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# Quality assessment of some brands of Ciprofloxacin tablets on sale in Abuja, Nigeria

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**Abstract**

The quality of the various brands of ciprofloxacin tablets in circulation within Abuja, the Federal Capital City of Nigeria, was assessed. Spectrophotometric evaluation showed that all the brands contained a chemical equivalent of ciprofloxacin within the limits of the official specification. However their antimicrobial activity as indicated by the zone of inhibition was less than that of the reference standard. Three of the ten samples tested failed the disintegration and dissolution tests as specified by the British Pharmacopoeia for film coated tablets.

*Keywords*: Ciprofloxacin; Quality assessment; Spectrophotometric evaluation; Microbial potency

## Introduction

The World Health Organization (WHO) at the International Conference on Primary Health Care, Alma-Ata, 1973, identified the supply of good quality essential drugs as one of the basic prerequisites for delivery of health care (WHO general report, 1988). However, the scourge of fake, substandard and adulterated drugs has seriously militated against the achievement of this especially in the developing countries.

Antibiotics are one of the most widely used, misused, abused and counterfeited class of drugs in Nigeria (Work shop paper presentation on decree No 17 of 1982). This has led to growing concern about the rapid development of resistant strains to commonly used antibiotics. In fact, experts are worried that in future, antibiotics may be unable to cure most of the infections which hitherto had been easily curtailed by them (Kolawole *et al.*, 2002; Chatley, 1999). The most common and widespread dangers associated with the use of substandard antibiotics are waste of resources, microbial resistance and the complication of diseases (Hossain *et al.*, 1999). Because of the rising population within Abuja, public health facilities are unable to cope with the pressure and as such most of the populace, especially those in the low-income bracket resort to indiscriminate drug purchase usually after a visit to private diagnostic laboratories.

Ciprofloxacin is one of the 4-quinolone carboxylic acid derivatives with a broad spectrum of antimicrobial activity. In recent times, there has been a proliferation of different brands of this antibiotic in Nigeria,

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many of which are incredibly cheap, hence the need for the assessment of their quality. A survey of the drug stores within the Federal Capital City (Abuja) has shown a stock of numerous generics of Ciprofloxacin tablets with a wide price variation.

While the International Pharmacopoeia suggests an HPLC method for the analysis of ciprofloxacin in tablet formulations, the use of a spectrophotometric method has also been reported (Eboka, 1996). This is of particular interest in the developing countries where HPLCs are not commonly available.

The objective of this study is to assess the quality of the various brands of ciprofloxacin tablets marketed within Abuja with a view to ascertaining their effectiveness. The quality parameters to be evaluated include disintegration time and dissolution profiles. The drug content of the various brands would also be determined and compared with their microbiological potency.

## Experimental

*Materials:* Ciprofloxacin crystals were obtained from Gemini Pharmaceuticals Ltd. (Representative of Bayer Pharmaceuticals in Nigeria) and used to prepare the reference standard. Ten brands of ciprofloxacin tablets were purchased from Pharmacy shops within the Federal Capital City, Abuja, Nigeria and coded alphabetically. Nutrient agar (BBL, USA) *Staphylococcus aureus* (Clinical isolate collected from Diagnostic Laboratory of National Institute for Pharmaceutical Research & Development, Idu, Abuja, Nig.) and sodium hydroxide (BDH, England).

*Packaging and product aesthetics:* The various products were assed for the tablet appearance, aesthetics and packaging quality.

*Melting point:* Method II of the BP (1993) for the determination of melting point was employed. A 1 g quantity of the reference ciprofloxacin powder was dried in a hot air oven at 100 °C for 1h. Some of this was then filled to a quarter of the length of a micro capillary tube and the melting point determined using an Electothermal melting point determination apparatus (Electrothermal Engineering Ltd. England).

*Uniformity of weight:* Twenty tablets were randomly selected and individually weighed on a balance (Mettler Toledo GmbH, USA) the mean weight and the standard deviation were then calculated from the weights obtained.

*Disintegration time:* The BP method for determination of disintegration time for film-coated tablets was used. An Erwerka BDT disintegration test apparatus (Erweka GmbH, Germany) was used to determine the disintegration time for six tablets. Simulated gastric fluid was used as the medium and maintained at a temperature of 30 ± 0.5 °C.

*Dissolution:* A BP (1993) type B (Erweka GmbH, Germany) dissolution apparatus was used at a speed of 50 rpm. The dissolution medium was buffer pH 4 solution (prepared and adjusted with glacial acetic acid) and 50% sodium hydroxide solution maintained at 37 ± 0.5 °C. 5ml samples were removed at 5 min. intervals and the drug concentrations determined using a Shimadzu UV 160 A spectrophotometer (Shimadzu, Japan) at a wavelength of 314 nm. The dissolution medium was used for all dilutions. The percentage drug released was plotted against time, to obtain the dissolution profile for each sample. The $T_{80\%}$ (time taken for 80% of the drug to dissolve) was determined.

*Content of active ingredient:* Twenty tablets of each brand of ciprofloxacin were weighed and powdered. Powder equivalent to 200 mg of ciprofloxacin was accurately weighed and dissolved in 0.1N sodium hydroxide 200 ml of solution. This was filtered and the filtrate further diluted with 0.1N sodium hydroxide to obtain a solution with an expected concentration of 10µg/ml of ciprofloxacin. The amount of ciprofloxacin contained per

tablet was determined spectrophotometrically. The percentage drug content of each brand was then calculated as in equation (1).

% Drug content = (Absorbance of test sample/ Absorbance of reference sample) x 100 ..... Eq 1

*Microbiological potency:* The method of Kings and Philip, (1986) was adopted with some modifications. The standard solution of ciprofloxacin was prepared by dissolving 50 mg of the ciprofloxacin reference standard in 25 ml of phosphate buffer pH 6 ± 0.1 in a 50 ml volumetric flask. The flask was agitated with a mechanical shaker (Vortex Genie 2, model – G-560E) for 45 min. and the volume made up to 50 ml with phosphate buffer pH 6.0. This solution was further diluted with phosphate buffer pH 6.0 to obtain a final concentration of 4 µg/ml. To prepare the test samples, 20 tablets of ciprofloxacin were weighed and powdered. Powder equivalent to 200 mg of ciprofloxacin was weighed and transferred in to a 200 ml volumetric flask containing 100 ml of phosphate buffer (pH 6.0). The flask was then agitated for 45 min. with a mechanical shaker and the volume made up to 200 ml with phosphate buffer (pH 6.0). The solution was filtered and diluted to obtain a final concentration of 4 µg/ml. The test microorganism was *Staphylococcus aureus* on nutrient agar. A 0.1 ml quantity of the standard and test samples of the drug were introduced into opposite cups in Petri plates. The plates were maintained at appropriate conditions (Temp. 25± 2°C / RH. 50±5%) to allow diffusion for 45 min. and then incubated at a temperature of 35 to 37 $^{0}$C for 24 h. After the incubation period, the zones of inhibition were then measured.

The comparative zone of inhibition was calculated relative to the zone of inhibition of the reference sample using equation 2.

Comparative Zone of Inhibition (%) = (Zone of inhibition of test sample / Zone of inhibition of reference sample) x 100 ..... Eq 2

## Results and Discussion

*Product aesthetics and packaging:* All the brands of ciprofloxacin tablets investigated (Table 1) were white oblong caplets with all their names and "500" embossed on either side of the caplets except sample J in which only the brand name was ink marked on one side. The tablets of the various brands were all packed in aluminum /plastic blister packs. The blister packs were all contained in cardboard boxes with well designed impression of the brand names. The manufacture and expiry dates and batch number were ink printed.

*Melting point:* The melting point of the ciprofloxacin crystals was 257 $^{0}$C. This falls within the official range of 255 – 257 $^{0}$C (Kings and Philip, 1986). This is an indication of purity and the suitability of the sample as a reference standard.

*Uniformity of weight:* All the tablets from the various brands showed significant weight uniformity with low percentage weight deviation (Table 2). Thus, there is satisfactory consistency in the weights of the tablets. Wide variation in tablets weight is undesirable, as this would also influence dosage uniformity.

*Contents of active ingredients:* The USP (1990) requires that ciprofloxacin tablets contain not less than 90% and not more than 110% ciprofloxacin. The various brands assayed were found to contain amounts of ciprofloxacin within the above range. The actual ciprofloxacin content varied from 95.9% for brand C to 101.7% for brand A. The result shows that all the brands investigated contained a chemical amount of ciprofloxacin within the official specification.

*Disintegration test/dissolution profile*

All the samples tested except B, E and I passed the disintegration test since they all disintegrated within 5 min. Samples B, E and I failed this test as they failed to disintegrate

within 30 min. (Table 2) as required by the BP (1993) for film-coated tablets.

The in-vitro release profiles of the various samples are shown in Fig.1. The USP (1990) specifies a release of not less than 80% of the drug from the tablet within 30 min. The result indicates that the brands G, H and J had initial high rate of release, releasing more than 80% of their drug content in about 10 min., thereafter stabilizing. Brand J had the highest dissolution rate. Although they passed the test, brands C and F had more gradual dissolution rate taking about 25 min. to release 80% of their drug content, their initial rate was quite low. Brands B, E and I failed to release up to 80% of the drug content within the test period of 35 min. The long disintegration time for these samples (Table 2) could be responsible for their unsatisfactory dissolution profile (Fig. 1). This could also lead to the absorption of sub-therapeutic amounts of these brands of ciprofloxacin when taken by patients and may result into inadequate blood levels, a slower or even non-attainment of the minimum inhibitory concentration in the blood and consequently treatment failure. The emergence of resistance strains of susceptible microorganisms could also result.

*Microbiological assay:* The anti-microbial activity of the test samples was determined by measuring their zones of inhibition against *S. aureus* relative to the reference sample. All the test samples had a lower level of activity than the reference sample. This does not correlate with the result of the drug content test where some of the test samples had higher values than the reference sample. This could indicate that while being chemically identical to the active drug (ciprofloxacin) some of the content of the samples may not be therapeutically equivalent probably containing material that could yield similar peaks with the UV spectrophotometer as the active material but not microbiologically equi-sensitive (Chaudhuri *et al.*, 1999). Sample B had the highest zone of inhibition of 88. 70% while sample I had the lowest value of 80.70%. Even though samples B, E and I failed the disintegration and dissolution tests as specified by the BP (1993) and USP (1990) they still exhibited a high zone of inhibition, which is comparable to those of the other brands. The relatively good anti-microbial activity exhibited by B, E and I despite failing disintegration and dissolution tests is essentially because anti-microbial activity is a function of the chemical amount of ciprofloxacin in the formulation while disintegration and dissolution are formulation parameters. Because the drug was used in the form of a solution for the anti microbial test the effects of disintegration and dissolution were bypassed.

**Conclusion**

Although all the brands investigated using the spectrophotometric analytical method contained a chemical amount of the drug within the limits of the official requirement for quality, comparative microbiological potency relative to the reference standard showed a lower level of anti-microbiological activity. The antimicrobial assay could be taken, as a more reliable result bearing in mind that the UV spetrophotometric method of analysis is not the official method of analysis for ciprofloxacin. Also the poor disintegration and release profile of some brands is certainly an important source of concern which cannot be overlooked as such defects could obviously lead to treatment failure due to poor bioavailability even if the drug contains exactly the labeled claim. This still highlights the need for all relevant authorities in the country to improve their regulatory activities and enforce such on every batch of the product that will enter the country's market.

**Table 1.** Some important particulars of the various brands of ciprofloxacin tablets investigated.

| Sample | Manufacture Date | Expiry Date | Batch Number | Country of Origin/ Address of source |
|---|---|---|---|---|
| A | April 2001 | March 2004 | 6732 | Germany |
| B | Aug. 2000 | July 2003 | 55 | Adipur |
| C | Oct. 2000 | Sept. 2003 | TE-149 | India |
| D | July 2000 | June 2003 | TE- 869 A | India |
| E | April 2001 | Mach 2004 | JCF-14 | Santa Cruz Medical stores |
| F | Feb. 2001 | Feb. 2006 | 029811 | Indonesia |
| G | Feb. 2001 | Jan. 2005 | CF-12 | Hamburg W/ Germany |
| H | Sept. 2001 | Aug. 2004 | MM-480 | Germany |
| I | Aug. 2000 | July 2003 | 56 | Adipur |
| J | March 2001 | Feb. 2004 | JCF-12 | Santa Cruz Medical stores |

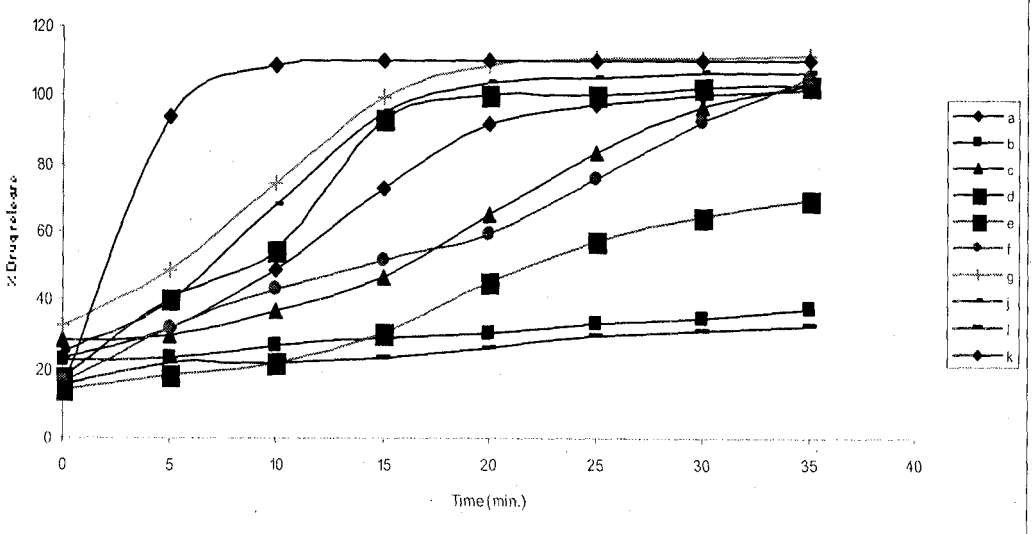
*Survey was conducted in March of the year 2002 when all the samples were within their viable shelf lives.

**Table 2**: Some determined quality parameters* of the various brands of ciprofloxacin tablets.

| Sample | % Uniformity of weight | % Drug content | Disintegration time | Comparative zone of inhibition |
|---|---|---|---|---|
| A | 0.99 (0.058) | 101.72 (0.500) | 65 sec. (0.00) | 82.70 (1.000) |
| B | 0.84 (0.010) | 101.34 (0.370) | >1h (0.0000) | 88.70 (1.000) |
| C | 0.86 (0.015) | 95.89 (0.468) | 30 sec. (1.000) | 87.10 (1.414) |
| D | 0.91(0.014) | 100.49 (0.900) | 32 sec. (1.000) | 85.50 (1.000) |
| E | 0.71 (0.017) | 103.09 (0.732) | >1h. (0.000) | 85.50 (1.414) |
| F | 0.95 (0.019) | 99.56 (0.245) | 80 sec. (0.141) | 83.90 (1.000) |
| G | 0.75 (0.018) | 99.97 (0.970) | 15 sec. (0.100) | 82.30 (1.000) |
| H | 0.90 (0.025) | 98.94 (0.900) | 43 sec. (0.400) | 82.30 (1.000) |
| I | 0.84 (0.010) | 100.59 (0.015) | > 1 h. (0.000) | 80.70 (0.000) |
| J | 0.95 (0.016) | 101.41 (0.559) | 80 sec. (0.577) | 87.10 (0.000) |

*Value of each parameter above is the mean of three readings with standard deviation in bracket.

Fig. 1: Disolution profile for the various brands of ciprofloxacin tablets



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