of administration, quality, purity, disintegration rate, dissolution rate and content uniformity of such generic drug products must be identical in order to ensure the safety of consumers and fitness of the drug for what it is intended to be used [6]. Bioavailability of generic drugs especially tablets dosage forms depends on the type and concentrations of binders, disintegration and types of lubricant [7]. Unregulated temperature and humidity causes the decomposition of active ingredients of pharmaceutical products during storage and transportation of the drug products [8].

* Corresponding author: Email: eogoko@noun.edu.ng; Phone: +2347067626107

Quality control of pharmaceutical products should be carried out regularly throughout the shelf life of drug products by the regulatory agencies and independent researchers. A combination of pharmaceutical and chemical assay methods have proved effective in quantitative and qualitative determination of active pharmaceutical ingredients in generic drugs, hence drug quality. Ciprofloxacin is a synthetic second generation fluoroquinolone bactericidal antimicrobial agent. The IUPAC name of ciprofloxacin is 1-cyclopropyl-6-fluoro-4-oxo-7-(piperazin-1-yl)-quinolone-3-carboxylic acid. It has a molecular formula $C_{17}H_{18}FN_3O_3$ and molecular weight of 331.34 g/mol. Ciprofloxacin is a broad spectrum antimicrobial drug that is effective in the treatment of urinary tract infections, acute uncomplicated cystitis in females, lower respiratory tract infections, acute sinusitis, skin structure infections, typhoid fever, bone and joint infection, uncomplicated urethral and cervical gonorrhoea among others [9-10]. It is also used to treat people who have been exposed to anthrax [11]. It prevent the multiplication of bacteria by inhibiting the reproduction and repair of their genetic material. [12]. The application of ciprofloxacin is associated with some adverse reactions also known as side effects which include; diarrhea, dizziness, headache, stomach upset, abdominal pain, nausea/vomiting and rash [5]. Quite a number of methods have been reported for analysis of ciprofloxacin tablets. Adegbolagun *et al* assessed the biopharmaceutical and chemical equivalence of ten brands of ciprofloxacin hydrochloride tablets in the market using thin layer chromatography and titrimetric techniques [13]. The authors observed that four out of the ten brands of ciprofloxacin hydrochloride tablets were not pharmaceutically equivalent [13]. Cazedey *et al* attempted to develop a simple but rapid UV-spectrophotometric procedure for evaluating ciprofloxacin hydrochloride in ophthalmic solution. The results revealed that the brands of ciprofloxacin hydrochloride were within the recommended permissible limits of British pharmacopoeia [14]. Qureshi *et al* carried out analysis of ciprofloxacin in different drug products using High Performance Liquid Chromatography. The results of the analysis shows the concentration of active ingredients were comparable with their labelled concentrations. The authors also observed that the quantification of ten out of eleven brands of ciprofloxacin were within the permissible limit [15]. Nandipati *et al* in a research to determine the active pharmaceutical ingredient in ciprofloxacin by ultra-performance liquid chromatograph observed that the six drug products analysed were within the recommended limits of British Pharmacopoeia specification [16]. Anah *et al* performed non aqueous titration and UV-spectrophotometric analysis of fifteen brands of ciprofloxacin hydrochloride, but observed that ten brands were within recommended standard specification whereas five brands were below the acceptable standard limits. These researchers concluded that the five substandard drug products may cause therapeutic failure and drug resistance by microbacterial [4]. In this paper, we seek to determine the physicochemical quality and concentration of the active ingredient in some brands of Ciprofloxacin using High Performance Liquid Chromatography (HPLC). The research also seek to ascertain if the levels of heavy metals in brands of Ciprofloxacin are within recommended and safe limits.
The molecular structure of Ciprofloxacin is shown below.

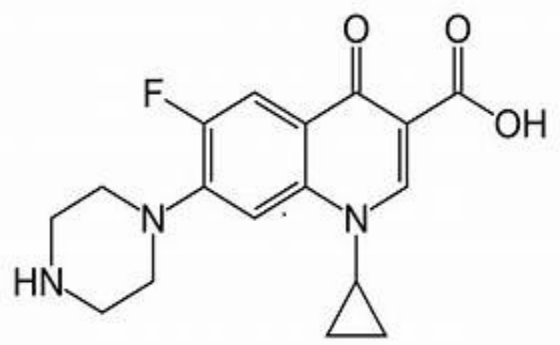


**Figure 1**: The chemical structure of Ciprofloxacin.

## 2.0 MATERIALS AND METHODS

### 2.1 Materials

#### 2.1.1 Reagents and equipment

Distilled water and de-ionized water were prepared using milli-q50 water distiller system (USA) and deionizer system (DM-6000 Dual bed Deionizer, USA) respectively. Concentrated nitric acid, phosphoric acid (85% wt), acetonitrile and tri-ethylamine were analytical grade and obtained from Sigma-Aldrich. Ciprofloxacin ethylene diamine analog reference standard was graciously provided from NAFDAC. Friabilator (YE-FT-02), Hardness tester (YE/HT/02), disintegration apparatus (YB/DT/01), analytical weighing balance (Metler Toledo, YE-AB-04), HPLC (Agilent 1260 infinity; version 2.1, Japan) and Atomic Absorption Spectrophotometer (Buck Scientific VPG 210) were the main

instrument or equipment used at the course of this study. Ten (10) brands of ciprofloxacin tablets were randomly procured from the distribution outlets in Idumota and Mushin, Lagos State. Brands of Ciprofloxacin were coded $C_1$-$C_{10}$.

**2.2 Methods**

**2.2.1 Uniformity of weight**

Twenty tablets of ciprofloxacin were randomly selected and the weight of each individual tablet was determined using analytical weighing balance (Metler Toledo, YE-AB-04). The average weight was then obtained and recorded.

**2.2.2 Disintegration Test**

Six tablets from each brand of ciprofloxacin tablets were employed for the test. Six tablets/capsules were placed in the basket of the disintegration apparatus (YB/DT/01) to which some quantity of de-ionized water was added to submerge the tablets and maintained at 37ºC. The time in minutes for all the tablets to completely disintegrate was then recorded.

**2.2.3 Hardness Test**

With the aid of a Hardness tester (YE/HT/02) the hardness of each ciprofloxacin sample was checked and the average calculated.

**2.2.4 Friability Test**

20 tablets for each sample were de-dusted and accurately weighed on a balance and the weight recorded. The de - dusted tablets were transferred to the drum of Friabilator (YE-FT-02) and allowed to rotate 100 times. The tablets were removed from the Friabilator, de-dusted again and re-weighed. Results were then calculated and recorded.

**2.2.5 Assay of Ciprofloxacin by High performance liquid chromatographic method (HPLC)**

0.025M phosphoric acid was prepared by adding 1.8 ml of concentrated phosphoric acid (85% wt) into a 1 litre volumetric flask containing about 600 ml of distilled water and was made up to the mark with distilled water. The pH of the solution was adjusted to 2.0 ± 0.1 by adding appropriate quantity of tri-ethylamine. 500 mg of the ciprofloxacin tablets was transferred into a 500 ml volumetric flask containing 400 ml of a mixture of 0.025M phosphoric acid solution prepared as above and acetonitrile in volume ratio of 87:13 respectively and then sonicated for about 20 min. The supernatant solution was made up to the mark (500 ml) by the addition of mixture of phosphoric acid and acetonitrile solution, and was filtered. 0.2 mg/ml of ciprofloxacin from the filtrate was then prepared by dissolving 1ml of the filtrate in 25 ml of solution of 0.025M phosphoric acid solution prepared as above and acetonitrile (volume ratio 87:13). The pH of 0.025M phosphoric acid was adjusted to pH 3.0 ± 0.1 with tri-ethylamine and then dissolved in acetonitrile to a volume ratio of 87:13 which constitutes the mobile phases. 0.2 mg/ml of United State Pharmacopeia (USP) ciprofloxacin reference standard was dissolved in solution of 0.025M phosphoric acid solution and acetonitrile in volume ratio of 87:13, this constitutes the standard solution. 0.05 mg/ml of United State Pharmacopeia (USP) ciprofloxacin ethylenediamine analog reference standard was dissolved in the standard solution. The solution was filtered and I ml of filtrate was then dissolved in solution of 0.025M phosphoric acid solution and acetonitrile in volume ratio of 87:13 to obtain the system suitability solution. The detector conditions are: wavelength (UV) is 278nm, Column: - 4.6 mm x 25 cm, 5µm packing L1, Colum temperature: 30ºc, flow rate: - 1.5ml/min, Injection volume: - 10µL.

**2.2.6 Heavy metal determination**

The method of American Public Health Association (APHA, AWWA, 2001) was adapted in the analysis of heavy metals using Atomic Absorption Spectrophotometer (Buck Scientific VPG 210). Serially diluted concentrations of stock solutions of the respective metals were used in preparation of calibrated curves. Each concentration (mg/ml) of the metal ion in the analyte sample was obtained by graphical extrapolation from the calibration curve [17-18].

**2.3 Statistical Analysis**

The mean, standard deviation, upper limit and lower limit were the simple statistical analysis carried out in this study

**3.0 RESULTS**

The results of uniformity of weight for ciprofloxacin tablets are presented in Table 1 below.

**Table 1:** Uniformity of weight for brands of ciprofloxacin tablets (mg)

| Sample | C1 | C2 | C3 | C4 | C5 | C6 | C7 | C8 | C9 | C10 |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 760.2 | 711.0 | 702.0 | 797.5 | 628.8 | 638.9 | 788.6 | 768.8 | 721.1 | 712.1 |
| 2 | 754.4 | 709.7 | 724.3 | 794.6 | 679.4 | 689.4 | 801.3 | 765.4 | 701.6 | 713.3 |
| 3 | 784.2 | 756.0 | 714.8 | 804.2 | 703.2 | 713.3 | 794.1 | 794.5 | 760.1 | 724.6 |
| 4 | 743.8 | 736.8 | 734.1 | 757.7 | 667.4 | 659.5 | 767.3 | 752.4 | 740.6 | 726.2 |
| 5 | 734.6 | 763.2 | 726.2 | 784.2 | 685.8 | 695.7 | 794.4 | 724.1 | 769.2 | 729.3 |
| 6 | 755.3 | 735.1 | 719.3 | 798.5 | 655.3 | 665.4 | 768.5 | 764.8 | 730.1 | 725.3 |
| 7 | 774.3 | 747.3 | 733.5 | 810.3 | 674.3 | 669.2 | 804.5 | 784.5 | 749.9 | 730.8 |
| 8 | 726.5 | 763.5 | 701.8 | 773.5 | 660.5 | 671.6 | 783.6 | 766.1 | 769.5 | 708.5 |
| 9 | 752.2 | 742.6 | 720.2 | 756.5 | 673.2 | 679.6 | 766.5 | 748.2 | 748.6 | 726.2 |
| 10 | 774.1 | 750.5 | 723.7 | 794.3 | 690.5 | 699.5 | 784.3 | 779.1 | 744.5 | 720.1 |
| 11 | 740.4 | 738.7 | 693.3 | 780.3 | 674.3 | 683.4 | 789.3 | 748.8 | 729.5 | 683.6 |
| 12 | 786.3 | 703.3 | 689.3 | 771.9 | 679.3 | 687.1 | 772.1 | 789.7 | 712.2 | 699.2 |
| 13 | 771.1 | 755.1 | 741.0 | 782.1 | 643.2 | 655.2 | 792.1 | 778.2 | 759.3 | 746.4 |
| 14 | 746.2 | 726.2 | 717.4 | 804.3 | 672.3 | 686.7 | 798.3 | 749.1 | 722.1 | 712.1 |
| 15 | 726.8 | 744.1 | 732.7 | 745.5 | 694.3 | 709.2 | 755.7 | 732.8 | 748.3 | 738.1 |
| 16 | 785.3 | 697.9 | 735.6 | 783.4 | 702.5 | 712.8 | 793.3 | 775.5 | 691.2 | 730.4 |
| 17 | 751.6 | 735.1 | 720.4 | 794.4 | 677.8 | 687.1 | 789.1 | 761.6 | 741.5 | 710.5 |
| 18 | 776.4 | 740.2 | 704.3 | 743.5 | 696.5 | 706.3 | 755.5 | 781.3 | 746.3 | 714.3 |
| 19 | 750.8 | 714.1 | 692.4 | 795.3 | 667.9 | 678.9 | 799.8 | 759.3 | 710.6 | 698.2 |
| 20 | 739.8 | 763.2 | 730.3 | 754.6 | 685.8 | 698.2 | 766.4 | 743.8 | 769.1 | 726.3 |
| mean | 756.7 | 736.7 | 717.8 | 781.3 | 675.6 | 684.4 | 783.2 | 763.4 | 738.3 | 718.7 |
| SD | 19.3 | 20.36 | 15.67 | 20.42 | 18.87 | 20.11 | 15.37 | 18.83 | 22.91 | 14.74 |
| Deviation | 57.09 | 61.08 | 47.01 | 61.26 | 56.61 | 60.33 | 46.11 | 56.49 | 68.73 | 44.22 |
| Upper limit | 813.8 | 778.8 | 764.8 | 842.6 | 732.2 | 744.7 | 829.3 | 819.9 | 807.0 | 762.9 |
| Lower limit | 699.6 | 675.6 | 670.8 | 720 | 619.0 | 624 | 737.1 | 706.9 | 669.6 | 674.5 |

Ciprofloxacin brands $C_7$ and $C_4$ recorded higher values for content weight uniformity of 804.5 mg and 810.3 mg respectively, while $C_5$ had the lowest weight uniformity value of 628.8 mg. The values of standard deviation ranged from 14.74 to 22.91. The results of disintegration test are presented in Table 2.

**Table 2**: Disintegration test for Brands of ciprofloxacin tablets (mg)

| Sample | C1 | C2 | C3 | C4 | C5 | C6 | C7 | C8 | C9 | C10 |
|---|---|---|---|---|---|---|---|---|---|---|
| Average DT time (min) | 3.01± 0.1 | 5.03± 0.2 | 3.02± 0.4 | 6.12± 0.1 | 4.05± 0.3 | 5.10± 0.2 | 4.06± 0.5 | 6.01± 0.1 | 4.03± 0.3 | 3.04± 0.2 |

The disintegration rate varies between 3.01 ± 0.1 to 6.01 ± 0.1 minutes among the ten different brands of ciprofloxacin assessed.
Table 3 shows the results for the hardness tests, which varies from samples to sample and brands to brands.

**Table 3**. Hardness for Brands of Ciprofloxacin (N)

| Sample | C1 | C2 | C3 | C4 | C5 | C6 | C7 | C8 | C9 | C10 |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 70.2 | 59.3 | 72.6 | 70.6 | 69.4 | 71.1 | 61.8 | 71.2 | 69.9 | 67.2 |
| 2 | 77.5 | 52.6 | 66.7 | 64.9 | 63.7 | 76.4 | 56.3 | 67.8 | 66.6 | 65.9 |
| 3 | 69.8 | 64.1 | 75.9 | 62.5 | 78.3 | 70.7 | 66.1 | 74.9 | 64.7 | 76.1 |
| 4 | 79.4 | 60.3 | 73.4 | 67.2 | 66.8 | 75.4 | 64.5 | 75.5 | 69.4 | 69.9 |
| 5 | 73.1 | 53.4 | 69.5 | 63.6 | 63.5 | 72.2 | 58.1 | 70.6 | 65.8 | 61.3 |
| 6 | 68.6 | 62.9 | 72.8 | 68.3 | 76.4 | 69.3 | 64.7 | 73.1 | 69.4 | 79.7 |
| 7 | 74.7 | 59.5 | 77.4 | 76.1 | 71.6 | 73.7 | 62.5 | 76.6 | 77.2 | 69.3 |
| 8 | 81.0 | 56.2 | 73.8 | 71.2 | 73.4 | 79.1 | 59.6 | 72.6 | 73.4 | 71.2 |
| 9 | 69.3 | 53.7 | 70.4 | 66.7 | 65.7 | 68.3 | 57.9 | 71.5 | 68.9 | 62.9 |
| 10 | 81.4 | 61.2 | 64.7 | 63.4 | 68.6 | 79.4 | 63.2 | 66.4 | 65.6 | 70.8 |
| sum | 745 | 583.2 | 717.2 | 674.5 | 697.4 | 735.6 | 614.7 | 720.2 | 690.9 | 694.3 |
| Mean | 74.5 | 58.32 | 71.72 | 67.45 | 69.74 | 73.56 | 61.47 | 72.02 | 69.09 | 69.43 |
| Max | 81.4 | 64.1 | 77.4 | 76.1 | 78.3 | 99.4 | 66.1 | 76.6 | 77.2 | 79.7 |
| Min | 68.6 | 52.6 | 64.7 | 62.5 | 63.5 | 68.3 | 56.3 | 66.4 | 64.7 | 61.3 |
| Final Hardness | 75 | 58 | 72 | 67 | 70 | 74 | 62 | 72 | 69 | 69 |

The maximum values of hardness ranged from 64.1 to 99.4 N whereas the minimum values ranged from 52.6 to 68.6 N. The mean hardness of ten different brands of ciprofloxacin therefore ranged from 58.32 N to 73.56 N.
Friability test is generally performed only on uncoated tablets and this test seeks to determine the extent of resistance to abrasion by such tablets [19]. The results of friability test are presented in Table 4.

**Table 4**. Mean friability for brands of ciprofloxacin tablets

| Sample | C1 | C2 | C3 | C4 | C5 | C6 | C7 | C8 | C9 | C10 |
|---|---|---|---|---|---|---|---|---|---|---|
| Initial weight (g) | 15.13 | 14.73 | 14.45 | 15.63 | 13.53 | 15.21 | 14.62 | 15.65 | 13.86 | 15.01 |
| Final weight (g) | 15.07 | 14.64 | 14.39 | 15.58 | 13.45 | 15.17 | 14.55 | 15.58 | 13.79 | 14.93 |
| %weight Loss (F) | 0.397 | 0.610 | 0.415 | 0.320 | 0.591 | 0.263 | 0.479 | 0.447 | 0.505 | 0.533 |
| SD | 0.001 | 0.005 | 0.003 | 0.002 | 0.001 | 0.004 | 0.001 | 0.002 | 0.005 | 0.003 |

The mean friability of the ten different brands of ciprofloxacin varies between one another, but approximate mean weight loss (friability) ranged from 0.263% to 0.610% in this study.
The concentration of ciprofloxacin in the ten different brands of the drug formulation analysed were determined using high performance liquid chromatography (HPLC) and results are shown in Table 5.

**Table 5** Concentration of ciprofloxacin (mg)

| Sample | Mean Composition by weight (mg) | Label weight claim (mg) | Percentage composition (%) |
|---|---|---|---|
| C1 | 511.5±0.11 | 500 | 102.3 |
| C2 | 515.5±0.02 | 500 | 103.1 |
| C3 | 502.9±0.05 | 500 | 100.6 |
| C4 | 502.6±0.01 | 500 | 100.5 |
| C5 | 484.1±0.03 | 500 | 96.8 |
| C6 | 499.2±0.10 | 500 | 99.8 |
| C7 | 526.6±0.13 | 500 | 105.3 |
| C8 | 530.4±0.08 | 500 | 106.1 |
| C9 | 503.7±0.15 | 500 | 100.7 |
| C10 | 492.9±0.07 | 500 | 98.6 |

The chromatogram of ciprofloxacin standard and a typical sample are shown in figure 1 and 2 respectively.

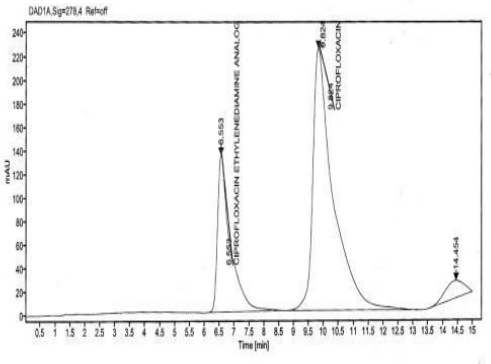


**Figure 1**: A chromatogram for ciprofloxacin reference standard

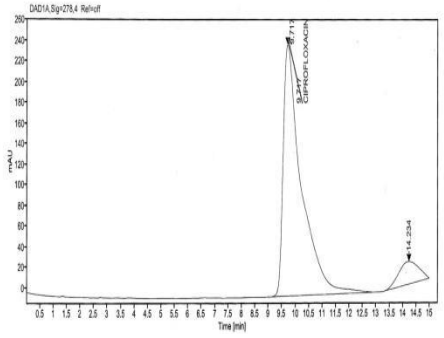


**Figure 2**: A chromatogram for ciprofloxacin sample

The composition of ciprofloxacin was computed using the equation below, based on information obtained from the chromatogram.

Result = (Ru/Rs) x (Cs/Cu) x ($Mr_1/Mr_2$) x100 --------- (1)
Where: Ru, Rs, Cs, Cu, $Mr_1$ and $Mr_2$ are peak response from the sample solution, peak response from the standard solution, concentration of ciprofloxacin hydrochloride reference standard in standard solution, normal concentration of ciprofloxacin in the sample solution, molecular weight of ciprofloxacin and molecular weight of ciprofloxacin hydrochloride respectively.
The mean composition by weight of ciprofloxacin in this study ranged from 484.1± 0.03 mg to 530.4 ± 0.08 mg. Label weight claim for all the ten brands of ciprofloxacin was 500 mg.

Table 6 revealed the disparity in the concentrations of heavy metals in different brands of ciprofloxacin.
**Table 6**: Heavy metal concentration in ciprofloxacin (ppm)

| Brand Code | Cu | Cd | Fe | Pb | Zn |
|---|---|---|---|---|---|
| **$C_1$** | 0.19 ± 0.10 | 0.13 ± 0.05 | 3.36 ± 0.11 | 0.00 ± 0.00 | 0.73 ± 0.01 |
| **$C_2$** | 0.16 ± 0.01 | 0.08 ± 0.01 | 0.68 ± 0.01 | 0.01 ± 0.00 | 0.81 ± 0.01 |
| **$C_3$** | 0.22 ± 0.05 | 0.09 ± 0.02 | 0.60 ± 0.01 | 0.01 ± 0.01 | 0.89 ± 0.02 |
| **$S_4$** | 0.17 ± 0.03 | 0.08 ± 0.01 | 0.63 ± 0.01 | 0.00 ± 0.00 | 0.96 ± 0.03 |
| **$C_5$** | 0.18 ± 0.04 | 0.12 ± 0.03 | 2.08 ± 0.10 | 0.02 ± 0.01 | 3.71 ± 0.10 |
| **$C_6$** | 0.19 ± 0.05 | 0.13 ± 0.02 | 1.07 ± 0.03 | 0.00 ± 0.00 | 0.53 ± 0.01 |
| **$C_7$** | 0.13 ± 0.01 | 0.07± 0.01 | 0.46 ± 0.01 | 0.00 ± 0.00 | 0.65 ± 0.01 |
| **$C_8$** | 0.22 ± 0.03 | 0.10 ± 0.02 | 0.76 ± 0.02 | 0.01 ± 0.00 | 0.79 ± 0.05 |
| **$C_9$** | 0.15 ± 0.02 | 0.06 ± 0.01 | 0.73 ± 0.01 | 0.00 ± 0.00 | 0.81 ± 0.02 |
| **$C_{10}$** | 0.20 ± 0.06 | 0.11± 0.01 | 1.98 ± 0.03 | 0.01 ± 0.00 | 2.17 ± 0.12 |

The concentration of Copper (Cu) in samples $C_1$ to $C_{10}$ of ciprofloxacin ranged from 0.13 ± 0.01 – 0.22 ± 0.03 ppm, while the concentrations of cadmium (Cd), Iron (Fe), Lead (Pb) and Zinc (Zn) in the ciprofloxacin ranged from 0.06 ± 0.01– 0.13 ± 0.05 ppm, 0.46 ± 0.01 – 3.36 ± 0.11 ppm, 0.00 ± 0.00 – 0.02 ± 0.01 ppm and 0.53 ± 0.01 – 3.71 ± 0.10 ppm respectively.

## 4. 0 DISCUSSION

Content uniformity of weight is an index that attempt to assess the amount of active pharmaceutical ingredient present in the formulation and quality of manufacturing practices. The mean content uniformity of weight ranged from 675.6 ± 18.87 mg to 783.2 ± 15.37 mg across the twenty samples of ten different brands of ciprofloxacin. The content uniformity of weight values for individual samples of ciprofloxacin were within the permissible limits (British Pharmacopeia [18]. The weight uniformity for tablets stipulates that not more than two weights out of twenty random weights should fall outside the upper and lower limits [20]. Another version of compendia specification for uniformity of weight recommended that not more than two weights out of twenty random weights should differ significantly from the mean weight by value greater than 5% [20]. The results of content uniformity of weights complied 100% with both specifications. The results of uniformity of weight in this study are in line with previous study conducted by Anah et al., 2019 [4]. The specification of disintegration rate necessitates that the time it required for a tablet or capsule to disintegrate at 37ºC should not exceed 30 minutes [21]. British Pharmacopeia recommended fifteen minutes disintegration time for uncoated tablets and thirty minutes disintegration time for coated tablets [20]. The results of disintegration test in this study (Table 2**)** were within the acceptable criteria of not more than 30 minutes, hence complied with the standard allowable limits. The Biopharmaceutical active ingredient in drug tend to be released more vigorously as the drug disintegrates. Disintegration is correlated with dissolution and bioavailability of active ingredient of the drug. Increase in rate of dissolution of any drug in tablet form, increases its oral absorption and consequently therapeutic efficiency. The capacity of tablets to endure handling without cracking or fragmenting is appropriately described as crushing strength or hardness. Hardness test is usually performed only on uncoated tablets. However, in case of coated tablet, the coating forms a protective shield which makes it difficult for the tablet to break into piece or chip away especially during usage or transportation. The results of the hardness test in this study (Table 3) complied with the specification of not less than 20 Newton [21]. The variation in hardness among brands of ciprofloxacin may be attributed to differences in manufacturer's formulation especially, methods of granulation, disparity in machine speed and the amount of lubricants added at the production stage [22-23]. Hardness can impact on the friability and disintegration rate of tablet form drugs. Consequently, increase in hardness of tablets, decreases the friability and the disintegration rate or time. The results of friability of the ten different brands of drug analysed (Table 4**)** varied markedly from one another, but were below 1%, indicating compliance to the compendia specification for friability of not more than 1%. The results for concentration of ciprofloxacin revealed a marked discrepancy in the composition of active pharmaceutical ingredients in the different brands of the analyte samples. The British Pharmacopeia stipulates that the composition of ciprofloxacin should not be lower than 95% and not higher than 105%

while the United State Pharmacopoeia recommended acceptable criteria that range from 90.0% - 110.0% for ciprofloxacin content. The assay results of ciprofloxacin samples ranged from 96. 8% - 106.1% with a relative standard deviation of 0.2%. Ciprofloxacin content in the drug formulation analysed were within the recommended specifications of 90.0% - 110.0% and within the maximum allowable standard deviation of 1.5% [21]. There was a marked differences in heavy metals concentrations among different brands of ciprofloxacin assessed (Table 6). The allowable limit for heavy metals concentration in ciprofloxacin sample is 20 ppm (European Pharmacopoeia).The concentrations of these heavy metals were within the permissible limits.

## 5.0 CONCLUSION

The physicochemical and trace metal analysis conducted on different brands of ciprofloxacin anti-biotic drugs conformed to the international standard as seen from the result of this study and are therefore fit to perform their therapeutic functions. It is therefore recommended that continues extensive monitoring of the drug industry should be paramount. Manufacturers and importers of drug products should be made to comply with all standard regulations.

**Acknowledgement**

The authors wishes to acknowledge the Mr. Ogbole Raymond Ojonye, Mr. Cyrus Ngemegwai and Mr. Kingsley Izuchukwu Chukwudi for their role in the laboratory works

**Conflict of Interest**

The authors declare no conflict of interest

**Contribution of the Authors**

Emeka C. Ogoko conceived and designed the study, supervised the laboratory works and prepared the manuscript. Henrietta I. Kelle co-supervised the laboratory works and reviewed the manuscript. Gana J. Babaman carried out the laboratory work.

## 6.0 REFERENCES

[1] World Health Organization. The international pharmacopoeia, World Health Organization (2006).
[2] Newton P, Green R, Fernandez M, Day N, White J. Counterfeit anti-infective drugs. *Lancet Infectious Diseases* 2006; 6: 602-613.
[3] Perur S. Fake drugs: The global industry putting your life at risk. Mosaic Newsletter 2018. Available from: https://mosaicscience,com/story/fake-drugs-global-antibiotics-amr-counterfeit-meds/
[4] Anah V U, Aniekan S E, Goodnews E C, Festus D E, Inimfon I U, Akanimo A E and Paschal C A. Quantitative and qualitative analysis of some brands of ciprofloxacin tablets sold in Uyo metropolis, Akwa Ibom State, Nigeria. *Nigerian Journal of Pharmaceutical and Applied Science Research* 2019; *8(3):15-22*
[5] US Food and Drug Administration, Center for Drug Evaluation and Research, Misplaced trust: Why FDA approval doesn't guarantee drug safety 2019. Available from: hhttp://www.drugwatch.com/featured/misplaced- trust-fda-approvalconcerns/
[6] Shah H. Generic captures new prescription markets. *Perspectives in Pharmacy Economics* 1994. 4: 3.
[7] Dahlgren D. Biopharmaceutical aspects of intestinal drug absorption. Regional permeability and absorption-modifying excipients. 2018 PhD Dissertation, Uppsal, Acta Universitatis.
[8] Khan AA . Decomposition and stabilization of pharmaceutical products. Slide share, 2018. Available from: https://www.slideshare.net/mobile/ArshadKhan63/decomposition-and-stabilization-of-pharmaceutical-products.
[9] Ejele A E, Ukiwe L N, Enenebeaku C K, Ejele N U. Evaluation of Drug Quality (III): Determination of Ciprofloxacin Hydrochloride Concentration in Pharmaceutical Tablets. *Nigerian Journal of Chemical Research* 2015; *20: 19-28.*
[10] Zhang G F, Liu X, Zhang S, Pan B, Liu M . Ciprofloxacin derivatives and their antibacterial activities. *European Journal of Medicinal Chemistry*, 2018; 146, 599-612.
[11] Plech T, Wujec M, Kosikowska U, Malm A, Rajtar B, Polz-Dacewicz M. Synthesis and in vitro activity of 1, 2, 4-triazole-ciprofloxacin hybrids against drug-susceptible and drug-resistant bacteria. *European journal of medicinal chemistry* 2013; 60: 128-13.
[12] Scales BS, Huffnagle G B. The microbiome in wound repair and tissue fibrosis. *The Journal of pathology*, 2013; *229*(2), 323-331.
[13] Adegbolagun OA, Olalade OA, Osumah SE. Comparative evaluation of biopharmaceutical and chemical equivalence of some commercially available brands of ciprofloxacin hydrochloride tablets. *Topical*

*Journal of Pharmaceutical Research*, 2007; 6(3): 737–745.
[14] Cazedey E C L, Salgado E R N. Spectrophotometric Determination of Ciprofloxacin Hydrochloride in Ophthalmic Solution. *Advances in Analytical Chemistry*. 2012; 2(6): 74–79.
[15] Qureshi HN, Rahman I, Marwat G. Comparative analysis of Ciprofloxacin in different Pharmaceutical products by High Performance Liquid Chromatograph. *Science, Technology and Development* 2012; 31(1): 69– 73.
[16] Nandipati S, Vanka KR, Uba S. The Separation and Quantitative determination of a ciprofloxacin in Pharmaceutical Formulation by Ultra Performance Liquid Chromatograph. *International Journal of Pharmacy and Pharmaceutical Sciences.* 2013; 5(3): 312–317.
[17] Ogoko E C and Ajani O S. Investigation on the quality of water from Jabi Lake in Abuja, Nigeria, *Journal of Chemical Society of Nigeria*, 2020; 45(5):881-889.
[18] Ogoko EC, Kelle H I and Njoku CP. Heavy metals contamination of solid waste disposal sites in Umuahia, Abia State. *Journal of chemical Society of Nigeria*, 2021; Vol. 46, No. 6, pp 0978- 0984.
[19] Osei-Yeboah F, Sun C, C. Validation and applications of an expedited tablet friability method. *International Journal of Pharmaceutics* 2015; 484(1-2): 146-155.
[20] British Pharmacopoeia Published by the Stationery Office Ltd (TSO) on behalf of the Medicines and Healthcare Products Regulatory Agency, Norwich, England, 2015.
[21] Pharmacopoeia, U. S. US Pharmacopoeia and National Formulary [USP39− NF34]. Rockville, Md: United States Pharmacopeial Convention, Inc., 2016.
[22] Birhanu G. Quality evaluation of the commonly prescribed antipsychotic drugs (chlorpromazine and thioridazine tablets) marketed in Ethiopia. *Int J. Pharm Sci Res*. 2014; 5(7):3031–3044.
[23] Okoye EI, Ndiwe I. Characterization of *Chrysophyllum albidum* and *Anacardium occidentale* gums as wet and dry binders in ciprofloxacin tablets. *Marmara Pharmaceutical Journal* 2016; 20: 122-130.