

## Evaluation of Drug Quality (III): Determination of Ciprofloxacin Hydrochloride Concentration in Pharmaceutical Tablets

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### ABSTRACT

The concentration of ciprofloxacin hydrochloride tablets in the Nigerian market was analyzed using both back-titration and UV-visible spectrophotometric methods. The results obtained showed that different brands contained different concentrations of the drug; some brands contained lower concentrations while others were in good agreement with stated label strength. It was observed that the results obtained from the back-titration method showed only two of the five brands were within the BP specification whereas results obtained from UV-visible spectrophotometric method were close to one another and all five brands analyzed were within the Pharmacopoeia specifications. The discrepancies in results from the two methods were interpreted in terms of differences in sensitivities of the methods. It was concluded that the UV-visible spectrophotometric method was more accurate and sensitive and gave better results than the back-titration method, which is dependent on individual judgement of the person performing the experiments.

### INTRODUCTION

Ciprofloxacin is the most widely used of the second-generation quinolone antibiotics since the late 1980s and early 1990s. It is the drug of choice for the treatment of urinary tract infections, acute uncomplicated cystitis in females, chronic bacterial prostatitis, lower respiratory tract infections, acute sinusitis, skin structure infections, bone and joint infections, infectious diarrhoea, typhoid fever, uncomplicated cervical and urethral gonorrhoea<sup>1</sup>.

Ciprofloxacin (1-cyclopropyl-6-fluoro-4-oxo-7-(piperazin-1-yl)-quinolone-3-carboxylic acid) is a synthetic fluoroquinolone antimicrobial agent. It is a relatively new,

second-generation fluoroquinolone antibiotic with an expanded spectrum of activity (broad spectrum antibiotic), active against both Gram-positive and Gram-negative bacteria<sup>2</sup>. Chemical and pharmaceutical inadequacies have been reported for several brands of the drug in Nigeria and other countries, which necessitated need to reevaluate various brands of drug<sup>3</sup>. Several researchers have evaluated the concentration of various brands of this drug and estimated the quantities of their active ingredients<sup>3-8</sup>. Adegbolagun *et al*<sup>3</sup> evaluated the biopharmaceutical and chemical equivalence of ten brands of commercially available ciprofloxacin hydrochloride tablets, including uniformity of weight, friability,

hardness, disintegration, dissolution rate, purity (using thin layer chromatography) and non-aqueous titration. The authors found that only 6 out of 10 brands were biopharmaceutically equivalent<sup>3</sup>

Cazedey *et al*<sup>4</sup> carried out the UV-spectrophotometric determination of ciprofloxacin hydrochloride in Ophthalmic solution in their attempt to develop a simple and rapid method for the determination of ciprofloxacin hydrochloride in ophthalmic solutions. Water was used as blank and the absorbance was measured at 275nm using UV-visible spectrophotometer. The calibration graph was linear over the concentration range studied and results obtained showed that different brands conformed to the British Pharmacopoeia specification<sup>4</sup>.

Manoranjan *et al*<sup>5</sup> carried out the UV-spectrophotometer determination of ciprofloxacin hydrochloride in pharmaceutical dosage form and quantitatively evaluated ciprofloxacin concentration in both bulk and pharmaceutical formulation using simple, sensitive and reproducible stability – indicating UV-spectrophotometer. The authors found that the drug was degraded more in 0.1M NaOH, 0.1M HCl and 3% H<sub>2</sub>O<sub>2</sub> solution<sup>5</sup>.

Qureshi *et al*<sup>6</sup> studied the comparative analysis of ciprofloxacin in different pharmaceutical products by High Performance Liquid Chromatography (HPLC). The results obtained from quantification of ciprofloxacin content of each product were compared with their labeled concentration and showed that ten out of the eleven ciprofloxacin brands were

within the allowed limits while one product was lower<sup>6</sup>.

Nandipati *et al*<sup>7</sup> determined the concentration of Ciprofloxacin in pharmaceutical formulations using Ultra Performance Liquid Chromatography (UPLC) and found that all six drug formulations analyzed were within allowed BP specification.

In this paper we report on the quantitative determination of Ciprofloxacin Hydrochloride concentration in pharmaceutical formulations of the drug in the Nigerian market using the back titration and UV–Visible spectrophotometric methods.

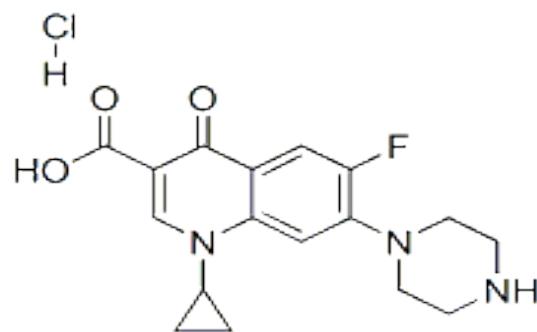


Figure 1: Structure of Ciprofloxacin Hydrochloride

## MATERIALS AND METHODS

### *Samples used in the Study*

Ciprofloxacin Hydrochloride crystals were bought from a Chemical shop at Onitsha Main market in Anambra State, Nigeria whereas the Ciprofloxacin Hydrochloride tablets containing 500mg per tablet of the drug were purchased from various Pharmacy shops in Owerri, Imo State, Nigeria.

## **Methodology**

Two methods were used in this study for the determination of concentration of the active ingredient in the drug, namely; back titration<sup>9</sup> and UV-visible spectrophotometric<sup>10</sup> methods were employed in this study to obtain the respective concentrations of Ciprofloxacin Hydrochloride in the tablets.

### **Back Titration Method**

3.68g of pure Ciprofloxacin hydrochloride crystal was weighed and dissolved in 1000mL of distilled water in a volumetric flask to obtain 0.01M solution of the drug. This was taken as the stock solution.

0.1M Na<sub>2</sub>CO<sub>3</sub> was prepared and used as the primary standard.

0.1M HCl was prepared and standardized with 0.1M standard Na<sub>2</sub>CO<sub>3</sub>.

0.1M NaOH was prepared and standardized with 0.1M standard HCl.

Then 25mL of the standardized 0.1M NaOH solution was mixed with 25mL of 0.1M ciprofloxacin solution and allowed to stand at room temperature for at least 1h. The excess NaOH solution was then back titrated against 0.1M HCl using phenolphthalein as indicator until the colour changed from pink to colourless. Three duplicate titrations were

made, titre values were recorded and the standard deviations obtained. This was used as the standard titration.

Similar experiments were repeated using 25mL of the different commercial Ciprofloxacin hydrochloride tablets, 25mL of 0.1M standard NaOH and 0.1M standard HCl using phenolphthalein as indicator until colour changed from pink to colourless.

### **UV-Spectrophotometric Method**

In the UV-spectrophotometric method, the absorbance of both the Ciprofloxacin hydrochloride standard and different Ciprofloxacin hydrochloride tablets were measured at the wavelength of maximum absorption using UV-Visible Spectrophotometer (Spectronic 300D). The corresponding concentrations of Ciprofloxacin hydrochloride tablets were obtained from the calibration curve.

### **Determination of Maximum Wavelength**

The stock ( $10^{-2}$ M) solution of Ciprofloxacin hydrochloride earlier prepared was used for determination of wavelength of maximum absorption. The absorbance of this solution was measured as a function of wavelength from 270–400nm, at intervals of 10nm. A graph of absorbance against wavelength was plotted (Fig. 2), from which the wavelength of maximum absorption ( $\lambda_{\text{max}} = 360\text{nm}$ ) was obtained.

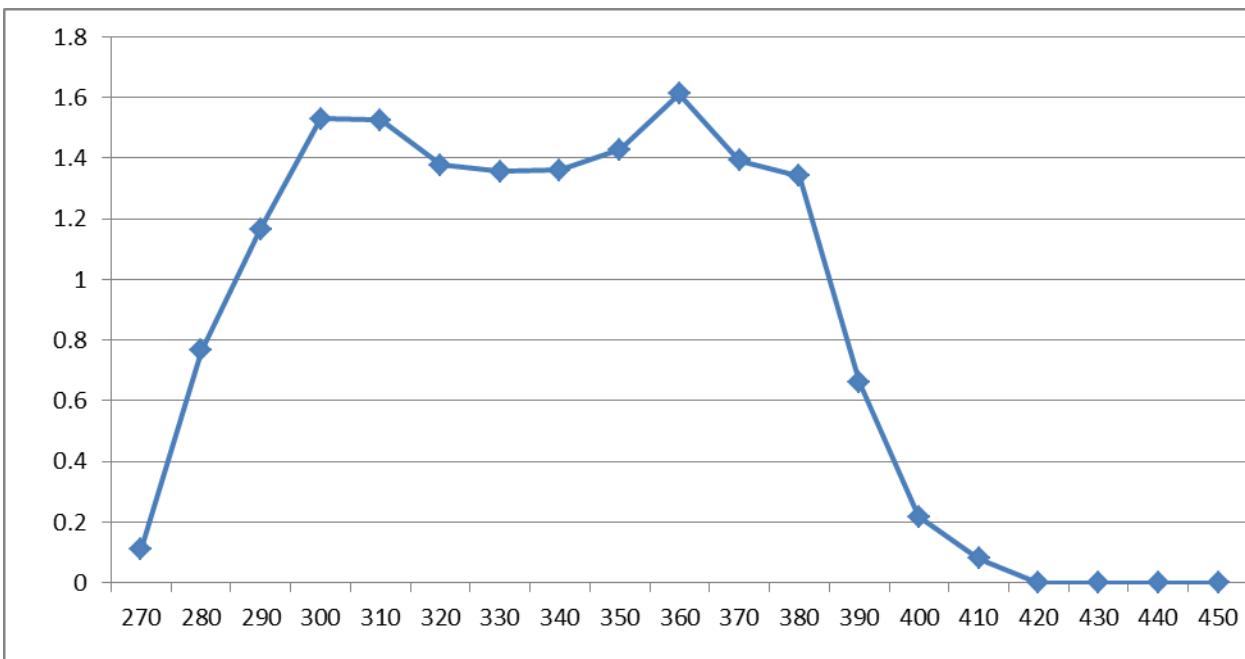


Figure 2: Graph of Absorbance against Wavelength

### ***Calibration Curve***

Different dilutions of the  $10^{-2}$ M standard solution were made to obtain other solutions of known concentrations. The absorbance of the various solutions was measured at the wavelength of maximum absorption (358nm). A graph of Absorbance against Concentration was made (Fig. 3). This is the Calibration Curve, which was used to determine the concentration of Ciprofloxacin hydrochloride in pharmaceutical tablets.

### ***Determination of Ciprofloxacin in Pharmaceutical Tablets***

Ten (10) tablets of each Ciprofloxacin hydrochloride brand were crushed, mixed, weighed and dissolved in 250mL distilled

water with stirring. The mixture was allowed to stand overnight. The next day, the solution was filtered and the absorbance was measured at 358nm using the UV–Visible Spectrophotometer (Spectronic 300D). The corresponding concentration was deduced from the calibration curve. This procedure was repeated for other Ciprofloxacin hydrochloride brands. The absorbance of each brand of Ciprofloxacin hydrochloride tablet was taken and the corresponding concentration was determined from the calibration curve. The concentration of each brand of ciprofloxacin hydrochloride tablet was obtained (mg/tablet) using equation below. The results are presented in Table 1.

$$\text{Conc (mg/tablet)} = \frac{(\text{molarity} \times \text{molecular weight} \times 1000)}{10}$$

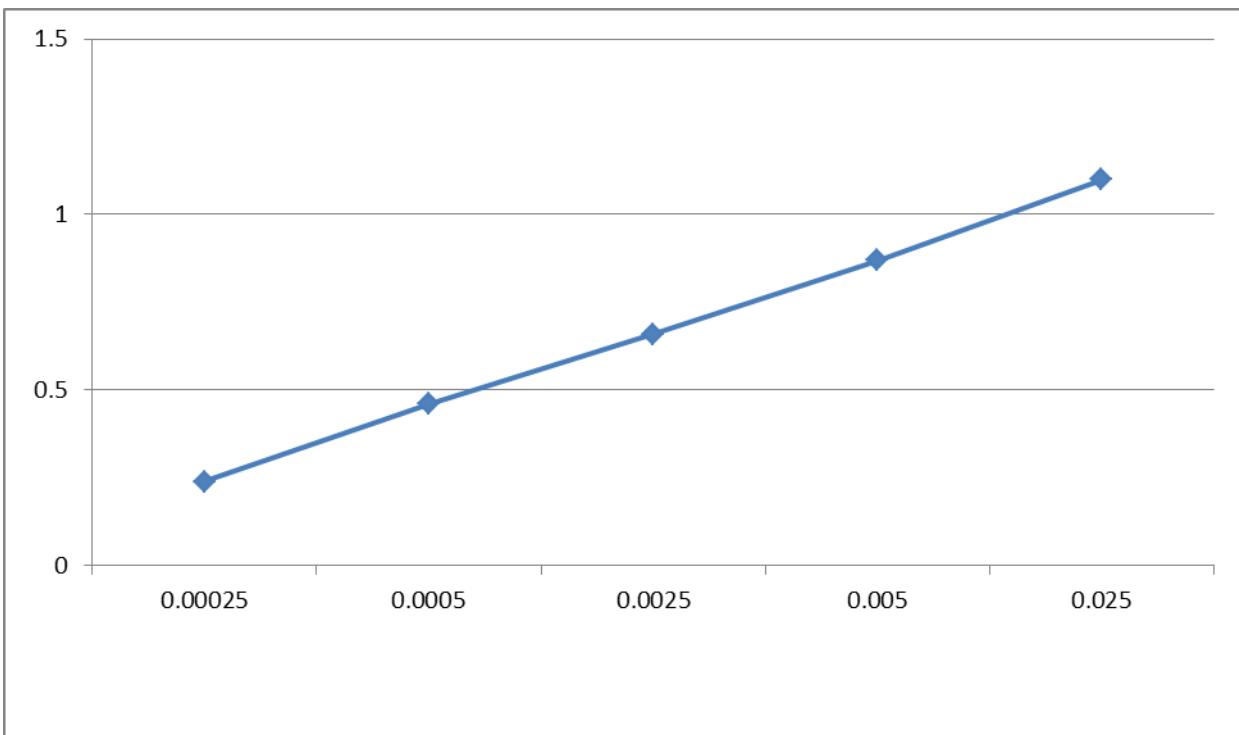
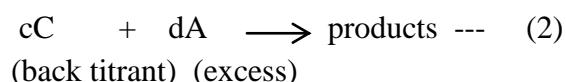
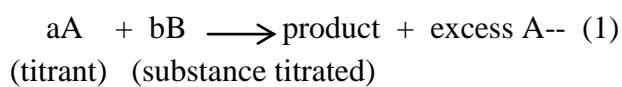


Figure 3: Calibration Curve (Absorbance against Concentration @  $\lambda_{\max}$ )

## RESULTS AND DISCUSSION

### *Analysis of Data*

The concentration of ciprofloxacin hydrochloride in the commercial tablets was calculated as follows<sup>10</sup>:



$$A_{\text{added}} - A_{\text{excess}} = A_{\text{net}} \quad (3)$$

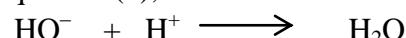
$$[(ml_A)(M_A) - (ml_c)(M_c)(d/c)] = \text{mmoles}_A \quad (4)$$

$$[(\text{mmoles}_A)(b/a)(\text{Mol wt}_B)] = mg_B \quad (5)$$

where:

A = NaOH, B = ciprofloxacin hydrochloride, C = HCl

From equation (2), it follows that



thus, ratio d/c = 1, whereas ratio b/a is not known.

In order to obtain ratio b/a, several assumptions were made, as follows:

(i) ***First assumption: b/a = 1***

We assumed the ratio: b/a = 1 and applied equations (4) and (5) simultaneously, using the data:

$$ml_A = 14.21\text{ml}; \quad M_A = 0.128\text{M}$$

$ml_C$  = titre of HCl (for the different brands)  
 $M_C$  = 0.1M; Formula  $Wt_B$  = 368g/mol

The results obtained based on first assumption:  $b/a = 1$ , are presented in Table 1 and showed that the ciprofloxacin hydrochloride concentrations in different capsules were below expectations hence this assumption was discontinued and discarded.

**(ii) Second assumption:  $b/a = 1:2$**

Results obtained based on second assumption:  $b/a = 1:2$  are presented in Table 1 and showed that the ciprofloxacin hydrochloride concentrations in the different capsules were far below expectations hence

this assumption was also discontinued and discarded.

**(iii) Third assumption:  $b/a = 2:1$**

The results based on the third assumption:  $b/a = 2:1$ , are presented in Table 1 and showed more acceptable values. The data showed there was relatively better agreement between the expected and experimentally derived values of ciprofloxacin hydrochloride concentrations in the various brands. Therefore the results obtained using the third assumption were used in the discussion contained in this study.

Table 1: Results Obtained from Various Assumptions of Molar Ratios of  $b/a$

Brands	Labelled strength	Manufacturer	Assumption 1 $b/a = 1$	Assumption 2 $b/a = 1:2$	Assumption 3 $b/a = 2:1$	Assumption 4 $b/a = 1:3$
1	500 mg/tablet	Foreign	226.04	113.02	457.84	74.59
2	"	"	224.22	112.12	453.76	73.99
3	"	Local	240.21	120.11	485.84	79.27
4	"	Foreign	235.52	117.75	476.22	77.73
5	"	"	223.91	111.95	452.56	73.89

**UV-Visible Spectrophotometric Method**

The molarities of ciprofloxacin hydrochloride in pharmaceutical tablets were obtained from the calibration curve while the corresponding concentrations were deduced from the molarities as follows:

$$\text{Conc (mg/tablet)} = \frac{(\text{molarity} \times \text{molecular weight} \times 1000)}{10} - 6$$

The results obtained are represented in Table 2, from which we see that the ciprofloxacin hydrochloride in the pharmaceutical tablets analyzed were close to each other and all were within the BP specification. Since the ciprofloxacin hydrochloride concentrations obtained using the UV-spectrophotometric method ranged from 496.53 to 522.28mg/tablet, it follows that all the Brands satisfied the Pharmacopoeia specification for

Table 2: Concentration of Ciprofloxacin Hydrochloride in Pharmaceutical Tablets

Brands	Labelled strength	Manufacturer	Results from Spectrophotometric method	Results from Titrimetric method (b/a = 2:1)
1	500 mg / tablet	Foreign	522.28	457.84
2	"	"	505.71	453.76
3	"	Local	496.53	485.84
4	"	Foreign	514.92	476.22
5	"	"	503.89	452.56

ciprofloxacin hydrochloride tablets of labeled strength 500mg/tablet, which lie between 475–525 mg/tablet representing  $\pm 5\%$ .

The results obtained in this study (especially from the UV-spectrophotometric method), suggested that none of the ciprofloxacin hydrochloride brands analyzed could be classified as fake or adulterated since most of the concentrations were within the BP specification. According to the British Pharmacopoeia<sup>11</sup> specifications for ciprofloxacin hydrochloride, the concentration of tablets of labeled strength value of 500mg/tablet should lie between 475–525mg per tablet, which represents  $\pm 5\%$ . A comparison of results obtained from the Titrimetric and UV-spectrophotometric methods for the various brands of ciprofloxacin hydrochloride tablets are given in Table 2, from which it could be deduced that when the back titration method was used, only two Brands (3 and 4) satisfied the BP specification. The other Brands (1, 2 and 5) were below this specification. However results obtained from the UV-spectrophotometric method showed that all

five brands conformed to the specification. The differences in results from the two methods have shown that the sensitivities of these methods are different: the UV-visible spectrophotometric method is more sensitive and gave better results than the Titrimetric method, which is dependent on personal judgement of the individual performing the experiments.

Several researchers have carried out different experiments to evaluate the contents of various brands of this drug and quantities of their active ingredients<sup>3 - 6</sup>. Analysis of the active chemical ingredient in a drug is one important aspect of drug quality, specification and control, which are essential for every serious manufacturing business. Drug analysis includes the identification, detection, separation and quantification of the drug. Various methods have been applied for drug potency determination in drug analysis, which includes titrimetry, spectrophotometry, chromatography or a combination of two or more of these methods may be applied. The objectives of drug specification and control include;

- i) the establishment of some important drug criteria such as its safety and practical standards, with respect to both dosage and quality to ensure conformity for all medication
- ii) determination of incompatibilities whether physical, chemical or biological so as to ascertain whether a drug conforms to specified standard of identify, strength, quality, purity, colour, flavour and physical appearance
- iii) to show whether the drug is properly constituted or not.

Drug standards are set by the pharmaceutical manufacturers, official compendia (such as the United States pharmacopoeia, British pharmacopoeia, the pharmaceutical codex) and regulations promulgated by the National Agency for Food, Drug Administration and Control. Each brand of a drug must satisfy these requirements which include its conformity to homogeneity, label claim, pharmaceutical elegance, regulatory standards and specified identity. Therefore drug analysis requires that drugs meet their label claims within specified limits and may vary in complexity from simple tests on drugs containing only one active ingredient to very complex chemical and biological tests on drugs containing two or more active ingredients. These analytical tests are mandatory to eliminate undesirable physiological reactions of a drug.

## CONCLUSION

We have determined the ciprofloxacin hydrochloride concentrations in tablet formulations of the drug in the Nigerian market, using both back-titration and UV-visible spectrophotometric methods. We found that the ciprofloxacin hydrochloride concentrations in the tablets studied by the back-titration method were close to one another although only two out of the five brands studied were within the BP specification. The results obtained when the UV-visible spectrophotometric method was used were also close to one another and all the five brands analyzed were within the Pharmacopoeia specification. The discrepancies observed in results from the two methods were interpreted in terms of sensitivities of the methods. The UV-spectrophotometric method was considered more sensitive and gave better results than the Titrimetric method, which is dependent on the individual judgement of the person performing the experiments. This notwithstanding, we may conclude that the methods we adopted in this study are relatively simple, accurate and ideal for verifying the quantity of ciprofloxacin hydrochloride in tablet, capsule or powder.

## ACKNOWLEDGEMENT

The Authors are grateful to Mr. Ifeanyi Ngwubike of the Department of Chemistry, Federal University of Technology, Owerri for his contribution to this study.

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*Received* 15<sup>th</sup> June 2015

*Revised* 27<sup>th</sup> September 2015

*Accepted* 10<sup>th</sup> October 2015