

Comparative Assessment of Ciprofloxacin Ophthalmic Solutions Marketed in Nigeria: Physicochemical and Microbiological Evaluation

Omotoso Abayomi Ebenezer^{1*}, Chinaka, Chioma Nnennaya¹ and Graham- Douglas Esther A¹

¹Department of Pharmaceutical and Medicinal Chemistry, University of Port-Harcourt, Port-Harcourt, Rivers State, Nigeria.

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*Corresponding Author:
Dr. Omotoso Abayomi Ebenezer
Email: abayomi.omotoso@uniport.edu.ng
Tel: +2348035662535

ABSTRACT

Background: Ciprofloxacin ophthalmic solutions are commonly used in the treatment of susceptible bacterial eye infections, so their quality must be reliable to ensure accurate dosing, acceptable ocular characteristics, and adequate antimicrobial performance. In Nigeria, comparing generic products with an innovator product is useful for medicine-quality monitoring and informed substitution. This study compared ten brands of ciprofloxacin eye drops available in Nigeria with an innovator product using physicochemical and microbiological tests.

Methods: Each sample was evaluated for appearance and clarity, volume, assay/content uniformity, viscosity, relative density, refractive index, surface tension, drop mass, drop volume, pH, electrical conductivity, and total dissolved solids. Antibacterial activity was determined against *Escherichia coli*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus* using susceptibility testing, minimum inhibitory concentration (MIC), and minimum bactericidal concentration (MBC) procedures.

Results: Most of the products satisfied the individual quality characteristics assessed. However, noticeable differences occurred in viscosity, electrical conductivity, and total dissolved solids. Ciprofloxacin content ranged from 97.14% to 102.90%, and every brand showed antibacterial activity against the organisms tested. When the physicochemical and microbiological findings were considered together, only one brand satisfied the operational criteria used in this study for pharmaceutical equivalence with the innovator product.

Conclusion: The results indicate that ophthalmic products carrying the same active ingredient and labelled strength can still differ in formulation-related characteristics. Continued post-marketing surveillance and assessment using several complementary quality parameters are therefore important for maintaining the quality of ophthalmic generics and supporting appropriate substitution decisions.

1. Introduction

Ophthalmic solutions are formulated specifically for application to the eye, making product quality an important consideration for safety, patient comfort, dosing accuracy, and overall performance. Because these preparations are administered directly to the ocular surface, they are expected to satisfy demanding quality requirements. Current regulatory guidance therefore places emphasis on factors such as microbiological quality, control of visible particles, container–closure integrity, stability, and relevant physicochemical properties.^{1,2} Parameters including pH, viscosity, surface tension, and related formulation

characteristics can affect how a drop is produced, spreads across the eye, remains on the ocular surface, and is tolerated by the patient.^{2,3,4}

In multidose ophthalmic preparations, the dispensing device is also an important part of dose delivery. The size and mass of a drop depend not only on the formulation but also on the construction and use of the dropper container. Previous comparisons of generic and branded ophthalmic products have reported differences in drop volume, dropper characteristics, pH, and viscosity, indicating that the formulation and delivery system should be considered together.^{5,6,7,8} Recent regulatory guidance similarly

identifies dispensing and delivery characteristics as relevant aspects of quality for topical ophthalmic products¹ Pharmaceutical equivalence is a key element of generic drug quality evaluation, although it is distinct from therapeutic equivalence and clinical interchangeability. For ophthalmic generics, contemporary regulatory thinking considers the qualitative and quantitative composition of a product alongside critical quality attributes and, where appropriate, evidence that the products perform comparably.^{4,9,10} Thus, physicochemical measurements and *in vitro* microbiological testing can provide useful evidence about pharmaceutical quality, but these laboratory findings alone cannot demonstrate equivalent clinical efficacy or interchangeability.

Ciprofloxacin belongs to the fluoroquinolone class of antibacterial medicines and is active against a range of susceptible Gram-negative and Gram-positive bacteria. Its principal antibacterial action involves inhibition of bacterial DNA gyrase and topoisomerase IV, thereby interfering with DNA replication and other essential cellular processes.¹¹ Ciprofloxacin ophthalmic formulations are used in the management of susceptible ocular infections, including conjunctivitis and other bacterial infections affecting the anterior eye. Consequently, assessment of antimicrobial activity provides useful additional information when marketed formulations are compared, although *in vitro* activity should not be taken as a replacement for clinical evidence of efficacy.

The Nigerian pharmaceutical market includes both innovator and generic medicines, which makes post marketing assessment of product quality particularly important. Studies conducted in Nigeria have reported instances in which medicines failed to meet pharmacopoeial requirements, and recent work on ciprofloxacin products purchased in Nigeria has also identified variation in drug content and antimicrobial performance.^{12,13,14,15} For ophthalmic preparations, such concerns are especially important because product quality and microbiological control have direct implications for patient safety. Against this background, the present investigation compared ten brands of ciprofloxacin ophthalmic solution marketed in Nigeria with an innovator product using a range of physicochemical measurements and *in vitro* antibacterial tests. The study was designed to determine whether the selected brands showed comparable characteristics according to the operational criteria adopted for pharmaceutical equivalence.

2. Materials and Methods

2.1 Materials

A ciprofloxacin hydrochloride USP reference standard was obtained from the National Agency for Food and Drug Administration and Control (NAFDAC). The other reagents and materials used were bromothymol blue, methyl red, Mueller Hinton agar, Mueller–Hinton broth, casein–soy agar broth, ferrous ammonium sulfate, sodium hydroxide, sulfuric acid, and hydrochloric acid. Double-distilled water was used for the procedures, and all reagents were of analytical grade.

2.2 Sample procurement and product identification

Ten (10) commercially available brands of ciprofloxacin eye drops were obtained from retail pharmacies located in Benin city (Edo state), Port Harcourt (Rivers state) and Uyo (Akwa-Ibom state) all in Nigeria. The study employed random sampling method in obtaining the samples. different Nigerian states and assigned the codes CA1–CA10. The primary and secondary packages were inspected for physical integrity and sealing, while information relating to labelled strength, manufacturing and expiry dates, batch number, manufacturer, country of origin, and NAFDAC registration was recorded. Ciloxan® (CA1), the innovator product, was used as the reference for the comparative evaluation.

2.3 Qualitative identification of fluoroquinolones

For the preliminary identification of fluoroquinolones, an aliquot of each ophthalmic preparation was mixed with 0.5 mL of 0.1% w/v ferrous ammonium sulfate prepared in sulfuric acid. Sodium bicarbonate was then added gradually until effervescence stopped. A yellow red colour was interpreted as a positive indication for a fluoroquinolone. A blank was run alongside the samples for comparison.¹⁶

2.4 Qualitative identification of ciprofloxacin

About 0.5 mL of 0.1 N hydrochloric acid was added to a portion of each sample and left for 2 min. The supernatant was subsequently removed and the remaining material was neutralized by adding 0.1 N sodium hydroxide dropwise until a precipitate formed. The precipitate was washed with distilled water, resuspended in 0.5 mL of water, and treated with 2–3 drops of bromothymol blue. The resulting colour of the supernatant was assessed after several minutes. Each determination was carried out in triplicate.¹⁷

2.5 Clarity

The samples were examined visually under suitable illumination against both black and white backgrounds.

Each container was gently swirled during inspection, and the samples were assessed for the presence or absence of visible particulate matter.^{3,12}

2.6 pH

The pH meter was first standardized using buffer solutions of pH 4.01 and 9.21 at 27 °C. Ten millilitres of each ophthalmic preparation were placed in a sterile 20 mL beaker, after which the electrode was immersed in the sample. The value was recorded once the reading had stabilized, approximately 20 s later. Measurements were made in triplicate¹⁸

2.7 Electrical conductivity and total dissolved solids

For electrical conductivity, the electrode of the PH/EC/TDS/temperature meter was rinsed with distilled water, dried, and placed into the sample. After the reading stabilized, the value was recorded. Total dissolved solids were measured using the same instrument with approximately 15 mL of sample. Each determination was performed three times.

2.8 Relative density

A clean pycnometer was oven-dried and weighed together with its stopper. It was then filled with distilled water and weighed again. After emptying and drying the pycnometer, it was filled with the test preparation and weighed. The relative density was calculated from the recorded weights using the procedure adopted for the study.

2.9 Refractive index

Refractive index was measured with an Abbe refractometer (model A 80251, BS). Before each determination, the prism was cleaned with methanol and dried. A thin layer of the sample was then placed on the prism, and the instrument was adjusted until a distinct light–dark boundary was obtained. The refractive-index value was recorded, with three measurements made for each sample.

2.10 Viscosity

The viscosity of each ophthalmic preparation was determined with a digital viscometer. Three measurements were obtained for every brand.

2.11 Surface tension

Surface tension was measured with a stalagmometer. Each sample was introduced into the capillary and allowed to produce drops under gravity. Approximately 30 drops were collected for the calculation, and the measurement was repeated in triplicate for each product.

2.12 Drop mass and drop number

For determination of the mass associated with a fixed volume, an automated micropipette was calibrated to 20 µL. A 20 µL portion of each sample was delivered into a glass beaker and weighed immediately on an analytical balance. Ten (10) measurements were recorded for each product. Drop mass was assessed by holding the bottle upright and then turning it approximately 90° from the horizontal. Gentle pressure was applied until a drop detached from the dropper tip, after which the pressure was released to allow the internal and atmospheric pressures to equalize. A 5 s interval was maintained between successive drops, and 30 drops were evaluated for each sample.

2.13 Volume uniformity

The contents of each ophthalmic product were transferred into an appropriate measuring cylinder, and the total volume was determined. The measurement was repeated three times for each brand.

2.14 Assay/content uniformity

A series of ciprofloxacin hydrochloride reference-standard dilutions covering 0.001–0.006 mg/mL was prepared as follows: In a 1 L volumetric flask containing about 500 ML of distilled water was added 10 mg of ciprofloxacin hydrochloride weighed with an analytical balance. The flask was shaken and made up to volume with distilled water. To prepared the different standard concentrations of Ciprofloxacin HCl (0.001, 0.002, 0.003, 0.004, 0.005, and 0.006 mg/mL) used for the calibration curve, 1, 2, 3, 4, 5, and 6 ML of the stock solution were made up to volume with distilled water in a 10 ML volumetric flask. Using water as the blank, absorbance was measured with a UV/visible spectrophotometer and a calibration plot of concentration against absorbance was constructed. The absorbance of each sample was then measured, and its concentration was estimated by interpolation from the calibration relationship.

2.15 Identification test

Benzalkonium HCl

The sample of the eye-drop was shaken gently and 2 ML of the eye-drop content was transferred into a dry and clean test tube. Thereafter 3 drops of 1% of Ferric chloride solution was added and the reaction mixture was gently mixed. The colour produced was observed. Development of a yellow/orange to reddish-brown colouration was taken as positive test.

Ciprofloxacin HCl

The eye-drop sample was gently shaken. About 1 mL of the

sample was transferred into a 100 mL volumetric flask and made to volume with distilled water. This was mixed thoroughly. The above procedure was repeated for the reference ciprofloxacin HCl sample. The solutions were separately scanned using a uv spectrophotometer, with distilled water as the blank from approximately 200 - 400 nm. The UV spectra of the two solutions were compared. The standard sample show wavelength of maximum absorption at 276 nm while the tested sample show 273 nm

2.16 Antibacterial susceptibility testing

Standardized suspensions of *Escherichia coli*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus* were spread onto Mueller–Hinton agar using sterile swabs. Wells were made in the agar and 0.1 mL of the relevant ophthalmic preparation was added to each well. The plates were allowed to stand for 15 min before incubation at 37 °C for 24 h. The diameter of each inhibition zone was measured in millimetres. All tests were carried out in triplicate.

2.17 Minimum inhibitory concentration

Approximately 3 mL of Mueller–Hinton broth was dispensed into test tubes and sterilized by autoclaving at 121 °C for 15 min. Once cooled to 40–45 °C, 0.1 mL of the test microorganism was inoculated into the broth. The MIC was taken as the lowest concentration of the preparation that prevented visible growth, following the procedure used in the study.

2.18 Minimum bactericidal concentration

The tubes from the MIC experiment in which no visible growth occurred were inoculated again with 0.1 mL of the corresponding microorganism and incubated for 20 h. The cultures were subsequently examined for growth, and the lowest concentration that demonstrated bactericidal activity was recorded as the MBC.

2.19 Statistical Analysis

Data were expressed as mean $\pm$ standard deviation (SD). SPSS Version 25 was used. Differences among the generic brands and the innovator product (CA1) were analyzed using one-way ANOVA, A p-value of < 0.05 was considered statistically significant.

All sampling were done before their expiry date. Sample sizes (n) for individual assays were selected in accordance with standard pharmacopoeial quality control guidelines and analytical testing protocols. High precision instrumental determinations (e.g. assay, pH, viscosity,

electrical conductivity, refractive index, and microbiological assays) were performed in triplicate with (n=3). Gravimetric assessment of small fixed volumes (20 μ L) was conducted with n =10 to evaluate delivery repeatability. For dynamic drop dispensing characteristics (drop mass and drop counts per volume), larger sample sizes (n $\geq$ 30) were evaluated to account for physical variations in container-closure mechanics and drop-formation dynamics.

RESULTS

Description of the eye drops.

All ten products were supplied in polyethylene containers fitted with dropper closures, and the seals were intact at the time of examination. Key package information, including manufacturing and expiry dates, NAFDAC registration numbers, batch numbers, and countries of origin, was clearly displayed (Table 1). The products had an average stated shelf life of two years, and all analyses were completed before expiry. The available product volumes were approximately 5.0–10.0 mL, and colour, clarity, and assay results were recorded. Every sample contained ciprofloxacin hydrochloride at the stated concentration of 0.35%, while benzalkonium chloride was identified as the preservative, with the amount varying between manufacturers.

Table 1. Some relevant information on the package of the different brands of ciprofloxacin eye drops and some tests on sample

Sample No	Brand Name	Country of Origin	Batch Number	NAFDAC Registration Number	MFD-EXP	Label Volume (ml)	Volume Uniformity (ml)	Assay (%)	Color and clarity
CA1	Ciloxan®	Belgium	20D22GC	04-6343	04/20-03/22	5	4.92 ± 0.00	100.00	Colorless and clear
CA2	Bactaforte®	India	VE9088	B4-0564	12/19-11/22	10	9.80 ± 0.17	102.90	Colorless and clear
CA3	Biosphere Ciprofloxacin®	India	DEA01030	A4-9808	01/20-12/21	10	10.00 ± 0.25	97.14	Colorless and clear
CA4	Ciflaxin®	Nigeria	75E0123	04-8090	05/20-04/23	5	4.60 ± 0.28	100.00	Colorless and clear
CA5	Ciprocet®	India	9EB11153	A4-0290	04/19-03/22	5	4.70 ± 0.19	97.14	Colorless and clear
CA6	Cipro-J®	Nigeria	56HL04	A4-5216	12/18-11/21	10	9.87 ± 0.09	97.14	Colorless and clear
CA7	Ciprotic®	India	X00B005	B4-6929	02/20-01/23	10	10.40 ± 0.11	97.14	Colorless and clear
CA8	Ivyzoxan®	Kenya	03106	04-5049	08/20-17/22	5	5.07 ± 0.09	97.14	Colorless and clear
CA9	La-Lid Ciprofloxacin®	India	VE-1722	B4-5202	01/19-12/21	10	10.07 ± 0.08	97.14	Colorless and clear
CA10	Ncipro®	India	70137	B4-6855	10/18-09/21	10	10.00 ± 0.00	97.14	Colorless and clear

Manufacturing (MFD) and Expiry (EXP) Dates are expressed as month/year

Physicochemical characteristics of the ophthalmic preparations

The measured physicochemical properties of CA1–CA10 are summarized in Table 2. The parameters assessed included viscosity, relative density, refractive index, surface tension, drop mass, number of drops per millilitre, pH, electrical conductivity, and total dissolved solids.

Table 2: Physicochemical Parameters of sample CA1 to Sample Ca10

Sample code	Viscosity (cps) [n=3]	Relative density (g/ml) [n=3]	Refractive index [n=3]	Surface tension × 10 ² (l/m ²)	Weight of 20 µl of sample (mg)[n=10]	Weight of a drop of sample (mg) [n =32]	Number of Drops per ml	pH [n = 3]	Electrical conductivity 10 ³ (msec./cm) [n = 3]	Total Dissolved Solids × 10 (ppm)[n=3]
CA1	1.0 ± 0	1.012 ± 0.001	1.3405 ± 0.007	4.03	45 ± 2.000	29 ± 0.002	32	4.45 ± 0.00	1.07 ± 0.21	0.54 ± 0.6
CA2	1.0 ± 0	1.004 ± 0.001	1.3350 ± 0.000	3.58	48 ± 0.003	30 ± 0.002	34	4.59 ± 0.02	20.20 ± 0.70	7.15 ± 0.5
CA3	3.0 ± 0	1.007 ± 0.001	1.3355 ± 0.000	4.89	49 ± 0.001	33 ± 0.001	28	4.85 ± 0.05	23.08 ± 0.96	11.57 ± 0.4
CA4	3.0 ± 0	1.004 ± 0.001	1.3340 ± 0.000	4.00	50 ± 0.002	30 ± 0.001	31	4.85 ± 0.07	10.73 ± 0.98	5.38 ± 0.4
CA5	1.0 ± 0	1.008 ± 0.002	1.3350 ± 0.000	5.19	49 ± 0.009	23 ± 0.002	32	4.73 ± 0.04	27.00 ± 1.05	13.58 ± 0.4
CA6	4.0 ± 0	1.003 ± 0.004	1.3355 ± 0.001	5.19	48 ± 0.002	31 ± 0.003	31	4.80 ± 0.02	20.05 ± 0.58	10.17 ± 0.2
CA7	2.0 ± 0	1.002 ± 0.006	1.3363 ± 0.000	4.77	50 ± 0.002	33 ± 0.004	31	4.77 ± 0.02	23.82 ± 0.31	11.90 ± 0.1
CA8	3.0 ± 0	1.010 ± 0.002	1.3365 ± 0.000	4.23	48 ± 0.001	32 ± 0.001	29	4.80 ± 0.01	23.68 ± 0.37	11.93 ± 0.1
CA9	1.0 ± 0	1.009 ± 0.006	1.3365 ± 0.000	3.94	50 ± 0.001	29 ± 0.005	32	4.62 ± 0.04	25.07 ± 0.28	12.58 ± 0.1
CA10	2.0 ± 0	1.003 ± 0.100	1.3363 ± 0.000	5.31	49 ± 0.049	35 ± 0.002	27	3.99 ± 0.01	0.98 ± 0.01	0.49 ± 0.0

The microbial Susceptibility Test for samples

Antibacterial susceptibility of the samples

Table 3: Microbial Susceptibility Test for Samples

Sample	Microbial Susceptibility Test Zone of Inhibition (mm)		
	<i>E. coli</i>	<i>P. aeruginosa</i>	<i>Staph. aerus</i>
CA1	26.0 ± 0.0	45.5 ± 0.7	38.0 ± 0.0
CA2	23.0 ± 0.0	41.0 ± 0.0	39.5 ± 0.7
CA3	24.0 ± 1.4	43.0 ± 1.4	37.0 ± 0.0
CA4	22.5 ± 0.7	43.0 ± 1.4	42.0 ± 0.0
CA5	26.0 ± 0.0	43.5 ± 0.7	42.0 ± 0.0
CA6	22.5 ± 0.7	43.5 ± 0.7	41.0 ± 1.4
CA7	24.5 ± 0.7	42.0 ± 0.0	38.0 ± 0.0
CA8	24.5 ± 0.7	41.5 ± 0.7	47.0 ± 4.2
CA9	25.5 ± 0.7	48.0 ± 1.4	39.5 ± 3.5
CA10	23.0 ± 0.0	44.5 ± 0.7	45.0 ± 7.1

The in vitro antibacterial activity of the ophthalmic preparations was evaluated against the selected microorganisms using the susceptibility test, and the resulting inhibition zones are presented in Table 3.

MIC and MBC findings for the samples

MIC represents the lowest tested concentration capable of preventing visible microbial growth, whereas MBC represents the lowest concentration that produces a bactericidal effect. The values obtained for the different products are presented in Table 4.

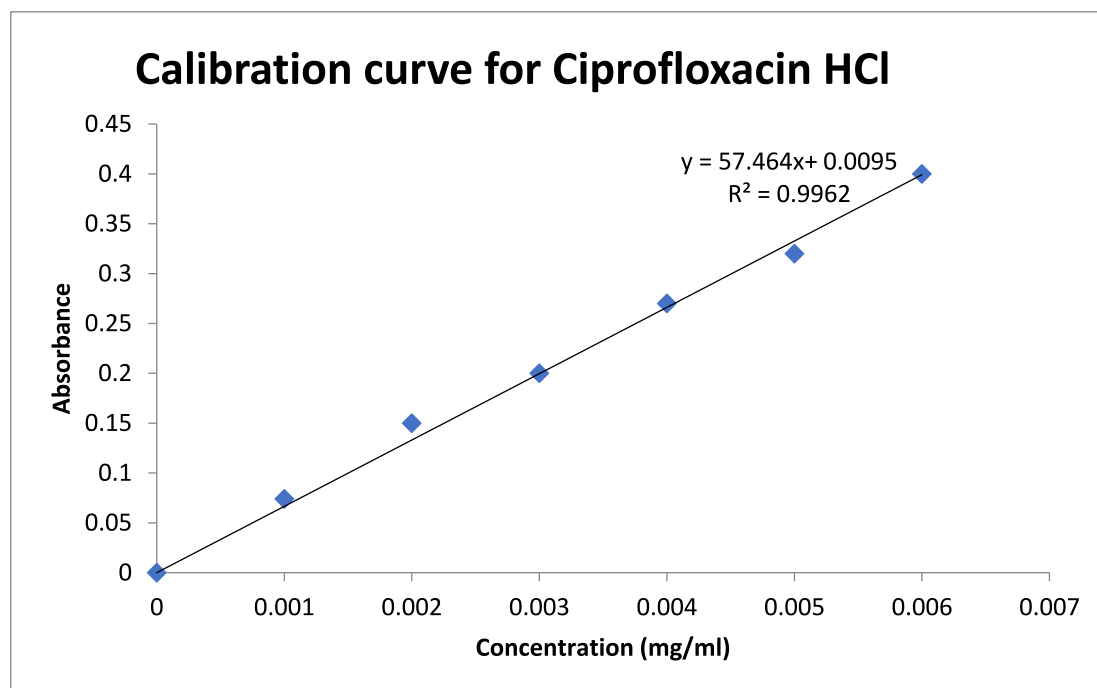
Table 4: Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC) for the Samples

Sample	Minimum Inhibitory Concentration (MIC)			Minimum Bactericidal Concentration (MBC)		
	<i>E. coli</i>	<i>P. aeruginosa</i>	<i>Staph. aerus</i>	<i>E. coli</i>	<i>P. aeruginosa</i>	<i>Staph. aerus</i>
CA1	0.075	0.075	0.075	0.3	0.15	0.15
CA2	0.150	0.075	0.075	0.3	0.15	0.15
CA3	0.150	0.075	0.075	-	0.15	0.15
CA4	0.075	0.075	0.075	-	0.15	0.15
CA5	0.075	0.075	0.075	-	0.15	0.15
CA6	0.150	0.075	0.075	-	0.15	0.15
CA7	0.075	0.075	0.075	-	0.15	0.15
CA8	0.075	0.075	0.075	-	0.15	0.15
CA9	0.1 50	0.075	0.075	-	0.15	0.15
CA10	0.150	0.075	0.075	-	0.15	0.15

- = no bactericidal endpoint was reached at the concentrations tested.

Calibration curve

The calibration analysis produced a regression equation of $57.46x + 0.0095$, with a correlation coefficient (R^2) of 0.9962.



3. Discussion

This investigation compared ten marketed brands of ciprofloxacin ophthalmic solution with the innovator product, Ciloxan® (CA1), using several physicochemical and microbiological measures rather than relying on drug content alone. Such a broad approach is useful because products carrying the same active ingredient and labelled strength may still differ in formulation composition and dispensing behaviour. Current approaches to the assessment of ophthalmic generics recognize the importance of multiple critical quality attributes, including physicochemical characteristics and the performance of the dispensing system.^{1,4}

Inspection of the packaging showed that all products were supplied in polyethylene containers with dropper closures and intact seals, and the main identifying information was present on the packages. The lack of visible particulate matter in the samples is relevant because particulate contamination is an important concern for preparations administered directly to the eye. Container-closure characteristics are also important because they contribute to product integrity and dose delivery.^{1,2} The more complete formulation information provided for the innovator product further highlights the usefulness of clear excipient labelling, particularly for multidose ophthalmic

preparations. Benzalkonium chloride was reported as the preservative across the products, although its concentration differed between manufacturers. Preservatives can help maintain microbiological quality in multidose ophthalmic products, but repeated exposure to benzalkonium chloride has also been linked with ocular-surface toxicity and disease, especially when exposure is prolonged.^{19,20,21} Since preservative concentrations were not directly measured and ocular-surface tolerability was not assessed in this study, these observations should be viewed as formulation information rather than evidence that one product is clinically safer than another. The refractive-index measurements were closely grouped across the brands and were also near the reported value for human tears. Refractive index is useful as a physicochemical descriptor during formulation characterization, but it should not be treated on its own as a measure of ocular compatibility or therapeutic equivalence.^{2,4} The relatively small variation observed therefore supports similarity for this particular attribute, while the broader product-quality judgement must take the other measured characteristics into account. The pH values of the products were acidic, and the study did not identify a statistically significant difference ($p < 0.05$) between the brands and the innovator. pH is important in ophthalmic formulation because it can affect drug

ionization, solubility, chemical stability, ocular comfort, and reflex tearing.² For ciprofloxacin preparations, pH-dependent ionization can influence formulation behaviour; consequently, pH is best interpreted alongside concentration, buffering capacity, tonicity or osmolality, and other formulation variables rather than in isolation. Ciprofloxacin content ranged from 97.14% to 102.90%, indicating that the labelled drug strength was generally maintained in the products examined. Nevertheless, comparable assay values do not by themselves demonstrate pharmaceutical equivalence. Products with similar active-ingredient content can still differ in excipients, viscosity, preservative levels, dispensing characteristics, or other critical attributes.^{1,4} The multidimensional approach used in this work therefore provides a broader basis for comparison. It is also important to distinguish the analytical procedure used here from a fully validated regulatory assay, since ICH Q2(R2) emphasizes demonstrating that an analytical procedure is fit for its intended purpose through appropriate validation characteristics.^{2,2} Drop behaviour is particularly relevant for ophthalmic preparations because the eye can retain only a limited amount of instilled liquid. In this study, neither the number of drops obtained per millilitre nor individual drop mass differed significantly from the innovator product. Earlier studies have shown that generic and branded eye drops may vary in drop size and dispensing performance,^{5,7,8} while USP guidance also identifies drop size and container-closure performance as relevant quality considerations.² The similarity observed here therefore supports comparable dispensing behaviour for the specific measurements performed, but it does not establish that the products will dispense identically under every condition of patient use. Surface tension and relative density are among the formulation properties that influence the formation of an ophthalmic drop. The surface-tension measurements were broadly similar to those of the innovator, and relative density showed only limited variation among the samples. These results suggest that the brands were generally comparable with respect to properties involved in drop formation. Although the mass of a fixed 20 µL volume varied between products, the study did not find this difference to be statistically significant ($p < 0.05$). Measuring both fixed-volume mass and the mass of an actual dispensed drop remains useful because formulation composition can influence density and, in turn, dosing behaviour. Previous work on generic ophthalmic products has likewise shown that formulation and container characteristics can interact to affect the delivered dose.^{7,8} Viscosity showed clearer differences between the brands. This parameter can affect the residence time of an

ophthalmic preparation, its spreading behaviour, the formation of drops, and its interaction with blinking. Contemporary ophthalmic research therefore regards viscosity as an important quality attribute that may work together with other formulation properties to influence product performance.^{2,4} The differences observed here are potentially relevant even though all products carried the same labelled ciprofloxacin concentration. However, because the measurements were performed in vitro, they cannot be used to directly predict differences in clinical ocular residence or tolerability.

Electrical conductivity and total dissolved solids also varied among the formulations. These measurements give indirect information about the ionic and dissolved components present in an aqueous preparation, but they are not established stand-alone indicators of pharmaceutical equivalence, efficacy, or safety. Differences could reflect variation in salts, buffers, preservatives, or other excipients. They are therefore more appropriately regarded as supporting physicochemical descriptors within the overall assessment rather than independent measures of product quality.^{1,2} Each of the ten products produced antibacterial activity against *E. coli*, *P. aeruginosa*, and *S. aureus*, although the inhibition zones and MIC/MBC patterns were not identical. The MBC values were obtained only for samples CA1 and CA2 which mean no bactericidal endpoint was reached at the concentrations tested for the other samples. The activity observed is compatible with the known antibacterial spectrum of ciprofloxacin against susceptible bacteria.¹¹ The lack of a statistically significant difference ($p < 0.05$) in susceptibility in the study indicates that the tested formulations retained measurable activity under the laboratory conditions used. Nevertheless, agar-diffusion results and MIC/MBC values are in vitro endpoints and cannot, on their own, establish equivalent clinical efficacy or therapeutic equivalence. When the physicochemical and microbiological findings are considered together, the products generally satisfied a number of individual quality requirements, but they were not consistently similar across all measured attributes. The finding that only one brand met the operational criteria for pharmaceutical equivalence with the innovator is therefore meaningful from a post-marketing quality-control perspective. It should not, however, be interpreted as proof of therapeutic equivalence or clinical interchangeability. Current regulatory approaches to ophthalmic generics emphasize assessment of product-specific critical quality attributes and, where necessary, additional evidence of comparable performance before equivalence or substitution claims are made.^{1,4} Several limitations should be acknowledged. Only ten

marketed brands were included, so the sample may not capture the full range of ciprofloxacin ophthalmic products available in Nigeria. The study was also laboratory-based and did not include sterility testing, direct preservative assay, validated container–closure integrity testing, stability studies, detailed characterization of excipients, or assessment of clinical tolerability. In addition, the study did not provide a detailed statistical-analysis section describing all statistical tests and assumptions used for comparisons between products. These limitations are important because sterility is a fundamental quality attribute for ophthalmic preparations, while regulatory guidance also emphasizes microbiological control, stability, container–closure performance, and dispensing characteristics.^{1,2} Future investigations should address these areas, particularly where the intended outcome is to inform regulatory substitution or interchangeability decisions.

4. Conclusion

The comparison of ten ciprofloxacin ophthalmic preparations marketed in Nigeria showed that most products met several of the individual quality characteristics examined, including acceptable labelled drug content and measurable in vitro antibacterial activity. At the same time, differences were detected in a number of physicochemical properties. When the complete set of findings was considered using the study's stated criteria, only one product was classified as pharmaceutically equivalent to the innovator. These findings illustrate why quality assessment of ophthalmic generics should extend beyond assay results alone and should continue as part of post-marketing surveillance, particularly in view of reports describing variability in the quality of medicines marketed in Nigeria.^{14,15} The results should nevertheless be understood as evidence of pharmaceutical-quality comparability rather than confirmation of therapeutic equivalence or clinical interchangeability. Future studies incorporating validated analytical methods, direct evaluation of preservatives and excipients, sterility assurance, container–closure testing, stability assessment, and appropriately designed comparative-equivalence studies would provide stronger evidence to guide substitution decisions.^{4,22}

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