COMPARATIVE EFFECT OF ENVIROMENTAL EXPOSURE ON THE QUALITY CONTROL ASSESSMENT OF CIPROFLOXACIN TABLET MARKETED IN GOMBE SOUTH, NIGERIA

Usman M.A,[*1] Auwal S,[*1] Zezi A.U,[*2] Ya'u J,[*2] Buba I[*2,3]

[*1]Department of Pharmaceutical and Medicinal Chemistry Ahmadu Bello University Zaria, Nigeria.
[*2]Department of Pharmacology and Therapeutics, Faculty of Pharmaceutical Sciences, Ahmadu Bello University Zaria, Nigeria.
[*3]Federal Teaching Hospital, Gombe.

* Corresponding author: (musaua@gmail.com)

Abstract

In Nigeria, ciprofloxacin is commonly prescribed in the treatment of infectious diseases. Massive importation with poor market regulations has allowed the product to be handled by non-professionals. This has led to poor storage and the drug being exposed to adverse environmental factors like; heat, light, moisture thereby causing deterioration of the product. The quality assessment test for environmentally exposed ciprofloxacin was compared with non-exposed tablet. The tests carried out were; Identification, assay, disintegration, friability and dissolution. From the results obtained, both the exposed and non-exposed responded positively to chloride test according to B.P 2002 specification, confirming the presence of ciprofloxacin hydrochloride. The percentage (%) content (assay) of the exposed and the non-exposed were 82.9 and 98.3 respectively (the acceptable range is 95-105%). The disintegration and friability tests for both the exposed and non-exposed were within the established specification of ≤30 min (for film coated tablet) and ≤ 1% respectively. The values obtained were 4.21 and 2.94 min for disintegration, and 0.16 and 0.00% for friability test respectively for the exposed and non-exposed. The percentage released for the exposed and non-exposed tablets were 66.0 and 98.0 respectively (the acceptable limit is ≥ 70%). In conclusion, exposure of ciprofloxacin to unfavorable condition such as sunlight, humidity, moisture and poor storage condition of Gombe South town (Billiri) lead to decrease in percentage content and percentage drug release of ciprofloxacin hydrochloride in the tablet sample indicating eventual low quality tablet.

Keywords: *BP 2002, Ciprofloxacin, Environmental Exposure, Gombe South, Quality Control.*

Introduction

In order to maintain quality, drug manufacturers are expected to test their products during and after manufacturing and at various intervals during the shelf life of the product (Akpabio *et al*., 2011). Quality control is a step taken to ensure that drugs conform to certain specifications. Ciprofloxacin is bactericidal drug that acts by inhibiting the bacterial DNA gyrase (topoisomerase) which is essential in the reproduction of bacterial DNA (Katzung *et al.,* 2009). Adverse reactions associated with ciprofloxacin administration are generally mild to moderate. The most commonly reported adverse reactions involve the gastrointestinal tract (nausea, vomiting and diarrhoea), metabolic or nutritional disorders, or the CNS (Vance-Bryan *et al.,* 1990). There are several brands available in the Nigerian market and due to its versatility it is commonly prescribed empirically by physicians for the treatment of infectious diseases. This led to an increased in importation of the drug into the Nigerian market that is poorly regulated. The choatic market led to

drugs being handle by hawkers (Adegbolagun *et al.,* 2007; Ngwuluka *et al.,* 2009; Ogar *et al.,* 2015). This study is aimed at simulating the environment of the drug hawkers in Gombe South who carry and sell drugs in boxes, bags, baskets and store them in a poor storage conditions and to carry out quality control assessment to know how these can affect the quality of ciprofloxacin.

Chemistry

Ciprofloxacin is a quinolone-carboxylic acid derivative with an extensive antibacterial spectrum of activity (Uduma *et al.,* 2011). Ciprofloxacin is 1-cyclopropyl-6-fluoro-1, 4-dihydro-4-oxo-7-(1-piperazinyl) 3quinolinecarboxylic acid. Ciprofloxacin hydrochloride is the monohydrochloride monohydrate salt of ciprofloxacin. It is a faintly yellowish to light yellow crystalline substance with a molecular weight of 385.8 g/mol. Its empirical formula is C 17 H 18 FN 3 O 3 HCl•H 3 O (Ali, 2014). Its melting process with decomposition is around 270°C to 385°C (Khan *et al.,* 2009).

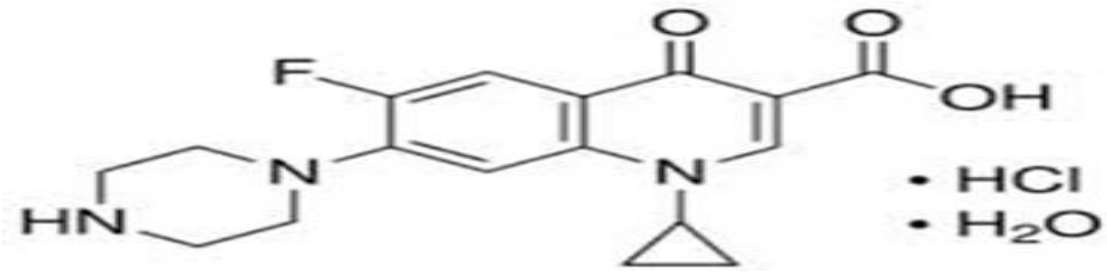

Figure: Chemical structure of Ciprofloxacin hydrochloride (1-cyclopropyl-6-fluoro-1, 4-dihydro-4-oxo-7-(1-piperazinyl)-3quinolinecarboxylic acid)

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Materials and methods

Drugs

Pharmaceutical grade (Standard) Ciprofloxacin powder (M&B–UK)

Ciprofloxacin tablet (EVANS) 500mg with

Brand name: Rapiflox^{R}

Batch number: E413

NAFDAC number: 04-3221

Manufacturing date: 02/05/14

Expiring date: 01/05/18

Reagents

The following solvents of analytical grade were used: 0.1M HCI (M&B–UK), Ethanol, Methanol, Chloroform, Acetone (Sigma-Germany), acetonitrile and Distilled water.

Phosphate buffer (pH 4 & 8) BDH (UK)

Apparatus and Equipments

The following apparatus and equipments were used:

UV spectrophotometer (Thermo-Scientific Helios Zeta UV-Vis, ser. no; UV2-164917) with1cm path length

Analytical weighing balance (DENVER-ISTRUMENT (Apx-200)

Friabilator

Disintegration apparatus (Erweka)

Dissolution apparatus (USP apparatus-basket method)

Method

The methodology of the study involved exposing some few sachets of the drug samples to Gombe South environmental condition for three (3) months. Drug hawker was used as a means of exposure and was selected from the market in Billiri town which is located in Gombe South (exposure zone). Quality control tests of the exposed and the non-exposed samples were carried out using B.P 2002 methods which include: Identification, Assay, Friability, Disintegration and Dissolution tests.

Results

Table 1: Results for the identification test of exposed and non-exposed ciprofloxacin

Sample	Observation	Remark
Exposed	White precipitate*	Passed
Non-Exposed	White precipitate*	passed

* The appearance of white precipitate indicate positive chloride test (BP, 2002)

Table 2: Results for the assay of exposed and non-exposed ciprofloxacin tablets

Sample	Normal range (%)	Yield (%)	Remark
Exposed	95-105	82.9	failed
Non-exposed	95-105	98.3	passed

The limit for ciprofloxacin tablet content as specified by BP 2002 is given in the table above

Table 3: Results for the disintegration test of exposed and non-exposed ciprofloxacin tablets

Samples	Average disintegration Time (min) ± SEM	Remark
Exposed	4.21± 0.76	passed
Non-exposed	2.94 ± 0.30	passed

Film coated tablets (e.g ciprofloxacin) should disintegrate within 30 min (BP, 2002). SEM = Standard error of the mean

Table 4: Results for the friability test of exposed and non-exposed ciprofloxacin tablets

Sample	Weight before test (g)	Weight after test (g)	Friability (%)	Remark
Exposed	6.42	6.26	0.16	passed
Non- exposed	6.39	6.39	0.00	passed

The (BP 2002) acceptable percentage (%) Friability is ≤ 1%.

Table 5: Results for the dissolution rate in 0.1N HCl at 45 min

Sample	% Release (t=45 min.)	Remark
Exposed	66.0	Failed
Non-exposed	98.0	Passed

Minimum percentage (%) drug released ≥ 70% (BP, 2002)

Discussion

The brand of the ciprofloxacin hydrochloride (Rapidflox^{R}) tablet was obtained directly from a pharmaceutical company (EVANS) in which half (5 packs) were given to hawkers in Billiri town of Billiri Local Government area of Gombe south for exposure to environmental forces like: sunlight, heat, and relative humidity for a period of three month. They were then subjected to a number of tests in order to assess the effect of the exposure on the drugs. Biopharmaceutical and chemical equivalent assessment were carried out. The assessment involved the use of both qualitative and quantitative method of evaluation. The qualitative method involved descriptive study through visual observation while the quantitative evaluation used tests such as: friability, disintegration, dissolution, as well as chemical content determination. The identification test revealed that both exposed and non-exposed samples contained ciprofloxacin hydrochloride as they gave white precipitates which indicate positive chloride test (BP 2002). The friability and disintegration test results obtained for the exposed and non-exposed were within official specification of film coated tablet. The percentage friability of the exposed was 0.16% and that of the non-exposed was 0.00%; both the former and the later passed the test, since both have percentage friability falling within the permissive limit of $\leq$ 1%.

The dissolution rate profile revealed that the non-exposed samples passed (98.0%) but the non-exposed sample failed, with 66% drug released. This could be due to the effects of the exposure. Also, the BP has provided guidelines for the equivalence studies of pharmaceutical active ingredient, the ascribed limit of active constituent in ciprofloxacin HCl tablet is 95-105%, from this research work, the percentage yield of ciprofloxacin from the exposed and non-exposed were 82.9% and 98.3% respectively. Thus, the percentage yield of ciprofloxacin from the non-exposed is within the permissible limit. Whereas, the percentage yield of the exposed brand is below the normal range indicating low quality probably due to the effects of the environmental exposure. In a similar study on products of photodegradation of quinolones antibiotics formed outside the organism under natural and artificial light conditions was found to be associated with loss of antibacterial activity, as well as occurrence of side effects and phototoxicity (Tiefenbacher *et al.*, 1994).

Conclusion

In conclusion, all the parameters measured in the quality control tests for the non-exposed ciprofloxacin tablet has a value within the acceptable range in the BP 2002 specifications while the dissolution and the assay parameters for the exposed sample did not. This is likely due to the effects of environmental factors such as: light, temperature, moisture as a result of poor storage condition etc.

Recommendation

In-vivo studies like bioavailability studies and microbiological assay of ciprofloxacin tablet and other antibiotics should be carried out in the exposed site (Gombe South).

All stake holders in the pharmaceutical industry should ensure proper storage of all pharmaceutical products especially antibiotics so as to prevent deterioration due to exposure to environmental forces like: sunlight, heat, dust and moisture.

References

Adegbolagun, O., O. Olalade, & S. Osumah. (2007). Comparative evaluation of the biopharmaceutical and chemical equivalence of some commercially available brands of ciprofloxacin hydrochloride tablets. *Tropical journal of pharmaceutical research, 6*(3), 737-745.

Akpabio, E., C. Jackson, C. Ugwu, M. Etim, & M. Udofia. (2011). Quality control and in vitro bioequivalence studies on four brands of ciprofloxacin tablets commonly sold in Uvo Metropolis Nigeria. *J. Chem. Pharm. Res, 3*(3), 734-741.

Ali, K. F. (2014). Estimation and veluation of the effect of pH on ciprofloxacin in drug formulations. *Journal of Chemical and Pharmaceutical Resaerch, 6(4)*, 910-916.

British Pharmacopoeia (2002). vol. I and II, Her Majesties Stationary office, University Press Cambridge.

Katzung, B., S. Masters, & A. Trevor. (2009). Basic and Clinical Pharmacology. MaGraw-Hill Companies. *Inc., New York.*

Khan, M. K., M. F. Khan, H. Khan, & G. Mustafa. (2009). Bioavailability of ciprofloxacin tablets in humans and its correlation with the dissolution rates. *Pak. J. Pharm. Sci, 22*(3), 329-334.

Ngwuluka, N., K. Lawal, P. Olorunfemi, & N. Ochekpe. (2009). Post-market in vitro bioequivalence study of six brands of ciprofloxacin tablets/caplets in Jos, Nigeria. *Scientific Research and Essays, 4*(4), 298-305.

Ogar J.N, Asira A.E, Eyimba M (2015). NAFDAC and Health care in Nigeria: A philosophical probe. *World Journal of public health, Water and food* 1 (1): 1-12

Tiefenbacher, E. M., E. Haen, B. Przybilla, andH. Kurz. (1994). Photodegradation of some quinolones used as antimicrobial therapeutics. *Journal of pharmaceutical sciences, 83*(4), 463-467.

Uduma, O. E., A. A. Agboke, R. C. Amadi, O. Okorie, and C. C. Opurum. (2011). Bioequivalence studies on some selected brands of ciprofloxacin hydrochloride tablets in the Nigerian market with ciproflox® as innovator brand. *Journal of applied pharmaceutical science, 1*(06), 80-84.

Vance-Bryan, K., D. R. Guay, & J. C. Rotschafer. (1990). Clinical pharmacokinetics of ciprofloxacin. *Clinical pharmacokinetics, 19*(6), 434-461.