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Quality Assessment of Various Brands of Ciprofloxacin Hydrochloride Tablets Sold In Uyo Metropolis

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ABSTRACT

Ciprofloxacin is a flouroquinoline antibiotic with a broad spectrum of activity used for the treatment of various bacterial infections including anthrax. The use of substandard or fake ciprofloxacin products will jeopardise their usefulness. Hence, the need for provisions of simple and cost-effective method(s) of assay that will encourage regular and quick sampling of ciprofloxacin tablets. Different brands of ciprofloxacin hydrochloride tablets purchased randomly from drug stores in the study centre, and coded A-J, were assayed for weight uniformity, friability, hardness, disintegration, dissolution rate using standard physical methods. Their percentage drug contents were determined using spectrophotometric and titrimetric methods. The spectrophotometric measurement was done at a wavelength of 276nm while the titrimetric method was based on oxidative reaction between ciprofloxacin and potassium permanganate yielding the oxide as a greyish pink colour at end point. All the brands met the requirements for weight uniformity, friability, disintegration and dissolution. Only one brand, sample E, failed the hardness test. The titrimetric and spectrophotometric assay showed that seven of the brands met the British Pharmacopoeia requirement for percentage drug content (95.0-105.0%). Statistical analysis showed no significant difference ($p<0.05$) between the results obtained from both the titrimetric and spectrophotometric methods. The two methods are reliable, simple and cost-effective and can be routinely used to assay ciprofloxacin tablets.

Keywords: Ciprofloxacin, antibacterial, titrimetric, spectrophotometric, assay.

INTRODUCTION

Ciprofloxacin is a broad spectrum second-generation fluorinated quinolone antibacterial drug available for oral, parenteral and ophthalmic administration (Ghelani, 2017; Drugs.com, 2018). It is in the 19th World Health Organisation (WHO) Model List of Essential Medicines (WHO, 2015). It is useful in the treatment of respiratory tract, urinary tract, reproductive tract and gastrointestinal tract infections as well as many other bacterial infections caused by susceptible strains (Dixon et al., 1999; Centers for Disease Control and Prevention, 2001; Stamm and Norrby, 2001; American Academy of Pediatrics, 2015). It acts by inhibiting DNA gyrase (a type II topoisomerase) and topoisomerase IV thereby inhibiting bacterial cell division (Bearden and Danziger, 2001). As with other fluoroquinolones, ciprofloxacin forms a chelate complex with antacids and metallic cations which leads to altered absorption and bioavailability of the drug (Uivarosi, 2013).

Due to the fact that different companies manufacture and distribute ciprofloxacin, there is the risk of purchasing substandard brands which could result in poor clinical outcome and threat to health. The results of consuming falsified, substandard or counterfeit drugs could be devastating (Weaver and Whalen, 2012; Ubajaka *et al*., 21016). Enhanced surveillance for counterfeit medicines and improvement in communication of risk information to stakeholders with the ultimate aim of protecting the consumer has been recommended (Mackey *et al*., 2015). Regular monitoring of drugs in circulation is one way of improving surveillance. For ciprofloxacin, this monitoring could be encouraged by provision of simple, easy to use, accurate and reproducible analytical assay procedure.

EXPERIMENTAL

Materials: Ten brands of 500mg ciprofloxacin tablets within their shelf-life purchased from different pharmacies in Uyo and coded A to J were used for this assay. The reagents were of analytical grade and used as purchased.

Extraction of pure ciprofloxacin: Ten tablets of brand A were pulverized and extracted using 40ml methanol, filtered and evaporated to obtain pure ciprofloxacin. Ciprofloxacin hydrochloride pure sample extracted was evaluated to ensure its authenticity. The extracted drug (0.1g), was accurately weighed and dissolved in 25mL of 0.01M NaOH in a 100mL volumetric flask. This was shaken and made up to volume with 0.01M NaOH.

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The resulting solution was then scanned for maximum wavelength of absorption (λmax) using UV-Vis Spectrophotometer at the wavelength (λ) range of 200-300nm. The highest absorbance was observed at a λ of 276nm which corresponds to that found in the literature.

Weight Analysis: Twenty tablets of each brand were randomly selected and weighed individually using electronic balance (Shimadzu, Japan). The mean weight, standard deviation and percentage deviation of each brand calculated.

Friability Test: Ten tablets of each brand were randomly selected and weighed together to obtain weight W_o. Each brand was subjected to friability test in a Roche friabilator at 25 revolutions per minute for 4 minutes after which each batch was reweighed to obtain weight W. The weight loss was calculated (W_o-W).

Hardness Test: Five tablets of each brand were randomly selected and subjected to crushing force using a Mosanto hardness tester. The average crushing pressure required for each brand was determined.

Disintegration Test: Six 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 37^0C. The time taken for each brand to disintegrate completely was recorded.

Dissolution Test: The dissolution profile of each brand of ciprofloxacin was measured according to the method described in British Pharmacopoeia (2008) using a digital tablet dissolution apparatus in 900ml of 0.1N HCl at 37^0C.

Spectroscopic assay: Pure ciprofloxacin sample 100mg was dissolved in 100ml of 0.01M NaOH to obtain a stock solution of 1mg/ml. From the stock solution 5ug/ml, 10ug/ml, 20ug/ml, 30ug/ml, 40ug/ml and 50ug/ml working solutions were prepared and their absorbance measured at 276nm. The absorbance versus concentration graph was plotted to obtain the standard calibration curve. Twenty tablets of each brand of ciprofloxacin tablet were pulverised and portions equivalent to 100mg of drug extracted with 100ml of 0.01M NaOH to give stock solutions of 1mg/ml of each of the brands. Aliquots of 10ug/ml of each brand were prepared from each stock and their respective absorbance measured at 276nm. These were extrapolated on the standard curve to obtain the respective extrapolated concentrations. The percentage recoveries were obtained by comparing the extrapolated concentrations with the expected concentrations (label claim).

Titrimetric assay: Portions of each brand of the powdered drug samples equivalent to 100mg ciprofloxacin were dissolved in 1M H_2SO_4, filtered and made up to 100ml using distilled water to give solutions of 10ug/ml. 25ml of each of the resulting solutions were transferred into 250ml conical flasks, 10ml of 0.02M standardized potassium permanganate ($KMnO_4$) added to each, thoroughly mixed and set aside for 15 minutes. The un-reacted oxidant in each sample was back titrated with 0.1M ferrous sulphate solution. A blank titration was performed simultaneously and the amount of ciprofloxacin in the measured aliquot calculated from the amount of $KMnO_4$ that reacted with the drug in the various samples. The potassium permanganate was standardized by the method described by Olaniyi and Ogungbamila (1998).

RESULTS AND DISCUSSION

All the brands complied with the British Pharmacopoeia (2008) specification for weight uniformity of uncoated tablets which is 5% of deviation from the mean value (Table 1). Strict adherences to Good Manufacturing Practice during the granulation and compression stages ensure tablet weight uniformity. All the brands passed the friability test as they all had a weight loss of less than 1% (Table 2). Good friability property ensures tablets do not chip during transportation as a result of abrasion and is an evidence of good finished product. One brand (E) showed a suboptimal crushing value of 3.9Kg/cm^2 as against the prescribed range of 4-10Kg/cm^2 (Table 3). All the brands tested disintegrated within the prescribed limit of 15 minutes (Table 4). The presence of suitable disintegrants in adequate proportions ensures the production of tablets which are free from disintegration problems (Jantratid *et al*., 2008). Figure 1 is a graphical representation of the dissolution profile of the different brands of ciprofloxacin. All the brands passed the British Pharmacopoeia (2008) specification of 70% dissolution in 30 minutes for uncoated tablets. The dissolution of drug from oral solid dosage forms is a necessary criterion for determination of drug bioavailability. It serves as useful tool in assessing the probable in vivo performance of a drug as well as in identifying unacceptable and substandard drug products (Shah, 2001; Jaman *et al.*, 2015).

From the quantitative assay results only seven out of the ten brands (70%) met the British Pharmacopoeia (BP) 2015 specification (95-105%) (British Pharmacopoeia, 2015). Adegbolagun et al., (2008) used a non-aqueous titrimetric method to assay ten brands of ciprofloxacin. They had recoveries of 19.7-87.27% for three brands, 90.03-90.62% for six brands and 96.17% for one brand.

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

Sample	A	B	C	D	E	F	G	H	I	J
Mean weight(mg)	736.8	763.0	805.5	756.5	974.5	736.8	660.5	748.9	782.0	866.0
SD (n=10)	±8.73	±6.62	±3.64	±8.45	±3.35	±8.73	±6.40	±9.33	±6.11	±6.64
% Deviation	1.18	0.87	0.45	0.01	0.34	0.01	0.97	1.25	0.78	0.77

Permissible percentage deviation is 5%

Table 2: Friability analysis of different brands of ciprofloxacin tablets

Sample	A	B	C	D	E	F	G	H	I	J
W_0(mg)	7368	7631	8056	7565	9745	9274	6605	7490	7820	8660
W(mg)	7363	7623	8046	7522	9702	9268	6600	7477	7816	8652
W_0-W	5	8	10	45	43	6	5	13	4	8
% Weight loss	0.67	0.1	0.12	0.57	0.44	0.065	0.076	0.17	0.05	0.09

Permissible percentage weight loss is 1%

Table 3: Hardness analysis of different brands of ciprofloxacin tablets

Sample	A	B	C	D	E	F	G	H	I	J
Average crushing strength (Kg/cm^2)	7.18	6.08	6.10	7.42	3.22	7.38	6.10	7.06	9.06	5.90

Permissible crushing strength is 4-10 Kg/cm^2

Table 4: Disintegration analysis of different brands of ciprofloxacin tablets

Sample	A	B	C	D	E	F	G	H	I	J
Mean disintegration time (min)	4.28	2.60	8.18	2.45	0.41	4.52	3.00	8.30	13.03	6.35

Permissible disintegration time is <15 minutes

They concluded that 70% (seven brands) of the brands assayed conformed to the compendium specification for content of active ingredient of ciprofloxacin. However, this is because they considered their results using United States Pharmacopoeia (USP) specification which allowed a wider range (90-110%) of recovery (United States Pharmacopoeia, 2000 and 2014). If they had applied British Pharmacopoeia specification, which is a narrower margin, only one of the brands which had 96.17% recovery would have passed the test. Some other workers had applied USP specification and had given pass mark to products that would have otherwise failed the test if they had used BP specification (95-105%). Earlier works by Getu and Awot (2010) and Igboasoiyi et al., (2014) employed the BP specification in arriving at their conclusions. There is need to harmonise the specifications (BP and USP) so that the manufacturers and researchers will be adequately guided. The BP range of 95-105% which is actually 100%±5.0 is recommended as it will challenge manufacturers to employing the finer points of quality assurance to ensure better products that will realise desired treatment outcomes

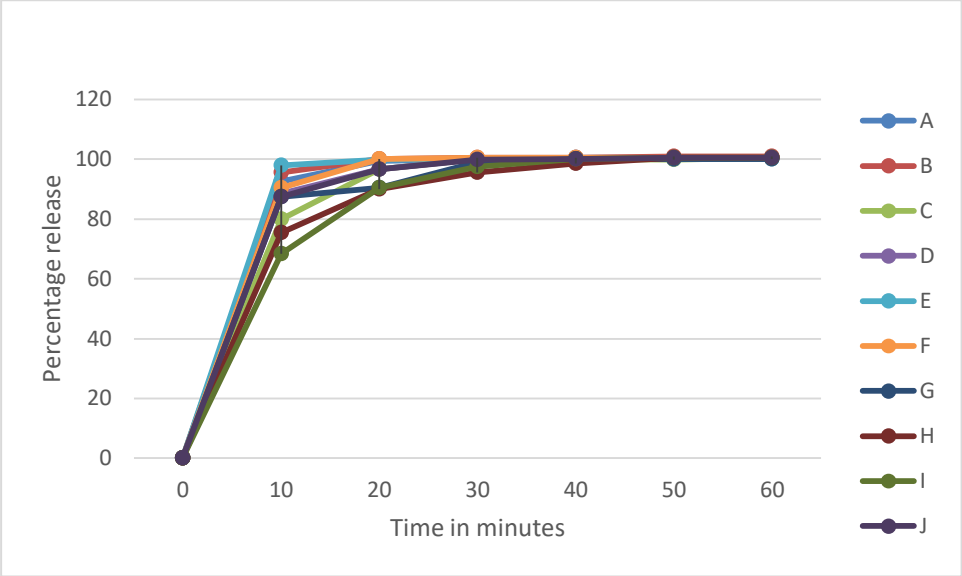

Figure 1: Graph of dissolution of different brands of ciprofloxacin tablets.

The spectrophotometric assay showed that all the brands tested had drug content of between 94.5% and 99.3% (Table 5) and the titrimetric assay showed drug contents of between 91.4% and 99.2% (Table 6).

Table 5: Result of UV-Vis spectrometry assay of ciprofloxacin 500mg

Sample	A	B	C	D	E	F	G	H	I	J
Recovery (%)	95.6	99.3	98.8	97.0	94.0	96.8	92.8	94.5	97.5	97.0

Table 6: Result of titrimetric assay of ciprofloxacin 500mg

Sample	A	B	C	D	E	F	G	H	I	J
Amount (mg)	475.6	496.2	490.5	486.0	468.1	483.0	460.5	456.8	488.7	485.0
% purity	95.1	99.2	98.1	97.3	93.6	96.6	92.1	91.4	97.7	97.0

The back-titration method using KMnO4 which has been described in this work is affordable and easily applicable. Statistical analysis using student t-test showed that the difference between the results obtained from the spectrophotometric and titrimetric assay methods were not significant at $P < 0.05$ confidence level for all the brands analysed. This shows that either of the methods is reliable and accurate. The two assay methods adopted in this study are simple, cost effective, reproducible and sufficiently sensitive and can be routinely used to quickly assay brands of ciprofloxacin HCl to ascertain the quality and purity.

CONCLUSION

Seven out of the ten brands analysed (70%) met the British Pharmacopoeia specification for tablet purity (95-105%). There is need to harmonise the compendia specifications on acceptable content of active ingredients. The two assay methods adopted in this study are simple, cost effective, reproducible and sufficiently sensitive and can be routinely used to quickly assay brands of ciprofloxacin HCl to ascertain the quality and purity.

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