

## Comparative Evaluation of Some Moxifloxacin Hydrochloride Tablet Brands Marketed in Nigeria Using Five Different Validated Analytical Methods

E. A. OMOTOSO <sup>\*A-F</sup>, E. B. UNAJI <sup>B-D,F</sup>

Department of Pharmaceutical and Medicinal Chemistry, Faculty of Pharmaceutical Sciences,  
University of Port Harcourt, Port Harcourt 500004, Nigeria.

A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of article.

### Abstract

**Background:** Assay of pharmaceuticals is an important aspect of quality control. It is necessary to compare the bioequivalence of generic brands of the any drug to an innovator/comparator brand as this forms the basis for comparing their therapeutic equivalence.

**Objective:** This study aimed to determine the most accurate method for the assay of moxifloxacin hydrochloride (MOX-HCl) tablet brands in Nigerian markets by using five different validated analytical methods and also verify their interchangeability.

**Material & Methods:** This study involved three brands of MOX-HCl including the comparator brand, Moxiget®. The study involves both quality control tests including: weight uniformity, diameter, thickness, friability, hardness, disintegration, dissolution and content of active ingredient (assay) methods including: phosphate buffered UV-Vis spectrophotometric, UV spectrophotometric, kinetic spectrophotometric, colorimetry and utilization of oxidation-reduction reaction methods.

**Results:** All the samples used for this study passed the quality control tests and thus were of standard quality and therefore pharmaceutically equivalent.

**Conclusion:** This study therefore conclude that phosphate buffered UV-Vis spectrophotometry provide the most accurate method to assay Moxifloxacin tablet, colorimetry assay method can serve as a substitute to the preferred method for the moxifloxacin assay and the three samples assayed in this work are interchangeable with the comparator brand (Moxiget®).

**Keywords:** Moxifloxacin HCl, UV-Vis spectrophotometry, Moxiget®, Quality control, Interchangeable analytical methods

### INTRODUCTION

All drugs marketed in Nigeria require registration with the National Agency for Food and Drugs Administration and Control (NAFDAC). An essential aspect of the registration process is the drug content uniformity evaluation. However, research evidence (Garuba, 2009) has shown that not only are unregistered medicines marketed in Nigeria, but randomly selected registered medicines do not always

meet the standard requirements. (Ndichu *et al.*, 2019). To the best of our knowledge, there is no known work on the quality control of brands of moxifloxacin marketed in Nigeria. Moxifloxacin being a fairly new medicine in the market, thus, the need to ascertain its quality. Moxifloxacin, an advanced new synthetic fluoroquinolone antibiotic with expanded spectrum of action, slightly yellow crystalline powder with the

molecular formula of  $C_{21}H_{24}FN_3O_4$  (401.43 g/mol), is chemically known as: 1-Cyclopropyl-6-fluoro-1, 4-dihydro-8-methoxy-7[(4aS,7aS)-octahydro-6H-pyrrolo [3, 4-b] pyridin-6yl]-4-oxo-3-quinolinecarboxylic acid monohydrochloride or 1-cyclopropyl-7- [(S, S)-2,8-diazabicyclo [4.3.0] non-8-yl] -6-fluoro-8methoxy-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid hydrochloride. It has activity against both *mycobacterium* gram negative, and gram-positive bacteria pathogens. The bactericidal activity of the drug is mediated by the inhibition of DNA gyrase (topoisomerase II) and topoisomerase IV.

Drug evaluation is important to determine chemical variation in medicines, identify deterioration due to treatment and storage, report substitution and adulteration as a result of carelessness, ignorance and fraud, check and ensure accuracy of identity, purity and quality of drug. Quality assurance covers all matters that influence the quality of product. It is the totality of the arrangements made with the object of ensuring that pharmaceutical products are of the quality required for their intended use (WHO 2007). Quality control include all measures taken such as setting specification, sampling, testing and analytical clearance, to ensure that products conform to established specifications for identity, strength, purity and other characteristics. (Raza *et al.*, 2014) To assess the quality of tablet dosage form, the tablets must meet the physical specifications and quality standards such as criteria for weight, weight variation, content uniformity, thickness, hardness, disintegration, and dissolution. The tests for quality are either Pharmacopoeia/Official tests such as content of active ingredient, uniformity of weight, uniformity of content, disintegration time and dissolution test or Non-Pharmacopoeia/ Non-official tests such as tablet porosity, tablet hardness, friability and thickness test. As early as 2009, a series of work has been carried out on moxifloxacin hydrochloride and most of them are based on development and validation of different analytical approaches to assay moxifloxacin in body fluids, bulk and pharmaceutical dosage forms. Desai *et al.*, (2015a) developed and validated a method for the simultaneous estimation of moxifloxacin hydrochloride (MOX) and bromfenac sodium (BROM) by RP-HPLC. The described method showed good linearity simple, rapid, precise and accurate, which is useful for the routine determination of studied drugs in bulk and in pharmaceutical dosage form. The same set of researchers in 2015b, Desai *et al.*, developed and validated a UV-spectroscopic method for simultaneous estimation of moxifloxacin HCl (MOX) and bromfenac sodium in combined dosage form. The method was developed using two wavelengths (275 nm: isosbestic point and 291 nm:  $\lambda_{max}$  of MOX). In 2015, Kalpana *et al.*, worked on

simultaneous estimation of moxifloxacin HCl and difluprednate in ophthalmic formulation by three spectrophotometric methods. Method 1 is the simultaneous estimation method, method 2 is the second order derivative method and method 3 is the ratio of second derivative method. Patel *et al.*, (2015) worked on simultaneous chromatographic determination of moxifloxacin HCl and difluprednate in eye drops using the developed and validated RP-HPLC and HP-TLC methods according to (ICH) guidelines. Rizk *et al.* (2015) developed and validated a simple isocratic RP-HPLC method with UV detection for the determination of moxifloxacin in human plasma using gatifloxacin as an internal standard. In 2016, Ashour *et al.*, validated a very rapid method for the quality control of moxifloxacin in bulk drug and tablets using rosuvastatin calcium as an internal standard with the instrumentation involving RP-HPLC. The precision was demonstrated by intra- and inter-day assay RSD% values which were less than 2%, while the recovery was 99.11–103.85%. In 2017, Akula *et al.*, developed and validated an RP-HPLC method for simultaneous estimation of moxifloxacin HCL and ketoprofen in bulk form in accordance with ICH guidelines. The response of the method was a linear function of concentrations over an established the range for the studied drugs. The developed method was successfully applied to quantitative determination of Moxifloxacin hydrochloride and Ketoprofen in pharmaceutical bulk formulation. So also in 2017, Alam *et al.* work on Flow Injection method for the determination of Moxifloxacin using silver nanoparticle - Tris (2,2-Bipyridyl)Ruthenium(III)-Ce(IV) Chemiluminescence Detection. The study concluded that utilization of silver nanoparticle enhanced effect of the weak chemiluminescence intensity of  $Ru(bipy)_3^{2+}$ -Ce(IV) system, though there was no significant interference from foreign species. The method has been applied for evaluation of moxifloxacin in commercial tablet and human urine. Patel *et al.*, (2017) worked on simultaneous spectrophotometric determination of moxifloxacin and prednisolone acetate in pharmaceutical preparation using the Q-Absorbance ratio method. In 2019, Attimard *et al.*, worked on simultaneous determination of moxifloxacin (MOX) and flavoxate (FLX) by RP-HPLC, first derivative and ratio first derivative spectrophotometric methods using valsartan as an internal standard. In 2019, Sankar *et al.*, developed and validated a HPLC stability-indicating method for the assay of moxifloxacin in oral pharmaceutical dosage forms. In 2020, Safwan *et al.* work on rapid spectrophotometric determination of moxifloxacin (MOX) and sildenafil (SC) in pharmaceutical preparations based on reaction with 4-

aminoantipyrine in the presence of  $KIO_4$  to yield red colored products exhibiting maximum absorption at 530 and 526 nm for moxifloxacin and sildenafil respectively.

The current study compared five different validated analytical techniques for the assay of moxifloxacin using three brands of moxifloxacin including the comparator brand. This study aims to establish which of the assay methods will be fast, precise, most

## **METHODOLOGY**

### **Materials**

All the reagents used were of analytical grade: Concentrated Hydrochloric acid, methyl orange, Potassium hydrogen phthalate, potassium permanganate, methyl orange, chloroform, sodium chloride, anhydrous sodium sulphate, ferric ammonium sulphate dodecahydrate, 2,2' bipyridyl were analytical grade, distilled water. Pure moxifloxacin hydrochloride sample obtained from AK Scientific (India). The different brands of moxifloxacin used; Moxiget<sup>®</sup> - Getz pharma (Private) Limited, Staxom<sup>®</sup> - MSN Laboratories (Private) Limited, P-Moxin<sup>®</sup> - Globela Pharma (Private) Limited were obtained from registered pharmacies in Nigeria.

### **Methods**

The labelling on the primary and secondary packages of the tablets were properly examined for the following details: Name & strength of active ingredient, batch number, NAFDAC registration number, brand name, manufacturing date, expiry date, manufacturing company and country of origin. The color, odor and shape of the studied brands were examined and noted. Twenty (20) tablets were weighed individually using an analytical balance. The average weight of the tablets and standard deviation were calculated. For friability Test: Ten (10) tablets were dusted and weighed together before they were placed in the tumbling chamber of the friabilator and rotated for four minutes. After 100 revolutions, the tablets were dusted and re-weighed after which the percentage friability was calculated. The hardness of the samples were tested thus: Ten (10) tablets per sample were randomly selected and the tablet were individually checked for their hardness by diametrically loading the tablet between the two platens of Monsanto hardness tester before adjusting the movable platen to compress the tablet until it cracked or broke using the. The values obtained were then recorded. With the aid of a micrometer screw gauge the thickness of the tablet samples were

effective and cost effective. Amongst other objectives of this work were provision of information on the quality of brands in use and thereby assisting the scientists including drug manufacturers, pharmacists and prescribers to choose the most cost-effective brands of the moxifloxacin, without compromising the medicine quality.

measured with the aid of a verniers caliper thus: Ten (10) tablets per sample were randomly selected and their thickness checked. Each tablet was placed between the jaws of the verniers caliper, (along the width to measure thickness) which was adjusted until a firm fit was obtained. The reading was then obtained from the scale.

**Disintegration Test:** The disintegration test was performed on six (6) tablets from individual brand as per procedure and specification. The disintegration time of six (6) tablets of each brand was determined at  $37 \pm 5^\circ\text{C}$  in distilled water using disintegration apparatus. The disintegration time is taken to be the time when no granule of any tablet is left on the mesh. About 700 mL of distilled water was taken in a 1000 mL beaker and the beaker was placed into the device. A tablet of the test brand was placed in each tube of basket rack and a plastic disc was placed over each tablet. The temperature of the media was maintained at  $37 \pm 5^\circ\text{C}$  while, a motor driven device helped to move the basket in an up and down motion through a distance of 5-6 cm at a rate of 28 – 32 cycles per min. The time at which all tablets disintegrate were recorded.

**Dissolution Test:** The in-vitro dissolution study for the tablets were carried out in USP XXIII type-II dissolution test apparatus (Paddle type) using 900 ml of Phosphate buffer pH 6.8 as dissolution medium at 50 rpm and temperature  $37 \pm 1^\circ\text{C}$ . At predetermined time intervals, 5 ml of the samples were withdrawn by means of a pipette fitted with a pipette pump. The volume withdrawn at each interval was filtered into a test-tube through a filter and replaced back in the dissolution apparatus with same quantity of fresh dissolution medium. The resultant samples were analyzed for the presence and quantity of the drug release by checking the wavelength of maximum absorption and measuring the absorbance at the  $\lambda_{\text{max}}$  using UV-Visible spectrophotometer after suitable dilutions. The determinations were performed in triplicate ( $n = 3$ ).

### **UV spectrophotometry (phosphate buffered)**

#### Preparation of Reagents

#### Preparation of buffer

The phosphate buffer of pH 6.8 was prepared using NaOH and KH<sub>2</sub>PO<sub>4</sub> in the following proportion; 100 ml of 0.1M KH<sub>2</sub>PO<sub>4</sub>: 44.8 mL of 0.1M NaOH. (Dhanlal De Lloyd, 2000) About 0.1M HCl was prepared and diluted to volume with distilled water. Standard solution of moxifloxacin was prepared by weighing and transferring about 200 mg of moxifloxacin HCl pure powder into a 200 ml clean & dry volumetric flask, then dissolved & diluted with freshly prepared phosphate buffer of pH 6.8 above to the volume. 2.0 mL was further collected from the prepared standard solution of moxifloxacin and diluted to 200 mL with phosphate buffer of pH 6.8 to the volume to get a concentration of 10 µg/mL. Assay: Dilutions of standard solution of moxifloxacin preparations were obtained (2, 4, 6, 8 & 10 µg/mL) by making up to volume with distilled water 2, 4, 6, 8 & 10 mL respectively of standard solution to 10mL in volumetric flasks. Absorbance of the dilutions were used to determine the wavelength, using phosphate buffer of pH 6.8 as the blank and these values were used to plot the calibration graph. Estimation of moxifloxacin in Tablets: Twenty (20) tablets of each branch were weighed and powdered. An amount of crushed powder equivalent to 100 mg moxifloxacin was transferred into 200 mL volumetric flasks. Phosphate buffer of pH 6.8 was added to 200 mL mark, mixed on a magnetic stirrer for 30 minutes before being filtered through filter paper. The first 5 ml of filtrate was discarded, before 2 mL of the filtrate was transferred to a 200 mL volumetric flask, this solution was diluted with phosphate buffer of pH 6.8 to the volume to form 5 µg/mL and absorbance was determined at 290 nm using phosphate buffer of pH 6.8 as the blank & the drug content is estimated from the calibration graph

### **UV spectrophotometry (Unbuffered)**

#### Preparation of Reagents

About 0.1M HCl was prepared. Standard solution of moxifloxacin was prepared by weighing and transferring about 200 mg of moxifloxacin HCl pure powder into a 200 mL clean & dry volumetric flask, then dissolved & diluted with freshly prepared 0.1M HCl to the volume. 2.0 mL of the prepared standard solution of moxifloxacin was further diluted to 200 mL with 0.1M HCl to the volume to obtain a concentration of 10 µg/mL. Assay: Dilutions of standard solution of moxifloxacin preparations were

obtained (2, 4, 6, 8 & 10 µg/mL) by taking 2, 4, 6, 8 & 10 mL respectively from standard solution into 10 mL volumetric flasks and made up to volume with distilled water. Absorbance of the dilutions were taken at the determined maximum wavelength using 0.1M HCl as the blank and these values were used to plot the calibration graph. Estimation of moxifloxacin in Tablets: Twenty (20) tablets of each branch were weighed and powdered. An amount of crushed powder equivalent to 100 mg moxifloxacin was transferred into 200 mL volumetric flasks. 0.1M HCl was added to 200 mL mark, mixed on a magnetic stirrer for 30 minutes before being filtered through filter paper. The first 5 mL of filtrate was discarded, before 2 mL of the filtrate was transferred to a 200 mL volumetric flask, this solution was diluted with 0.1M HCl to the volume to form 5 µg/mL and absorbance was determined at the same wavelength as before using 0.1M HCl as the blank & the drug content is estimated from the calibration graph

### **Kinetic spectrophotometry**

#### Preparation of Reagents

Stock standard solution of moxifloxacin (100 µg/mL) was prepared by dissolving 10 mg of the pure moxifloxacin in 2.0 mL of 0.05 M NaOH, and further diluted to 100 mL with double distilled water in a 100 mL volumetric flask. Aqueous solution of potassium permanganate (0.005M) was freshly prepared by dissolving 79.02 mg of pure KMnO<sub>4</sub> with hot distilled water and made up to mark in a 100 mL volumetric flask, followed by filtration through sintered glass. Aqueous solution of 0.5M NaOH was prepared by dissolving 2.0 g of NaOH with distilled water and making up to the mark in a 100 mL volumetric flask.

Aqueous solution of 0.005M HCl was prepared by transferring 0.42 mL of concentrated HCl into a small quantity of distilled water in a 1 L volumetric flask and making it up to volume with distilled water. Blank solutions of 0.5M NaOH and 0.005M KMnO<sub>4</sub> were prepared by adding 1.5 mL of 0.5M NaOH and 1.5 mL of 0.005M KMnO<sub>4</sub> respectively into separate different 10 mL volumetric flask and making each up to the mark with distilled water at ambient temperature (25 ± 2°C). Assay of standard solution of moxifloxacin (Fixed Time Method): Aliquot (0.1, 0.4, 0.8, 1.2 and 1.6 mL) of standard moxifloxacin solutions were transferred into series of 10 mL volumetric flasks. 1.5 mL of 0.5M NaOH and 1.5 mL of 0.005M KMnO<sub>4</sub> were added to each of the flasks and the volumes made up to the mark with distilled water at ambient temperature (25 ± 2°C). A fixed time of 12 min was selected for the fixed time method. At this pre-selected

fixed time, the absorbance of each sample of moxifloxacin solution was measured at determined wavelength of maximum absorbance ( $\lambda_{max}$ ) against the reagent blank. The calibration curve was obtained by plotting the values obtained. Assay of moxifloxacin in tablet samples: twenty (20) of moxifloxacin tablets were weighed and powdered. An accurate quantity of the powdered moxifloxacin tablets equivalent to 100 mg of active drug was weighed and extracted into 50 mL of 0.005 M HCl solution. This solution was stirred for 15 min before being filtered with filter paper into a 100 mL volumetric flask to isolate the insoluble excipients. The residue was washed with two 10 mL portions of 0.005M HCl solution and the washings were added to the filtrate. Volume was made up to the mark with the same solvent. 2.0 mL of the prepared solution was collected and diluted further to 10 mL with same solvent. An aliquot of 0.5 mL of the tablet solutions were treated as for Assay of moxifloxacin in tablet outline under the above recommended procedures. The content of the tablets was determined from the plotted calibration graph.

#### **Spectrophotometric method utilizing oxidation-reduction reaction**

##### **Preparation of Reagents**

Standard stock solution (8  $\mu\text{g}/\text{mL}$ ) was prepared by dissolving 80 mg of pure moxifloxacin in convenient quantity of distilled water in 100 mL volumetric flask followed by dilution to the mark with the same solvent. 1.0 mL was taken from the obtained solution and further diluted to 100 mL to produce 8  $\mu\text{g}/\text{mL}$  of pure moxifloxacin standard stock solution. Aqueous solution of 1M HCl was obtained by transferring 8.33 ml of concentrated HCl solution into 100 mL volumetric flask containing about 20 mL of distilled water and making up to volume with distilled water. Iron (III) – bipyridyl reaction mixture was prepared by mixing 0.16 g of 2, 2' bipyridyl, 2.0 ml of 1M HCl and 0.16 g ferric ammonium sulphate dodecahydrate in a 100 mL volumetric flask and then then diluted to mark with distilled water.

Blank solution was obtained by measuring 3.5 mL of Iron (III) bipyridyl into a 10 mL volumetric flask and heating on a boiling water bath for 30 minutes. Mixture was then cooled to room temperature ( $25\text{ }^{\circ}\text{C} \pm 1\text{ }^{\circ}\text{C}$ ) and made up to volume with distilled water. Assay of standard solutions of moxifloxacin: Different concentration of the standard solutions of moxifloxacin (0.8, 1.6, 2.4, 3.2 & 4.0  $\mu\text{g}/\text{mL}$ ) were obtained by transferring an aliquot (1, 2, 3, 4 & 5 mL respectively) of the 8  $\mu\text{g}/\text{mL}$  stock solution to a series of 10 mL calibrated flasks. 3.5 mL of Iron (III) bipyridyl was added to each of the calibrated flask and

heated on a boiling water bath for 30 minutes. The mixtures were cooled to room temperature ( $25\text{ }^{\circ}\text{C} \pm 1\text{ }^{\circ}\text{C}$ ) and volume made up to mark with distilled water. The absorbance values of the colored complexes formed were measured at determined wavelength of maximum ( $\lambda_{max}$ ) absorbance against the reagent blank. Assay of moxifloxacin in tablet samples: An accurately weighed quantity of the pulverized tablets equivalent to 80 mg of the studied drug was extracted with distilled water. Mixture was filtered through a filter paper and washed with water. The filtrate and washing were collected in a 100 mL standard flask and diluted to volume with distilled water. 1.0 mL was taken and further diluted to 100 mL. 2.5 mL of this solution was transferred in a 10 mL volumetric flask and the analysis was completed using the above-mentioned assay method.

#### **Colorimetric method**

##### **Preparation of Reagents**

Standard Stock Solution of moxifloxacin (100  $\mu\text{g}/\text{mL}$ ) was prepared by dissolving 10 mg of pure drug in suitable quantity of 0.1M HCl and made to volume in a 100 mL volumetric flask. The mixture was warmed at  $50^{\circ}\text{C}$  in a water bath for 5.0 min, agitated for another 5.0 min, cooled to room temperature, and diluted to volume with distilled water. Methyl Orange reagent (0.001M) was prepared by dissolving the appropriate weight of methyl orange (32.733 mg) in 10 mL of 96% ethanol and this was further diluted to 100 mL using distilled water.  $\text{KC}_8\text{H}_5\text{O}_4\text{-HCl}$  buffer of pH 3.5 was prepared by mixing 100 mL of 0.1M potassium hydrogen phthalate ( $\text{KC}_8\text{H}_5\text{O}_4$ ) and 16.4 mL of 0.1M HCl in a beaker. 0.1M  $\text{KC}_8\text{H}_5\text{O}_4$  was prepared by dissolving 2.0422 g of the powder in sufficient distilled water to mark in a 100 mL volumetric flask. HCl (0.1M) was prepared by diluting 0.833 mL of concentrated HCl in sufficient distilled water to mark in a 100 mL volumetric flask. Blank solution was obtained by mixing 2.0 mL of  $\text{KC}_8\text{H}_5\text{O}_4\text{-HCl}$  buffer and 2.0 mL of 0.001M methyl orange solution in a 10 mL calibrated flask. The mixture was extracted twice with 10 mL chloroform by shaking for 2.0 min and then allowed to stand for clear separation of the two phases. The chloroform layer was passed through anhydrous  $\text{Na}_2\text{SO}_4$  and the filtrate made up to mark with chloroform. Assay: Aliquot (0.1, 0.5, 1.0, 1.5 and 2.0 mL) of moxifloxacin stock solution (100  $\mu\text{g}/\text{mL}$ ) was transferred to 10 mL measuring flasks. 2.0 mL of  $\text{KC}_8\text{H}_5\text{O}_4\text{-HCl}$  buffer was added followed by 2.0 mL of 0.001M methyl orange solution. The mixture was extracted twice with 10 mL chloroform by shaking for 2.0 min and then allowed to stand for separation of the two phases. The chloroform layer was passed through anhydrous sodium sulphate and filtrate was made up

to volume with chloroform. The absorbance values of the yellow coloured complexes were measured at determined wavelength of maximum absorbance against corresponding reagent blank. The obtained values were used to plot the calibration graph. Assay of moxifloxacin in tablet samples: Ten tablets were crushed and powdered. An accurately weighed powder equivalent to 10 mg of moxifloxacin was dissolved in

20 mL of 0.5M HCl with shaking for 5.0 min and filtered. The filtrate was diluted to 100 mL with distilled water in a 100 mL volumetric flask to give 100 µg/mL stock solution. An aliquot of the diluted drug solution was treated as described above.

## RESULTS AND DISCUSSION

The packaging and labelling of the three brands were investigated and found to contain the necessary information such as name & strength of active ingredient, batch number, NAFDAC registration number, brand name, manufacturing date, expiry date, manufacturing company, country of origin and aluminum packaging material required by regulatory bodies. The three brands of the tablets were labelled 400 mg each. The results of qualitative test and general appearance test also showed that the three brands were consistent with their respective literature. All the assayed brands were found to be within the USP limit ( $\pm 5\%$  deviation). This test is important because, it can be correlated to the uniformity of content. (Zaid *et al.*, 2011). The results for the tablet thickness showed that all brands were within the limit ( $\pm 5\%$  deviation).

(CDER, 2015; USP 2020, & BP 2021). Tablet thickness is determined majorly by compaction characteristics of the material and compression force, other factors include the amount of granules filled into the die. Tablet thickness is important in packaging operations. (Ofoefule, 2002).

Friability test is important in order to ensure that the tablets will not break or chip during coating, packaging or routine handling during distribution chain. (Felton, 2013). The result from this study showed that all brands were within acceptable limit (not more than 1%) thus, very minimal friability. This will help to ensure that drug remains in the right state for consumer acceptability and reduce the risk of losing API that may arise from fraying.

**Table 1: Label Information on the three brands of moxifloxacin tablets evaluated**

Brand code	Batch No.	MFG Date	EXP Date	Label Strength	Price/ 400 mg tablet (₦)	Country of Origin
M-01	208F31	10/20	10/22	400 mg	360	Pakistan
M-02	BT1806019A	06/18	05/23	400 mg	150	India
M-03	GT18296	08/18	07/21	400 mg	150	India

**Table 2: Physiochemical parameters of the tested brands of Moxifloxacin Hydrochloride marketed in Nigeria**

Batch Code	Weight Uniformity (mg) (n=20)	% Friability (n=10)	Thickness (mm) (n=10)	Hardness (kg/m <sup>2</sup> ) (n=10)	Disintegration (min) (n=6)	% Content of Active ingredient
<b>M-01</b>	614.8 $\pm$ 0.004	0.03	5.01 $\pm$ 0.03	4.60 $\pm$ 0.32	3.24 $\pm$ 0.12	100.11
<b>M-02</b>	722.7 $\pm$ 0.006	0.01	5.58 $\pm$ 0.03	4.40 $\pm$ 0.21	2.68 $\pm$ 0.95	101.02
<b>M-03</b>	761.0 $\pm$ 0.008	0.07	5.28 $\pm$ 0.03	6.45 $\pm$ 0.37	4.07 $\pm$ 1.64	101.49

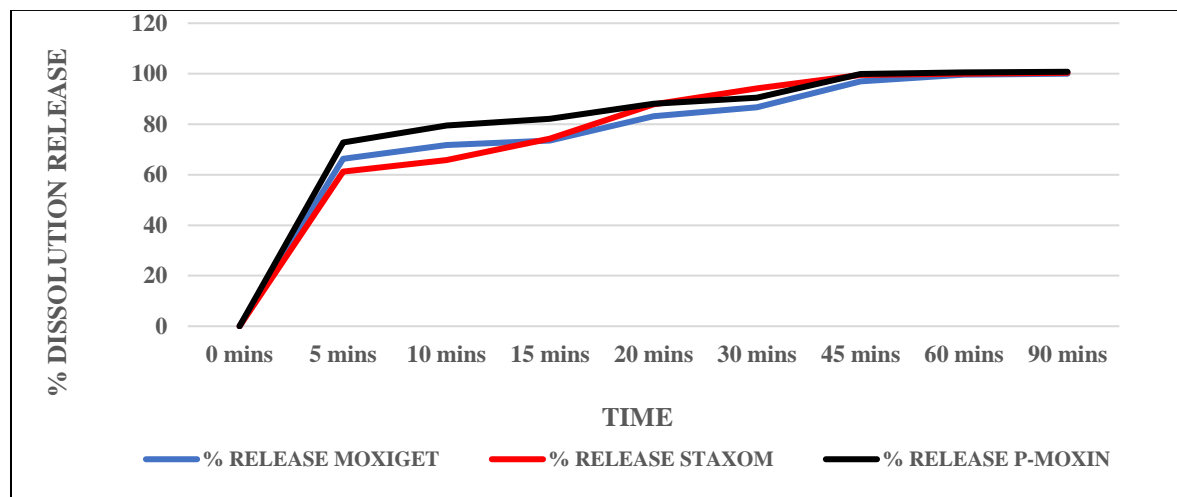
All values are recorded as Mean  $\pm$  SD

The hardness of all the brands under study falls within the acceptable limit (ranges from 4 – 6 kg and up to 8 kg for film coated tablets) (Ansel and Allen, 2014). A tablet that is not hard enough will frail easily and lose parts of API while a drug that is too hard may not disintegrate properly to release API at the necessary parts of the body.

All our samples, disintegrated within 30 min which is the standard limit (USP, 2017). For the medicinal agent in a tablet to become fully available for absorption, the tablet must first disintegrate and discharge the drug to the body fluids for dissolution. (Ansel and Allen, 2014).

The content of active ingredient test is aimed at verifying the amount of active pharmaceutical ingredient in the tablets for the purpose of estimating the potency of the sample under consideration and

comparing them to the label claim. The monograph (USP, 2017) has not stated the limit for UV analysis of moxifloxacin. In vitro dissolution testing is important because it provides a reasonable prediction of correlation with the product's in vivo bioavailability. Dissolution profile of the three brands were performed to provide information regarding biological bioavailability and brand to brand consistency. The dissolution profile of the various sampled brands of moxifloxacin HCl tablets are depicted in Figure 1. According to the USP specifications for moxifloxacin, the amount of moxifloxacin in solution for each tablet at time 30 minutes is not less than 75% (Q) and according to USP, not less than Q + 5% of the label claim. The released amount of Moxifloxacin across the brands were within the USP limit.



**Figure 1: Dissolution profile of the various sampled brands of Moxifloxacin HCl tablets**

Generally,  $f_1$  values up to 15 (0-15) and  $f_2$  values greater than 50 (50-100) ensure sameness or equivalence of the two curves and, thus, of the performance of the test and reference products. (Hambisa *et al.*, 2019). This approach has been adopted by USFDA in comparing release profiles of a reference and a test drug. The  $f_1$  of brand M-02 and M-03 with respect to M-01 was 4.01 and 5.34 respectively, and  $f_2$  was 67.9 and 63.4 respectively. The values are within the limit values, so it can be said that samples M-02 and M-03 are pharmaceutically equivalent to sample M-01 and therefore interchangeable. The reference and the test products are said to be equivalent if the difference between their dissolution efficiencies is within appropriate limits ( $\pm 10\%$ ). (Anderson *et al.*, 1998).

In order to ascertain the interchangeability of drug products with the comparator product, the release

profiles were also compared by calculating dissolution efficiency (DE) for various brands tablets included in the study. The difference between the D.E of comparator sample M-01 and test samples (M-02 and M-03) were 1.12 and 1.25 respectively. The value is within the given limit and thus infers interchangeability between test brands and the comparator brand.

A method is the application of a technique to a specific analyte in a specific matrix. Ultimately, the request of the analysis determines the best method. Consideration is usually given to some or all of the following design criteria: accuracy, precision, sensitivity, selectivity, robustness, ruggedness, scale of operation, analysis time and availability. We can also compare analytical methods with respect to the equipment needs, the time needed to complete the analysis and the cost per sample. Besides technical

efficacy, the ultimate goal of assaying of pharmaceutical products is to check how cost effective the best method will be compared to the comparator method. When one considers the criteria according to which an analytical method is selected, precision and

accuracy are the first to be considered. Therefore, for the purpose of this study, will be comparing the methods against technique using accuracy, precision, time, equipment and cost of sample analysis.

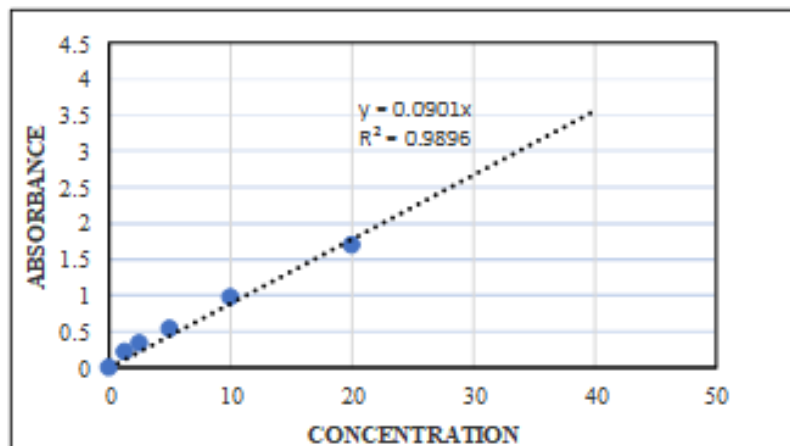


Figure 2: Calibration curve plot for pure moxifloxacin HCl

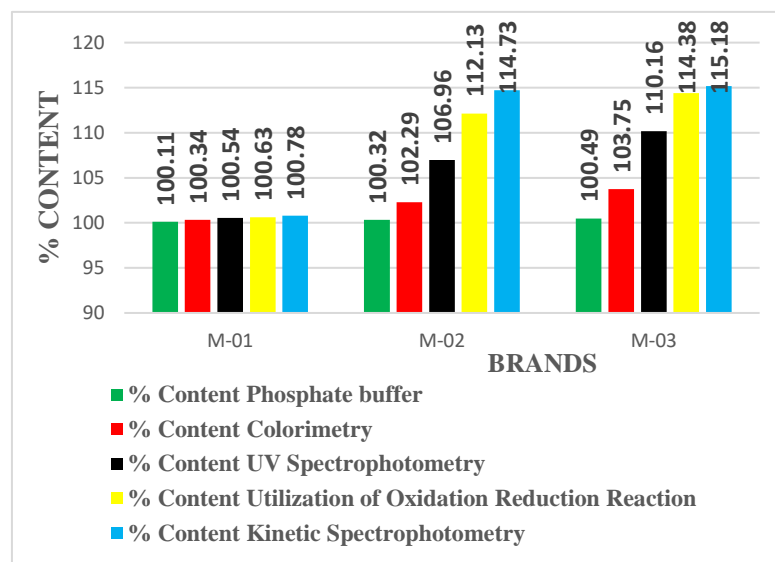


Figure 3: Comparison of percentage content of studied brands using various assay methods

Sample M-01 gives consistent results (Fig 3) with all the methods of analyses employed. There was no significant difference in the amount of moxifloxacin contained in the sample. This is not the same with samples M-02 and M-03, where the assay results were inconsistent. Method which employed UV assay using phosphate buffer gave the percentage content of 101.32 % while the kinetic spectrophotometry method gave percentage content of 114.73 % for the same

sample M-02. The other methods used to assay sample M-02, shows results which falls in-between the above range of values. Therefore, there is a significant difference ( $p > 0.05$ ) in the amount of moxifloxacin contain in sample M-02. The same scenario seems to be playing out when sample M-03 was analyzed using the five assays methods deployed in this study. The method which employed phosphate buffer UV assay gave the percentage content of 100.49 % while the



kinetic spectrophotometry method gave percentage content of 115.18 % for the same sample M-03. An interesting scenario play out here, the three samples under study gives a consistent amount of moxifloxacin when assayed using the phosphate buffered UV method, so also a similar trend was noticed for colorimetric method across the three samples, that is consistent amount of moxifloxacin were obtained. Similar scenario does not play out when unbuffered UV-Vis spectrophotometric, oxidation-reduction and kinetic spectrophotometric methods were used for the assay. In the later instances, the amount of

moxifloxacin assayed were not consistent and they were significantly different ( $p > 0.05$ ) from one sample to another. It can be seen that UV-Vis spec., oxidation-reduction and kinetic spectrophotometric methods give unusually high amount of moxifloxacin when samples M-02 and M-03 were assayed. This may be due to the fluctuations in the pH of the analyte, Moxifloxacin being more acidic may behave differently under UV when buffered and when not buffered, because the result was more constituent when the analyte was buffered.

**Table 3 Values for f1, f2 and Dissolution efficiency**

Sample Comparison	f2	f1	Dissolution Efficiency	Difference of Dissolution Efficiency
M-01			88.46	-
M-02 VS M-01	67.89	4.01	89.58	1.12
M-03 VS M-01	63.41	5.34	90.83	1.25

**Table 4: Comparison of other parameters of assay methods**

Analytical Technique	Parameters				
	Precision RSD ( $\leq 2\%$ )	Accuracy Mean $\pm$ SD N=3 (%)	Time (Hour)	Cost ₦	Instrument
Buffered UV/Vis Spectrophotometer (290 nm)	0.17	0.64 $\pm$ 0.62	2.5	1,000	UV/Vis Spectrophotometer
UV Spectrophotometry (257 nm)	0.92	5.89 $\pm$ 4.90	3.5	1,100	UV/Vis Spectrophotometer
Kinetic Spectrophotometry (274 nm)	0.17	10.23 $\pm$ 8.19	4.5	1,750	UV/Vis Spectrophotometer
Utilization of Oxidation Reduction Reaction (250 nm)	0.01	9.05 $\pm$ 7.38	4.0	11,600	UV/Vis Spectrophotometer
Colorimetry (310 nm)	0.26	2.13 $\pm$ 1.71	5.5	4,950	UV/Vis Spectrophotometer

The same might as well suffice for the inconsistency when the sample was assayed with oxidation-reduction and kinetic spectrophotometric methods, some of the design criteria such as sensitivity or selectivity, robustness, ruggedness of the method. In other to compare the performance characteristics of the methods, out of the five criteria we intend to use, one of them is constant for all of them: instrumentation, which is UV-Vis spectrophotometer. Technically, accuracy is how close the result of an

experiment is to the “true” or expected result. The order of accuracy in this study is: phosphate buffer UV method (0.64) > colorimetric method (2.13) > unbuffered UV method (5.89) > oxidation-reduction reaction method (9.05) > kinetic spectrophotometric method (10.23). The accuracy depends on the signal source which is same for all the methods, but the difference is in the way in which the samples were handled. Precision (Table 4) refers to the reproducibility of measurements within a set, just like

accuracy, it depends on the same factors. For this study the order of reducing precision of the methods: oxidation-reduction reaction (0.01) > kinetic spectrophotometric and phosphate buffer UV method (0.17) > colorimetric (0.26) > unbuffered UV method (0.92). This study reveals that oxidation-reduction method is more precise (Table 4) than the remaining methods including the comparator method (phosphate buffer UV). Precision does not translate to accuracy. From the above results, phosphate buffered UV method is the most accurate method of all the test methods employed in this study. The method with the

least cost of analysis is the phosphate buffered UV method followed by the UV Spectrophotometry. But minimizing cost of analysis may decrease the accuracy. Usually, the most important design criterion is accuracy, but when the urgency of getting result arises, as in faking of pharmaceutical products and in clinical laboratories, analysis time may become the critical factor.

## CONCLUSION

All the samples tested gave good physicochemical parameters, dissolution profile, dissolution efficiency and acceptable assay result according to USP standard. Thus, they are said to be pharmaceutically equivalent and interchangeable with one another. The most

accurate method to assay moxifloxacin in pharmaceutical solid dosage form is by using phosphate buffered UV spectrophotometry. In absence of this, a good alternative is the colorimetric method.

## REFERENCES

- Akula G, Nagarani P, Phanindra S, Nirmala R, Jaswanth A. (2017). Validated RP-HPLC method for simultaneous estimation of moxifloxacin hydrochloride and ketoprofen in bulk form. *Int. J. Pharm. and Bio. Sci.* 7 (4):143-150
- Alam S.M. and Wabaidur S.M. (2017) Flow Injection Determination of Moxifloxacin using Silver Nanoparticle with Tris(2,2-Bipyridyl)Ruthenium(III)-Ce(IV) Chemiluminescence Detection, *Ind. J. Pharm. Sci.* 79(3): 402-410
- Anderson N.H., Bauer M, Boussac N, et al. (1998) An evaluation of fit factors and dissolution efficiency for the comparison of in vitro dissolution profiles. *J Pharm Biomed Anal.* 17(4-5): 811-822
- Ansel H.C. and Allen L.V. (2014). *Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems*. Tenth Edition. Baltimore, Philadelphia: Lippincott Williams and Wilkins. 270-275
- Ashour S, Kattan N, (2016) New, Simple and Validated RP-HPLC method for quality control of Moxifloxacin SOJ. *Pharm. Pharm. Sci.* 3(3): 1-6.
- Attimarad M, Chohan M.S. and Balgoname A.A. (2019) Simultaneous Determination of Moxifloxacin and Flavoxate by RP-HPLC and Eco-friendly Derivative Spectrophotometry Methods in Formulations *Int. J. Environ. Res. P. H.* 16(7): 1196.
- British Pharmacopoeia Commission. *British Pharmacopoeia 2021*. London: TSO; 2021.
- Center for Drug Evaluation and Research (CDER) (2015). "Guidance for Industry: Size, Shape, and Other Physical Attributes of Generic Tablets and Capsules". United States Food and Drug Administration.
- Desai S., Dalwadi H., Desai K. (2015) Development and Validation of UV Spectroscopic Method for Simultaneous Estimation of Moxifloxacin Hydrochloride and Bromfenac Sodium in Combined Dosage Form. *J. Pharm. Sci. Bioscientific Res.* 5(6):410
- Felton, L.A. (2012). *Remington Essentials of Pharmaceutics*. UK: Pharmaceutical Press.
- Garuba H.A., Kohler J.C., Huisman A. (2009) Transparency in Nigeria Public Pharmaceutical Sector: perception from policy makers. *G. Health.* 5:14 doi: 10/186/1744-8603-5-14
- Kailash N. T., Swati S.A., Neha G. S. and Seema R.S. (2012), Development and Validation of UV-Spectrophotometric Methods for Determination of Moxifloxacin HCL in Bulk and Pharmaceutical Formulations *Der. Pharma. Chem.* 4 (3): 1180-1185
- Ndichu E.T., Ohiri K, Sekoni O, Makinde O, Schulman K. (2019) Evaluating the quality of antihypertensive drugs in Lagos State, Nigeria. *PLoS ONE* 14(2): e0211567. <https://doi.org/10.1371/journal.pone.0211567>
- Ofoefule, S.I. (2002). *Textbook of Pharmaceutical Technology and Industrial Pharmacy*. Nigeria: Samakin (Nig.) Enterprise. 2nd ed. 123-137
- Patel P.U., Suhagia B.N., and Patel M.M. (2015). "Spectrophotometric methods for estimation of moxifloxacin in pharmaceutical formulations," *Ind. Drugs*, 42(10): 654-657.

- Patel P.B, Patel S.A. (2017) Spectrophotometric Method Based on Q-Absorbance Ratio for Simultaneous Determination of Moxifloxacin and Prednisolone Acetate in Pharmaceutical Preparation Inter. J. Pharm. Pharm. Res. 8(4):46-53
- Raza W., Liung N., Liu D., Wei Z., Huang Q. (2016) Volatile organic compounds produced by *Pseudomonas* fluorescence WR-1 restrict the growth and virulence traits of *Ralstonia solanacearum*. Micro. Res. 192: 102-113,
- Rizk M.F. Belal, F. Ibrahim F., Ahmed S.M., and El-Enany N.M. (2015) A simple kinetic spectrophotometric method for the determination of certain 4-quinolones in drug formulations, Sci. Pharm.. 68(1): 173–188.
- Safwan A. (2020) Rapid Spectrophotometric Methods for the Determination of Moxifloxacin and Sildenafil in Pharmaceutical Preparations Based on Reaction with 4-Aminoantipyrine Acta Sci. Pharm. Sci. 4(4): 02-10
- Sankar R., Deepthi K.D., Babu P.S., Rachana G., Geethika A.S., Bhargavi J., *et al.*, (2019) Development and Validation of a Stability-Indicating Method for Assay of Moxifloxacin in Oral Pharmaceutical Dosage Forms by HPLC IOSR J. Pharm. 9(4 series 1): 30-41
- United States Pharmacopoeia 40-National Formulary 35. (USP 40/NF 29), (2017). Thirty Fifth edition. United States Pharmacopoeia Convention, Stationery Officer, USA
- United States Pharmacopoeia and National Formulary (USP 43–NF 38). United States Pharmacopoeial Convention; 2020.
- World Health Organization. (2007). The International Pharmacopoeia. World Health Organization, Geneva.
- Zaid, A.N., Al-Ramahi, R.J. Ghoush, A.A. and Zaarob Y.A. (2013). Weight and content uniformity of lorazepam half-tablets: A study of correlation of a low drug content product. Saudi Pharm J. 21(1): 71–75

\*Address for correspondence: Omotoso EA  
Department of Pharmaceutical and Medicinal Chemistry,  
Faculty of Pharmaceutical Sciences,  
University of Port Harcourt.  
Port Harcourt 500004, Nigeria  
Telephone: 09056204652  
E-mails: Abayomi.omotoso@uniport.edu.ng

Conflict of Interest: None declared  
Received: October, 2023  
Accepted: December, 2023