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Research Article

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Physical Characteristics of Ofloxacin Tablets Sold in Uyo and Quantitative Assay by Novel Ion-Pair Complexation Technique

Arnold C Igboasoiyi*, Marlene D Ekpo and Amarachi P Egeolu

Department of Pharmaceutical and Medicinal Chemistry, Faculty of Pharmacy, University of Uyo, Uyo, Akwa Ibom State, Nigeria

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ABSTRACT

Ofloxacin is a flouroquinoline antibiotic frequently prescribed for the treatment of various bacterial infections Quality assessments were carried out on ten brands of ofloxacin tablets, purchased randomly from pharmacy stores in Uyo, Akwa Ibom State, Nigeria and coded A-J. These were subjected to standard physical tests to determine their respective disintegration times, weight uniformity, hardness, friability characteristics and dissolution profiles using standard methods. Quantitative assay was by a spectrophotometric measurement of the ion-pair complex of the drug with bromothymol blue (BTB). All the brands met requirements for weight uniformity and disintegration characteristics. All the brands except brands B, E and F passed the USP specification of 80% dissolution in 30 minutes for uncoated ofloxacin tablets. The f1 and f2 values of the various brands, in comparison with the innovator product (brand I) showed that brands A,B,D,E,H and J could be used interchangeably with brand I. Brands F and J showed suboptimal friability values. Brand B showed suboptimal hardness value. The calibration curve for reference ofloxacin with BTB at 410 nm was linear over a concentration range of 0.00-20.00 µg/ml. The variation of absorbance with concentration showed excellent correlation with coefficient of correlation (r) of 0.9999 and coefficient of determination (r2) of value 0.9998. All the brands met the USP requirement for content of active ingredient (100.0-110.0%). The recovery of the drug from tablets ranged between 97.54-100.3%. The spectrophotometric assay method used is a simple, sensitive, economical and extraction-free method. It is recommended for routine quantitative analysis of ofloxacin tablets.

Keywords: Ofloxacin; Antibiotic; Spectrophotometric assay; Bromothymol blue

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INTRODUCTION

Ofloxacin is a broad spectrum second-generation fluorinated quinolone antibacterial drug which is active against most Gram-negative aerobic bacteria, many Gram-positive aerobic bacteria and some anaerobes [1-3]. It is useful in the treatment of respiratory tract infections, urinary tract infections, reproductive tract infections, and gastrointestinal tract infections caused by susceptible bacteria strains [4-6]. It is used in conjunction with other drugs to treat Helicobacter pylori infection and duodenal ulcer infection [7-11]. It acts by inhibiting DNA gyrase, a type II topoisomerase, and topoisomerase IV, which is an enzyme necessary to separate replicated DNA in bacteria, thereby inhibiting bacterial cell division [12,13]. Like other fluoroquinolones, ofloxacin forms a chelate complex with antacids and metallic cations which leads to altered absorption and bioavailability of the drug [14].

Many companies manufacture and distribute ofloxacin. Many brands of ofloxacin manufactured in different countries are available in Akwa Ibom State, Nigeria. Falsified and counterfeit drugs, when consumed result in devastating outcomes [15,16]. With the presence of several brands and generics of the drug in the market, there is the probability of making inappropriate decision on the suitable brand to purchase, which could lead to the purchase

of substandard brands of the drug with ultimate poor clinical outcome and threat to health. Improve surveillance of counterfeit medicines and communication of risk information to stakeholders is encouraged [17]. Previous works on some anti-infective agents showed that some brands did not comply with compendia (British Pharmacopoeia and United States Pharmacopoeia) for percentage drug content [18,19]. Therefore, the need to evaluate the quality of various brands of ofloxacin in the market cannot be overemphasised. The study employed a novel easy-to-use, accurate, reproducible and simple analytical procedure for the assay of ofloxacin.

Spectrophotometric assay of ofloxacin based on ion-pair complexation (reaction) is a simple, sensitive, economical and extraction-free spectrophotometric method. Spectrophotometry as a whole is characterized by its speed and simplicity, accuracy and inexpensive instrument needed. Hence, it is an important alternative to other analytical techniques with clear advantages in terms of analysis. Few ultraviolet spectrophotometric methods have been reported for determination of ofloxacin in dosage forms. The most widely used technique has been visible spectrophotometry and methods based on diverse reaction chemistries such as oxidative coupling reaction using Ce(IV)-MBTH [20], condensation with citric acid acetic-anhydride. [21], complex formation with iron(III)nitrate nonahydrate, iron(III)chloride in HCl medium [22], ion-pair complex with tropaeolin and supracene violet 3B 200 or with bromophenol blue (BPB) and bromocresol purple (BCP) [23]. Most of the above visible spectrophotometric methods suffer from one or other disadvantages such as use of expensive reagents, use of heating step, poor sensitivity, liquid-liquid extraction step and close pH control.

EXPERIMENTAL SECTION

Materials

Ten brands of 200mg ofloxacin tablets within their shelf-life were bought from different pharmacies in Uyo and coded A to J. These were used for the assay. The reagents were of analytical grade and used as purchased.

Extraction of Pure Ofloxacin

Ten tablets of the innovator brand (Tarivid) were pulverized and 10ml dichloromethane added and shaken for 20 minutes to allow the extraction of ofloxacin into the liquid phase. The mixture was filtered using a Whatman filter paper and the filtrate was placed in a petri dish to allow for evaporation of dichloromethane. The dichloromethane evaporated, leaving the dried ofloxacin powder which appeared as pale yellow crystals with bitter taste. The ofloxacin pure sample extracted was evaluated to ensure its authenticity.

Weight Analysis

20 tablets of each brand were randomly selected and weighed individually using electronic balance (Shimadzu Japan). The average of three weight determinations of each tablet was obtained. The mean weight, standard deviation and percentage deviation of each brand were calculated.

Friability Test

Five tablets of each brand were randomly selected and weighed together to obtain weight W0. Each brand was subjected to friability test using a Veego Friability Test Apparatus at 25rpm for 4 minutes after which each batch was reweighed to obtain weight W. The percentage weight loss was calculated (W0-W).

Hardness Test: Five tablets of each brand were randomly selected and subjected to crushing force using a manual hardness tester and the pressure at which each tablet crushed was recorded. The average crushing pressure required for each brand was determined.

Disintegration Test

Five tablets of each brand were randomly selected and put in a digital tablet disintegration test apparatus using 900ml distilled water as the disintegration medium at 37°C ± 0.5°C. The time taken for each of the tablets to disintegrate completely was recorded and the average disintegration time for each brand determined.

Dissolution Test

This test was carried out using a digital tablet dissolution test apparatus. 0.1N HCl (900 mL) was used as the dissolution medium with bath temperature of 37°C ± 0.5°C. For each brand of Ofloxacin, the test was carried out in 3 replicates. The duration of the test was 30 minutes and 10 ml dissolution sample were withdrawn at 5, 10, 15, 20 and 30 minutes and replaced with equal volume to maintain sink condition. The withdrawn samples were filtered using the Whatman filter paper and assayed by UV-VIS spectrophotometer at 294nm against the reagent blank. The concentration of each sample was determined from a calibration curve obtained from standard samples of Ofloxacin

and the amount of drug released calculated as concentration (mg/mL) × dissolution bath volume (mL). The percentage drug release was calculated.

Standard Graph for Ion-Pair Complexation Spectrophotometric Assay

Standard solution of ofloxacin (25 mg/L) was prepared using dichloromethane as solvent. The standard solution (2 ml) was transferred into a 5 ml volumetric flask, and 1 ml of 0.03% Bromothymol blue in dichloromethane was added and made up to mark using dichloromethane. The solution was scanned in a range of 360nm to 480nm against 1 ml blank solution to obtain the wavelength of maximum absorbance. From the standard solution was taken 0.25 ml, 0.50 ml, 1.00 ml, 2.00 ml and 4.00 ml and transferred into different 5ml volumetric flasks. 1ml of 0.03% bromothymol blue in dichloromethane was added to each volumetric flask, made up using dichloromethane and the absorbance of the yellow-coloured chromogen was measured at 410nm (wavelength of maximum absorbance) against the reagent blank. A standard graph was obtained by plotting the increasing absorbance values versus concentration of ofloxacin.

Spectrophotometric Assay of Various Brands of Ofloxacin Tablets

Five tablets of each brand were randomly selected, weighed and pulverized. Portion equivalent to 2.5 mg ofloxacin were transferred into 100 ml volumetric flasks, 30 ml of dichloromethane added to each and shaken for 20 minutes. It was then made up using dichloromethane and filtered using a Whatman filter paper. Aliquots of 0.25 ml, 0.50 ml, 1.00ml, 2.00 ml and 4.00 ml of each brand were transferred into different 5ml volumetric flasks and made up using dichloromethane. The absorbances were measured at 410nm against the reagent blank and the concentrations and percentage purity were calculated.

RESULTS AND DISCUSSION

All the brands complied with the British Pharmacopoeia [24] specification for weight uniformity of uncoated tablets which is 5% of deviation from the mean value (Table 1). Strict adherence to Good Manufacturing Practice during the granulation and compression stages ensures tablet weight uniformity. Two brands (F and J) failed the friability test with a weight loss of more than 1% (Table 2). Poor friability property could result in chipping of tablets during transportation as a result of abrasion, and it is an evidence of poor production. Only one of the brands (B) tested showed a suboptimal crushing strength for the hardness test with a value of 3.9Kg/cm2 as against the prescribed range of 4-10 Kg/cm^2 (Table 3). The British Pharmacopoeia specifies that uncoated tablets should disintegrate within 15 minutes and the film coated tablets in 30 minutes, while the United States Pharmacopoeia [25] specifies that both uncoated and film coated tablets should disintegrate within 30 minutes. All the brands tested disintegrated within the prescribed limit of 15 minutes (Table 4). The presence of suitable disintegrants in adequate proportion ensures the production of tablets free of disintegration problems [26]. Figure 1 is a graphical representation of the dissolution profile of the different brands of ofloxacin. The USP specifies that up to 80% of an immediate-release ofloxacin tablets is expected to dissolve in 30 minutes. All the brands except brands B, E and F passed the USP specification of 80% dissolution in 30 minutes for ofloxacin tablets. The dissolution of drug from oral solid dosage forms is a useful index in predicting the probable in vivo performance of a drug as well as identifying unacceptable and poor quality drug products [27,28]. The difference factor (f1) and the similarity factor (f2) were calculated to compare the dissolution profile of the various brands with the innovator product (Table 5). Two dissolution profiles are considered similar and bioequivalent if f1 is between 0 and 15 and f2 is between 50 and 100 [29]. The f1 and f2 values with respect to brand I which is the innovator brand is shown in Table 5. All the brands gave f1 values between 0 and 15 and f2 values between 50 and 100 except C, F and G which gave f2 values below 50. The brands A, B, D, E, H and J can be used interchangeably with the innovator product (brand I). Figure 2 represents Calibration curve of ofloxacin pure sample.

From the ion-pair complexation spectrophotometric assay, all the brands complied with the United States Pharmacopoeia specified limit of percentage purity (90%-110%) (Table 6). The ion-pair complexation spectrophotometric assay of ofloxacin using bromothymol blue in dichlorometane as solvent is a novel method for assay of ofloxacin which is very simple, rapid and cost effective. It requires dye and reagents which are cheap, readily available and can be applied at ambient temperature. The colour development is instantaneous and does not involve strict pH adherence or a complicated extraction step. It is suitable for quality control and routine analysis of ofloxacin.

Table 1: Weight uniformity analysis of different brands of ofloxacin tablets

Sample	A	B	C	D	E	F	G	H	I	J
Mean weight (mg)	724.9	509.4	414.3	569.0	610.0	254.5	385.1	247.9	400.1	414.4
SD (n=10)	±6.3	±7.0	±5.6	±10.5	±3.3	±4.3	±5.3	±2.3	±4.6	±2.1
% Deviation	1.8	1.4	1.3	1.8	0.5	1.7	1.4	0.9	1.2	0.5

Permissible percentage deviation is 5%

Table 2: Friability analysis of different brands of ofloxacin tablets

Sample	A	B	C	D	E	F	G	H	I	J
W0(g)	3.60	2.51	2.08	2.83	3.04	1.25	1.91	1.23	1.99	2.10
W(g)	3.59	2.50	2.06	2.81	3.03	1.23	1.10	1.22	1.98	2.05
W0-W	0.01	0.01	0.02	0.02	0.01	0.02	0.01	0.01	0.01	0.05
% Weight loss	0.28	0.39	0.96	0.71	0.33	1.60	0.52	0.81	0.50	2.50

Permissible percentage weight loss is 1%

Table 3: Hardness analysis of different brands of ofloxacin tablets

Sample	A	B	C	D	E	F	G	H	I	J
Average crushing strength (Kg/cm2	4.80	3.90	4.30	4.10	4.20	5.80	4.10	5.10	4.20	6.70
±SD (n=10)	0.36	0.37	0.79	0.30	0.51	0.24	0.37	0.24	0.24	0.40

Permissible crushing strength is 4-10 Kg/cm2

Table 4: Disintegration analysis of different brands of ofloxacin tablets

Sample	A	B	C	D	E	F	G	H	I	J
Mean disintegration time (min)	5.23	3.68	4.97	1.11	4.62	7.53	10.43	7.35	13.16	1.74
±SD (n=10)	6.85	9.45	11.62	4.44	9.35	9.09	11.85	10.32	7.09	2.73
% Deviation	2.09	4.27	4.07	6.70	3.33	2.01	1.85	2.34	0.89	2.61

Permissible disintegration time is 15 minutes

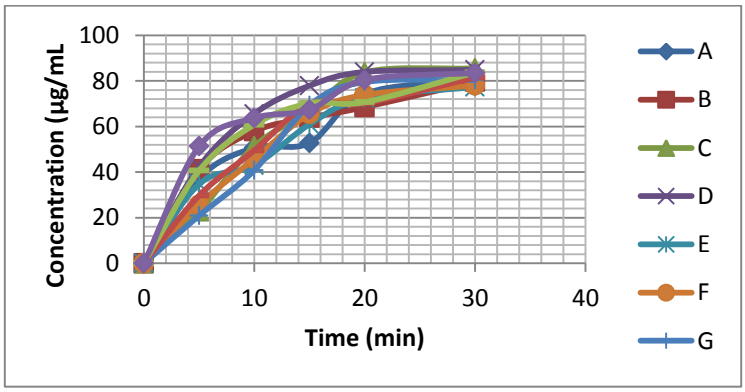

Figure 1: Graph of dissolution test result of different brands of ofloxacin tablets

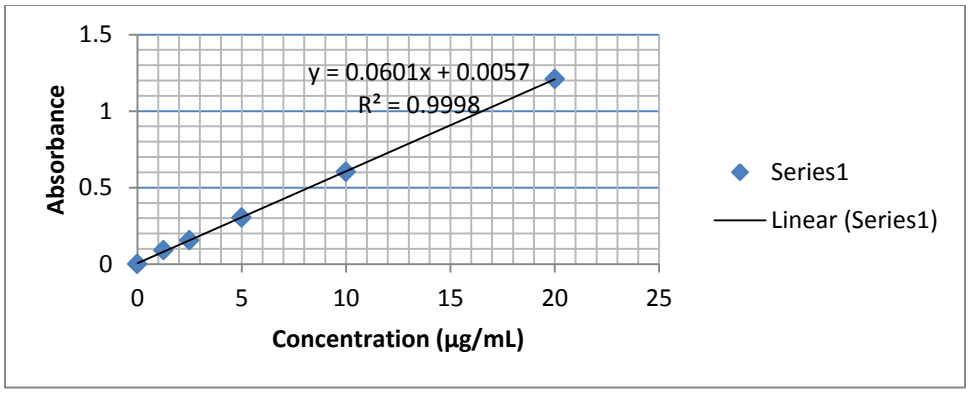

Figure 2: Calibration curve of ofloxacin pure sample

Table 5: f1 and f2 values of the various brands of ofloxacin tablet 200 mg compared with the innovator brand I.

Sample	A	B	C	D	E	F	G	H	J
f1	9.30	4.57	4.92	8.42	11.51	12.35	10.78	7.78	6.26
f2	51.22	70.44	47.97	56.86	50.22	47.70	43.90	57.21	72.27

Table 6: Result of ion-pair complexation spectrophotometric assay

Sample	A	B	C	D	E	F	G	H	I	J
Percentage content %	100.25	98.24	98.89	98.75	97.57	97.97	99.60	99.22	98.16	97.74
±SD (n=5)	5.07	0.86	0.67	0.83	1.53	1.03	1.46	1.45	0.33	1.47

CONCLUSION

All the brands met the British Pharmacopoeia specification for tablet purity. The spectrophotometric assay method used, and which was based on ion-pair complexation (reaction) of ofloxacin with bromothymol blue in dichloromethane as solvent, is a simple, sensitive, economical and extraction-free method. It is recommended for routine quantitative analysis of ofloxacin tablets.

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