AN ASSESSMENT OF *IN-VITRO* QUALITY CONTROL OF DIFFERENT BRANDS OF CIPROFLOXACIN 500 MG TABLETS MARKETED IN ZARIA

[1*]Yunusa, I., [1]Mahdi, M.A., [2]Awwalu, S., [3]Aliyu, Y., [4]Mohammed, R.B., [3]Babawuro, A.A. and [1]Zezi, A.U.

[1] Department of Pharmacology and Therapeutics, Ahmadu Bello University, Zaria
[2] Department of Pharmaceutical and Medicinal Chemistry, Ahmadu Bello University, Zaria
[3] Department of Pharmaceutics and Industrial Pharmacy, Ahmadu Bello University, Zaria
4 Department of Pharmaceutical Microbiology, Ahmadu Bello University, Zaria

* *Corresponding author: ibryaes@gmail.com*, +2348061524258

ABSTRACT

Ciprofloxacin is a 4-fluoroquinolone antibiotic with a broader spectrum of action than nalidixic acid and more favourable pharmacokinetics, which allows its use in systemic infections. It is used to treat various infections. There are many different brands of Ciprofloxacin Hydrochloride (500 mg) tablets available in the Zaria metropolis and the quality of these brands is important for product usage. The present study aimed to evaluate the quality of five brands of ciprofloxacin hydrochloride tablets marketed in Zaria metropolis. Five brands of ciprofloxacin hydrochloride tablets (500 mg) were purchased from retail pharmacies. Each brand was assigned different codes, and its pharmaceutical quality was evaluated using official and unofficial in-vitro quality control tests, namely identification by Fourier Transform Infrared Spectroscopy, weight variation, friability, hardness, disintegration time, dissolution test and analysis by Ultraviolet spectrophotometric method to determine content. All brands evaluated passed the in-vitro quality control tests required for the tablets according to USP and BP standards. The results showed that the overall quality of all ciprofloxacin hydrochloride tablet brands tested was satisfactory as they met the requirements of official and unofficial quality control tests.

Keywords: Ciprofloxacin HCl, dissolution, disintegration, friability, hardness, quality control.

INTRODUCTION

Ciprofloxacin, a synthetic antibacterial agent derived from nalidixic acid, belongs to the fluoroquinolone class and features a fluorine atom located at the sixth position of the naphthyridine ring. Extensive structure-activity studies have been published, indicating that the presence of fluorine contributes significantly to the broad-spectrum antibacterial activity of this compound against a wide range of pathogens, including both gram-negative and gram-positive bacteria (Majalekar & Shirote, 2020). Accidentally discovered in 1962, ciprofloxacin has emerged as a pivotal component in the management of various infectious diseases, such as urinary tract infections, gastrointestinal and abdominal infections, and sexually transmitted infections, The efficacy of this medication renders it a valuable resource in the healthcare sector, particularly in the fight against bacterial infections that show resistance to alternative antibiotics (Murugaiyan *et al*., 2022).

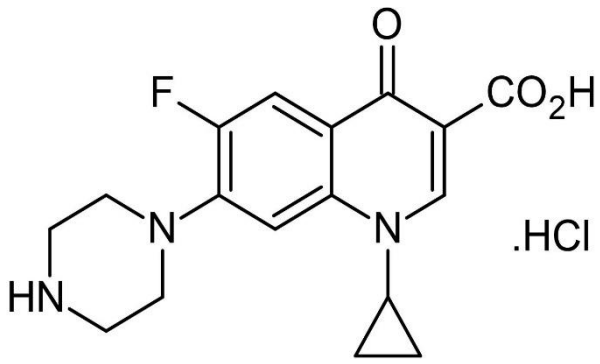

Figure 1: Chemical structure of ciprofloxacin hydrochloride

Quality control is a procedure or set of procedures intended to ensure that a manufactured product adheres to a defined set of quality criteria listed in the official monographs or meets the requirements specified by regulatory bodies such as the National Agency for Food and Drugs Administration and Control (NAFDAC) and World Health Organization (Derby, 2020). *In-vitro* quality control assessment of a tablet involves comprehensive evaluation which includes physical examination of the sample of tablet with the label information, identification test, uniformity of weight, disintegration and dissolution rates and assay (Muhammad *et al*., 2021). This is usually carried out by regulatory bodies, designated laboratories and those in academia. WHO (2010) reported that "substandard medicines are

pharmaceutical products that do not meet their quality standards and specifications. Each pharmaceutical product that a manufacturer produces has to comply with quality assurance standards and specifications, at release and throughout its shelf-life, according to the requirements of the territory of use. Normally, these standards and specifications are reviewed, assessed and approved by the applicable national or regional medicines regulatory authority before the product is authorized for marketing." There are many diverse brands of Ciprofloxacin Hydrochloride (500 mg) tablets readily available within the Zaria metropolis and the quality of these brands is imperative for product utilization. The present study aimed to carry out the *in-vitro* quality control evaluation of five brands of ciprofloxacin hydrochloride tablets marketed within the Zaria metropolis in Kaduna State, Nigeria.

MATERIALS AND METHODS

Drugs, Chemicals and Equipment

Ciprofloxacin hydrochloride standard powder (Sigma-Aldrich) and five different brands of ciprofloxacin tablets purchased from retail Pharmacy outlets in Zaria and coded, analytical grade methanol (BDH, Germany), distilled water (was obtained from Pharmaceutics Laboratory, Ahmadu Bello University, Zaria), Ultraviolet-visible spectrophotometer (SPS-100, Cambridge, England), Fourier transform infrared machine (Agilent, Germany), Friabilator (Erweka, TA3, Germany), Dissolution apparatus (Erweka, Germany), Disintegration apparatus (Erweka, Germany), Analytical balance (Mettler Gallenkamp), Melting point apparatus (Erweka, England), Manual tablet hardness tester (Vinsyst Technologies, India), Centrifuge (Mettler Gallenkamp, England), Refrigerator (Haier Thermocool, Nigeria), Vernier calliper, and Mortar and pestle.

In-vitro Quality Assessment Tests

Physical assessment of the ciprofloxacin tablet brands: The five (5) brands of ciprofloxacin (500 mg) tablet were examined for batch number, manufacturing date and expiry date. The physical assessment of the tablets from the various brands was carried out taking note of their colours, shapes, presence or absence of scoring. The diameter and thickness of the tablets from the various brands were also measured with the aid of a vernier calliper as described in BP 2013.

Identification test of the ciprofloxacin standard powder and the various brands of ciprofloxacin tablets

a. *Identification test of ciprofloxacin standard powder using FTIR*: A small quantity of the standard ciprofloxacin powder obtained was analyzed using Agilent Technology Cary 630 FTIR machine (USP, 2006) Identification of the ciprofloxacin powder was achieved by superimposing the FTIR spectrum obtained with a standard IR spectrum of ciprofloxacin.
b. *Identification test of the various brands of ciprofloxacin tablets*: One tablet from each brand of ciprofloxacin tablet was grinded and made into a solution with 20 mL methanol. The solution was shaken for 30 minutes, filtered and the filtrate was allowed to evaporate to dryness at room temperature for 48 hours (about 2 days). A small quantity of the dried filtrate for each brand of the ciprofloxacin tablet obtained was analyzed using Agilent Technology Cary 630 FTIR machine (USP, 2006). Identification of the ciprofloxacin powder was achieved by superimposing the FTIR spectrum obtained with a standard IR spectrum of ciprofloxacin.

Assay of the ciprofloxacin tablet brands using Ultraviolet-Visible Spectroscopy

Sample preparation and determination of wavelength of maximum absorption (λmax)

Ciprofloxacin stock solution (1 mg/mL) was prepared by dissolving standard ciprofloxacin powder (100 mg) in 20 mL of distilled water. The solution was then made up to 100 mL with distilled water. The solution, after ten-fold dilution, was scanned within 200 to 600 nm to obtain λ_{max}.

Construction of calibration curve

A calibration curve of ciprofloxacin in distilled water was constructed by preparing a series of working solutions within the concentrations range of 10 to 160 µg/mL from the stock solution. The absorbance was measured at the λ_{max} of the ciprofloxacin previously determined. The absorbance obtained was plotted against their corresponding concentrations. The calibration curve generated was used to determine the concentration of ciprofloxacin for both the assay and dissolution rate test.

Extraction and quantification

Ciprofloxacin tablets (20) were grinded into a fine powder and a portion of the powdered tablets equivalent to 100 mg of ciprofloxacin HCl was carefully weighed and transferred into a 100 mL volumetric flask and was extracted by addition of 10 mL of distilled water. The volumetric flask was shaken for a few minutes to enable the complete dissolution of the drug and the solution was made up to the volume with distilled water and filtered. The filtrate containing ciprofloxacin was analyzed by taking the absorbance at the obtained λ_{max}. The concentration of ciprofloxacin was extrapolated from the calibration curve generated above.

Weight variation: Uniformity of weight test for ciprofloxacin was conducted by weighing 20 tablets individually and the mean weight was determined. The percentage deviation of each of the tablets from the mean was determined.

Hardness test: A manual tablet hardness tester was used to carry out the crushing strength test of ciprofloxacin tablets of each brand (n = 6) as described in BP (2013).

Friability: The ciprofloxacin tablets (n = 10) from each brand were weighed and placed in a friabilator operated at 25 revolutions per minute. After four minutes (100 revolutions), the tablets were removed, dusted with tissue paper, weighed and the difference in the tablet's weight was determined. The percentage loss was calculated using the formula:

$$\text{Friability (\%)} = \frac{\text{Initial weight of ten tablets - Final weight of ten tablets}}{\text{The initial weight of ten tablets}} \times 100$$

Disintegration test: The disintegration test was carried out using the Erweka disintegration apparatus as described in BP, 2002. The medium employed for the disintegration test was 900 mL of distilled water at 37 ± 2°C. Ciprofloxacin tablets (n = 6) were selected from each brand and a tablet was placed in each of the six units of the disintegration apparatus. The disintegration apparatus was turned on and the time taken for the tablet fragment to completely pass through the mesh Erweka disintegration apparatus was taken with the aid of a stopwatch.

Dissolution test: The dissolution rate for ciprofloxacin tablets from each brand was determined using the Erweka dissolution apparatus. One tablet was placed into the rotating paddle, the apparatus was assembled and the medium (900 mL distilled water) was allowed

to equilibrate at 37°C. Thereafter, the apparatus was allowed to run at 50 rpm for 45 minutes and a sample of 5 ml was withdrawn from a zone midway between the surface of the dissolution medium and the top of the rotating paddle. The absorbance of ciprofloxacin from the solution was determined using an ultraviolet-visible spectrophotometer at λ_{max} determined against a blank (distilled water) after 100-fold dilution. The percentage release of ciprofloxacin at 45 minutes was determined for each brand at this wavelength using concentrations derived from the calibration curve constructed previously.

RESULTS AND DISCUSSIONS

Results

The label information and the physical appearance of the five brands of ciprofloxacin tablets revealed information as indicated in Tables 1 and 2.

Table 1: Label information of ciprofloxacin tablet brands

Code	Batch No.	NAFDAC No.	Manuf. Date	Expiry Date	Manufacturer
A	+	+	03/2021	02/2024	Imported
B	+	+	05/2021	04/2024	Imported
C	+	+	05/2022	04/2025	Indigenous
D	+	+	08/2021	07/2024	Imported
E	+	+	09/2022	08/2025	Indigenous

+ indicates presence while – indicates absence

Table 2: Physical characteristics of ciprofloxacin tablet brands

Code	Presence of score	Presence of logo	Mean Thickness (mm) ± STD	Mean Diameter (mm) ± STD
A	+	-	6.73 ± 0.04	9.56 ± 0.14
B	-	+	6.34 ± 0.09	8.26 ± 0.12
C	+	+	4.61 ± 0.11	9.24 ± 0.07
D	+	-	5.18 ± 0.03	8.40 ± 0.08
E	+	-	5.05 ± 0.02	9.4 ± 0.06

All the brands (A – E) were white, uncoated, and oblong with smooth surfaces. + indicates presence while – indicates absence

Results of Identification of ciprofloxacin standard powder and the five brands of ciprofloxacin tablet using FTIR

The superimposed FTIR spectra of ciprofloxacin standard powder and each of the five brands of ciprofloxacin against ciprofloxacin BP reference IR spectrum are presented in Figures 2-7.

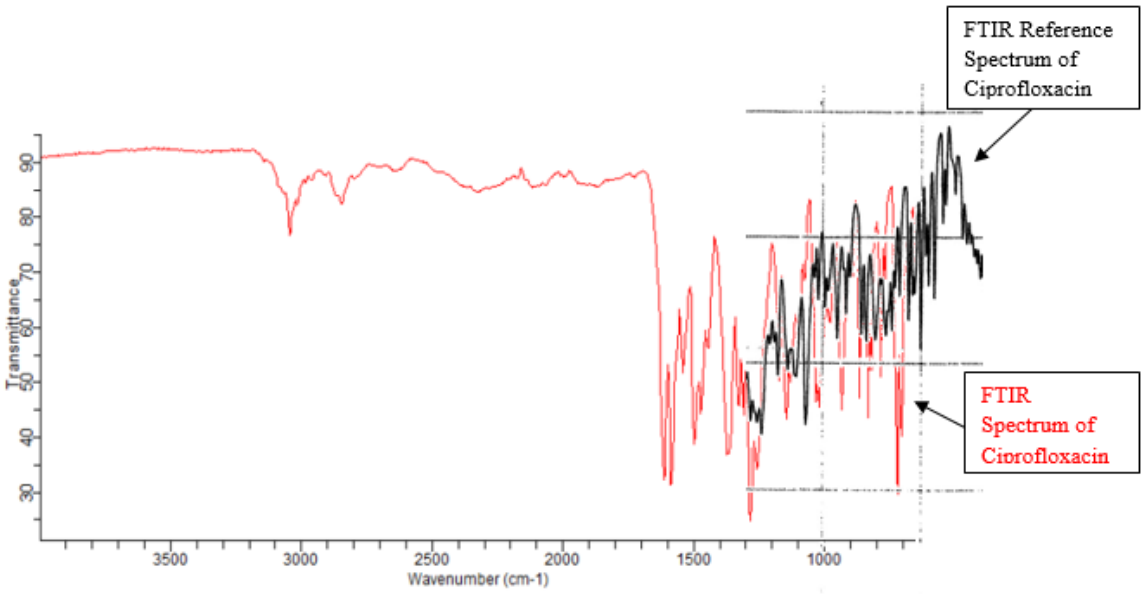

Figure 2: Superimposed FTIR spectra of ciprofloxacin standard powder against ciprofloxacin BP reference

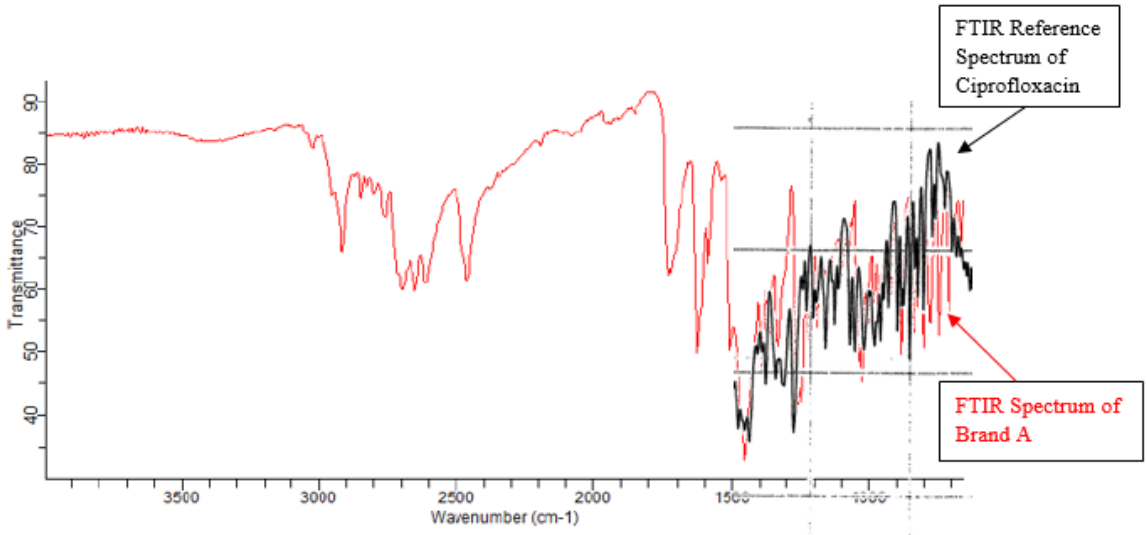

Figure 3: Superimposed FTIR spectra of brand A ciprofloxacin against ciprofloxacin BP reference

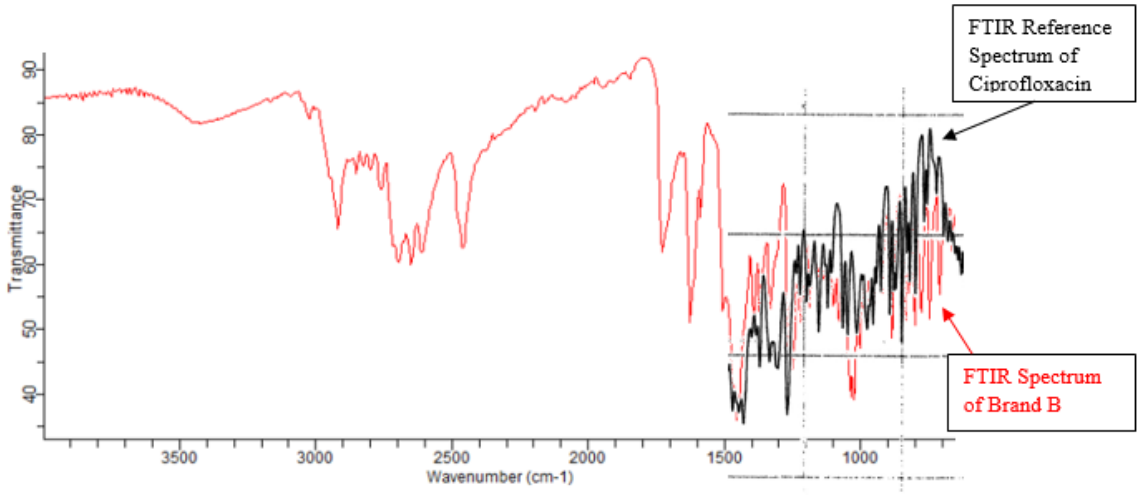

Figure 4: Superimposed FTIR spectra of brand B ciprofloxacin against ciprofloxacin BP reference

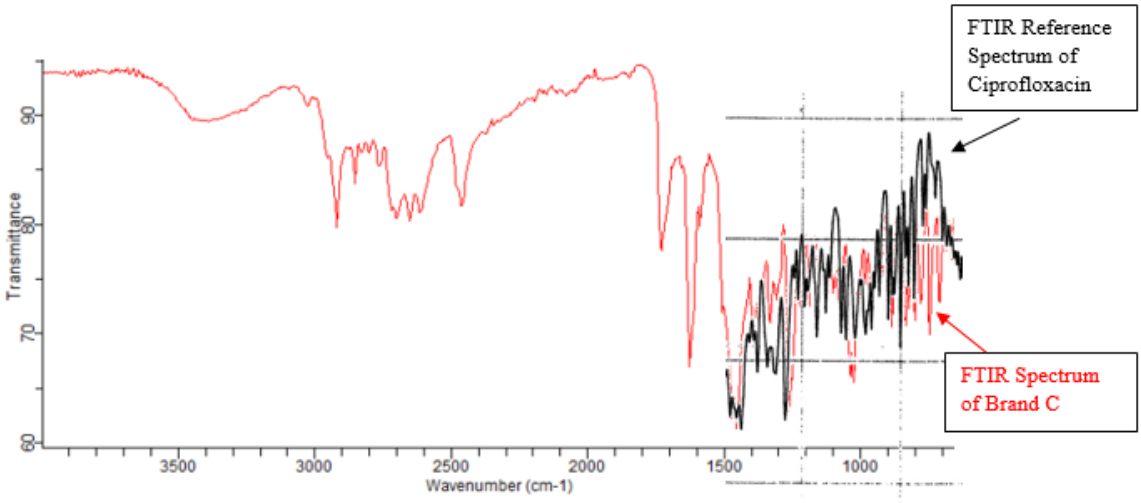

Figure 5: Superimposed FTIR spectra of brand C ciprofloxacin against ciprofloxacin BP reference

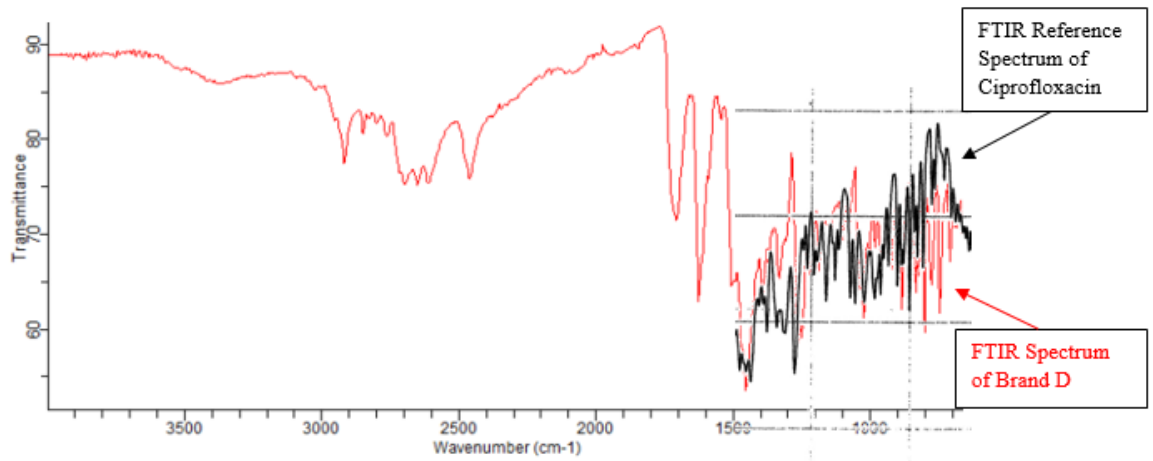

Figure 6: Superimposed FTIR spectra of brand D ciprofloxacin against ciprofloxacin BP reference

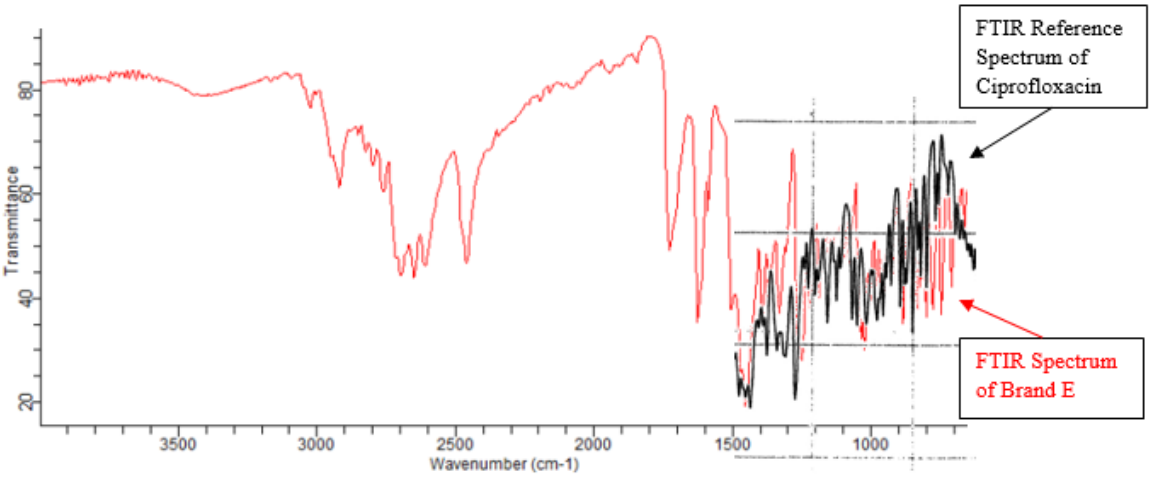

Figure 7: Superimposed FTIR spectra of brand E ciprofloxacin against ciprofloxacin BP reference

Assay, disintegration and dissolution rate for the different brands of ciprofloxacin tablets

The five-point calibration curve prepared within the range of 10 – 160 µg/mL of ciprofloxacin hydrochloride powder in distilled water is shown in Figure 8.

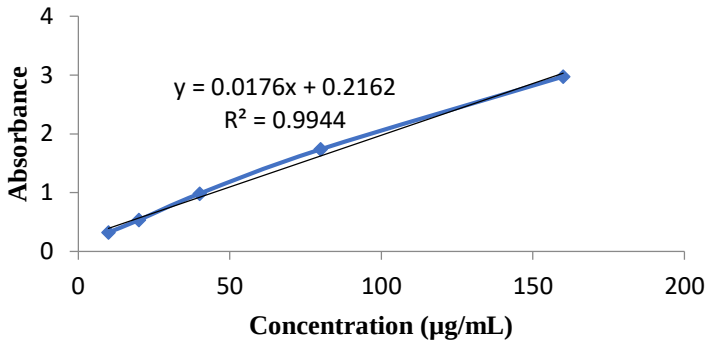

Figure 8: Calibration curve for ciprofloxacin hydrochloride in distilled water

The percentage content, mean disintegration time and the dissolution rate for each brand of ciprofloxacin tablet evaluated are shown in the Table 3.

Table 3: Assay, mean disintegration time and the dissolution rate of ciprofloxacin tablet brands

Code	Percentage Content (%)	Mean Disintegration Time (min) ± SD	Percentage Drug Release at 45 minutes (%)
A	96.36	0.25 ± 0.09	95.43
B	103.18	5.28 ± 0.77	98.64
C	97.50	2.48 ± 1.58	93.34
D	99.77	12.69 ± 1.53	91.61
E	98.64	14.20 ± 0.42	96.26

SD: standard deviation

Weight variation for the different brands of ciprofloxacin tablets

The results obtained for the weight variation determined for the five brands of the ciprofloxacin tablets are shown in Table 4.

Table 4: Weight variation for the five brands of ciprofloxacin tablets

Code	Mean weight (mg) ± SD	Range of % deviation	Number of tablets that deviate ± 5 % from mean weight
A	920.40 ± 9.00	0.28 – 1.59	None
B	1024.50 ± 8.73	0.34 – 1.31	None
C	746.50 ± 21.06	0.60 – 2.89	None
D	702.30 ± 3.40	0.19 – 1.10	None
E	727.30 ± 9.29	0.51 – 2.24	None

SD: standard deviation

Crushing Strength (Hardness) and percentage friability results for the different brands of ciprofloxacin tablets

The hardness and percentage friability evaluated for the five brands of the ciprofloxacin tablets are shown in Table 5.

Table 5: Mean crushing strength and percentage friability for the five brands of ciprofloxacin tablets

Code	Mean Crushing Strength (Kgf) ± SD	Percentage friability (%)
A	14.6 ± 0.548	0.03
B	14.4 ± 0.548	0.00
C	12.4 ± 0.548	0.00
D	12.6 ± 0.548	0.06
E	14.4 ± 0.548	0.00

SD: standard deviation

Discussion

The tablet samples examined were registered with the National Agency for Food and Drug Administration and Control, NAFDAC and have a reasonable shelf life as seen in Table 1. This is an indication that the drug products met NAFDAC requirements for pharmaceutical products in Nigeria. The brands of the tablet sample obtained were mostly imported as only 40 % of the brands were manufactured by indigenous pharmaceutical companies. The country of origin for all the tablet brands imported was India. Analysis carried out by the National Bureau of Statistics' foreign trade reports in 2022 revealed that the top 10 import trading partners were China, the Netherlands, India, Belgium, the United States, South Korea, the United Arab Emirates, the United Kingdom, Germany and Norway (NBS, 2023).

The tablet samples have an impressive appearance. The tablets were scored (Table 2) and the scoring permits accurate subdivision of the tablet to provide doses of less than one tablet and also facilitate breaking of the tablet for ease of swallowing a dose consisting of one or more whole tablets (Jacques & Alexandridis, 2019). The tablet thickness test for all five brands of tablet samples revealed that none of the tablets deviated from ±5 % from the mean thickness. The thickness of the tablet is the only dimensional variable which is related to the important process of tablet compression and should be controlled within ±5 % variation for patient adherence and acceptance as well as to make the tablet packaging easier in blister packs (Ahamad, 2023). The tablet samples have a mean diameter which is within the range specified by the United States Food and Drug Administration, USFDA and it recommends that the diameter of the tablet should be 8 mm or less than 8 mm and should not exceed 22 mm (about 0.87 in). The tablet samples were white, uncoated, and

oblong with a concave smooth surface. The diameter and oblong shape of the tablet influence esophageal transit, and techniques of administration (such as patient position, and use of fluids). It enables easy oesophagal transit when a patient is in an upright position and when taken with a fluid such as water.

The standard powder and the tablet samples of ciprofloxacin revealed the presence of the active ingredient using the method specified in the official monograph (BP 2013). The fingerprint region for standard powder and that of the different brands namely - A, B, C, D and E superimposed with that of the reference spectrum (Figure 2-7). This confirmed the presence of the ciprofloxacin active ingredient in the standard powder and the brands of tablets.

The calibration curve prepared for quantification of ciprofloxacin in distilled water (Figure 8) was found to be linear within the range of 10 – 160 µg/mL (R^2 = 0.9944) and the assay of all the brands of ciprofloxacin tablet (Table 3) showed that the percentage content is within the limit specified in the official book. The acceptable limit for the percentage content of ciprofloxacin tablet according to BP 2013 is 95 - 105% while USP and IP are 90 - 110%. The crushing strength of 4 kgf is usually considered to be the minimum force and 15 kgf is usually considered to be the maximum force for satisfactory tablets according to BP 2013. All the brands passed the test with a crushing strength greater than 4 kgf and less than 15 kgf (Table 5). The BP 2013 specification for uncoated tablets is that for tablets weighing more than 324 mg, not more than two of the individual weights should deviate from the average weight by more than 5%. The entire tablet brands passed the test as none of the tablets deviated from their average weight by 5% (Table 4). BP 2013 specification for friability is that a maximum weight loss of not more than 1% of the weight of the tablets

is considered generally acceptable. All the brands passed the test with a friability of less than 1% (Table 5). The disintegration time is the mean time needed for the tablets to break into particles, small enough to pass through the screen into the disintegration medium until no particle remains in the unit. The time limit for disintegration of uncoated tablets in water at 37°C should not exceed 15 minutes according to BP 2013. All the brands passed the test with a disintegration time of less than 15 minutes (Table 3). The percentage of drug release in distilled water at 45 minutes according to BP 2013 should be more than 80%. The tablet sample passed the test as more than 80% of the drug for each brand was released at 45 minutes (Table 3).

Anizor *et al,* 2023 conducted a similar study to assess the quality of eight brands of ciprofloxacin tablets marketed in Anambra State, South Eastern Nigeria and found that the brands of ciprofloxacin tablets met most of the criteria laid in the official monographs, though they differ slightly in terms of various parameters like weight variation, hardness, friability, disintegration and dissolution.

CONCLUSION

The study attempted to evaluate the *in-vitro* quality of ciprofloxacin tablets of five brands marketed in the Zaria and the evaluation showed that the ciprofloxacin tablet brands tested for identity, assay, weight variation, hardness, friability, disintegration and dissolution complied with the Pharmacopoeial specifications described in the BP and USP.

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