Al-Ameed Journal for Medical Research and Health Sciences

Manuscript 1019

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Tareq Maqlam

Abdullah H Maad

ORIGINAL ARTICLE

A Comparative Evaluation of Local and Imported Ciprofloxacin Tablets Marketed in Yemen

Tareq Maqlam [a,b,*], Abdullah H. Maad [c,d,**]

[a] Supreme Board of Drugs and Medical Appliances, Yemen
[b] College of Medicine and Health Sciences, Hadhramout University, Hadhramout, Yemen
[c] Department of Pharmaceutics, College of Pharmacy, University of Al-Ameed, Karbala, Iraq
[d] Department of Pharmacy Practice, Faculty of Clinical Pharmacy, Hodeidah University, Hodeidah, Yemen

Abstract

Ciprofloxacin is one of the most common antibacterial drugs used mainly for gastrointestinal and urinary tract infections. This study aimed to compare the quality specifications of two Yemeni ciprofloxacin hydrochloride tablet products with two non-Yemeni brands. Samples were randomly selected from different batch numbers and subjected to physicochemical testing in accordance with pharmacopeial monographs. Additionally, microbiological susceptibility testing was performed against *Staphylococcus aureus* and *Escherichia coli*. All tested products complied with pharmacopoeial standards for weight uniformity (<5 %), hardness, friability, disintegration (within 15 min for non-coated tablets), dissolution (≥80 % within 30 min), and assay (95−105 %). Antibacterial activity tests showed significant efficacy against *Escherichia coli* and *Staphylococcus aureus*, with brand D demonstrating the highest activity. These findings suggest that Yemeni ciprofloxacin tablets meet quality standards comparable to non-Yemeni products, supporting their potential as effective alternatives.

Keywords: Antibacterial, Ciprofloxacin, Tablets, Quality control

Introduction

Drug quality control is a fundamental aspect of public health that ensures the safety, efficacy, and reliability of medications. Inadequate quality control can lead to the distribution of substandard drugs, resulting in treatment failures, increased healthcare costs, and the promotion of antimicrobial resistance (Razak et al., 2016). Pharmaceutical products to exhibit the required quality, they should comply certain pharmacopoeia and non-pharmacopoeia specifications. These specifications provide the effectiveness, safety, stability of product and compliance of the consumer (Sankula et al., 2023). Tablets are the most common used pharmaceutical products; their quality are evaluated officially by the testing the identity, uniformity of content, weight variations, assay of active ingredients, disintegration of the tablet, dissolution of the drug and non-officially through evaluation of their hardness and attrition resistance. Post-market surveillance encompasses all activities conducted to collect data and insights about a product after it has received marketing authorization and entered the market. This ongoing monitoring supports product refinement, formulation of standards, and the development of evidence-based regulatory policies. Post marketing quality of pharmaceutical product is a responsibility of good manufacture and good storage (Sankula et al., 2023). Ciprofloxacin, a broad-spectrum fluoroquinolone antibiotic, plays a significant role in the treatment of various infectious diseases, including urinary tract infections, respiratory infections, and gastrointestinal infections. Its effectiveness and widespread usage make it a crucial component in managing bacterial infections, particularly in settings with rising antibiotic resistance (Tomczak et al., 2021). Despite its importance, there is a notable gap in research regarding the quality of ciprofloxacin products available in Yemen. Limited studies have

Received 28 February 2025; revised 10 April 2025; accepted 12 April 2025.
Available online 12 May 2025

* Corresponding author.at: Supreme Board of Drugs and Medical Appliances, Yemen.
** Corresponding author at: Department of Pharmaceutics, College of Pharmacy, University of Al-Ameed, Karbala, Iraq.
E-mail addresses: tareqmaqlam1984@gmail.com (T. Maqlam), dr.ph.abdullah.maad@gmail.com (A.H. Maad).

https://doi.org/10.61631/3005-3188.1019

been conducted to evaluate the quality and efficacy of ciprofloxacin in this context, raising concerns about the potential impact on treatment outcomes and public health (Al-Mehdar & Al-Akydy, 2017). Yemen is a growing country, manufacture various pharmaceutical products through various factories under the supervision of ministry of health, the quality of products are evaluated by the factories and supreme board of drugs and medical appliances (SBDMA) (Maqlam et al., 2024). Several studies have evaluated the quality control of pharmaceutical products marketed in Yemen, highlighting challenges related to manufacturing practices, regulatory oversight, and storage conditions (Al Kamarany et al., 2024). Yemen is an importer country of drugs from various drug exporters as India, China, Jordan, Egypt and other countries (Al-Worafi, 2020). To improve medicine affordability, particularly for low-income communities in developing nations, the World Health Organization (WHO) has long promoted the adoption of generic alternatives (Ozawa et al., 2019). However, this strategy has not conclusively validated the interchangeability of brand-name and generic products. Price disparities between branded and generic medicines can exceed 90 %, yet studies consistently reveal significant variations in therapeutic outcomes among marketed products containing identical active ingredients (Malvankar-Mehta et al., 2019). These findings underscore concerns about bioequivalence and clinical equivalence despite regulatory approval. The surge in generic ciprofloxacin formulations correlates with its escalating prescription rates in clinical practice. Physicians frequently select ciprofloxacin as the first-line treatment for many infections, both empirically and, at times, following laboratory investigations (Kållberg et al., 2021). This growing demand has driven higher importation and encouraged local pharmaceutical industries to manufacture their own ciprofloxacin brands (Tuitert, 2021). To ensure the quality of these products, healthcare providers must verify their efficacy and safety, necessitating ongoing post-marketing surveillance (Maad et al., 2024; Mgboko, 2021). This study aims to compare the quality of conventional ciprofloxacin tablets manufactured by Yemeni pharmaceutical companies with those produced in other countries and available in the Yemeni drug market. Four brands of ciprofloxacin HCl 500 mg tablets (two Yemeni and two non-Yemeni) were randomly collected from the market. Pharmacopoeial quality control assessments, including weight uniformity, hardness, friability, assay, disintegration, dissolution, and *in vitro* antibacterial activity, were conducted to evaluate their physicochemical properties and overall quality.

Materials and methods

Materials

Four commercially available ciprofloxacin tablet brands (labeled 500 mg per tablet), procured from retail pharmacies in Hadhramout, Yemen, were analyzed. These were anonymized as Brands A, B, C, and D for comparative evaluation (see Table 1). The reagents used in the study included hydrochloric acid and ferric chloride (DH, UK). The Mueller-Hinton agar media was supplied by Scharlu (Spain).

Evaluation tests

This study assessed the quality of ciprofloxacin tablets through various evaluation procedures based on the standards of the United States Pharmacopoeia (USP) and the British Pharmacopoeia (BP) (Pharmacopeia, 2016, Pharmacopoeia, 2013).

Uniformity of weight

Twenty tablets from each brand were individually weighed using an analytical balance, and the average variation from the mean was recorded (Gupta et al., 2020).

Hardness test

Tablet fracture resistance was determined using a Monsant (UK) tablet hardness tester. Ten tablets were randomly selected from each brand, and the force required to crush each tablet was measured and recorded as the hardness value (Gupta et al., 2020).

Friability test

Ten tablets from each brand were weighed and subjected to mechanical stress using a Roche friability tester (Erweka GmbH, Germany) at 25 rpm for 4 min. The tablets were then reweighed, and the percentage friability was calculated by comparing the initial and final weights (Gupta et al., 2020).

Disintegration test

To a disintegration medium consist of 0.1 N HCl at 37 °C using tablets disintegration tester (Nottingham, UK), a number of six tablets from each ciprofloxacin brand were added. The time taken for

Table 1. Ciprofloxacin tablets products involved in the study.

Code	Dosage form	Strength in mg	Country of origin
A	Tablet	500 mg	Yemen
B	Tablet	500 mg	Yemen
C	Tablet	500 mg	India
D	Tablet	500 mg	Jordan

complete disintegration of each tablet was recorded in minutes (Gupta et al., 2020).

Dissolution test

A quantity of six tablets of each brand were selected randomly and dissolved in sink condition for determining of percent of dissolved drug in 30 min. A nine hundred ml of 0.1 N HCl was prepared as dissolution medium which was maintained at 37 C° in the instrument. A quantity of 5 ml of dissolution sample was taken for analysis after 30 min and replaced with five ml of dissolution medium. The withdrawn filtered sample were assayed using UV/Visible spectrophotometer at 277λ (nm) and compared to standard reference. The percent of each analyte was estimated from a standard calibration curve (Tessema et al., 2022).

Assay test

A 1 % w/v ferric chloride solution was prepared, along with a standard solution of pure ciprofloxacin at a concentration of 100 mcg/ml. A number of five tablets from each product brand were powdered and 100 mg of the samples were accurately weighed and dissolved in 100 ml solution of 0.1 N hydrochloric acid (HCl) which further diluted to 100 mcg/ml concentration for each product. One ml of ferric chloride was added to 5 ml of each brand and the pure sample and completed to 50 ml with HCl 0,1 N. The UV absorbance of all samples was determined separately at 438 nm against the blank reagent using UV/Visible spectrophotometer (Jenway, UK). The content percent was estimated for all products separately using calibration curve of standard material and the results were recorded and compared to pharmacopoeia specifications (Moed et al., 2019).

In vitro antibacterial activity

In vitro antibacterial activity was studied for all tested products against two standard bacteria species using both cup plate method and disc diffusion Kirby-Bauer method. The studies species are *S. aureus* and *Escherichia coli* (Alsawi et al., 2024).

For the cup plate method, Mueller-Hinton agar plates were inoculated with standardized bacterial suspensions (0.5 McFarland standard, approximately 1.5×10^8 CFU/mL^{-1}). Wells of 6 mm diameter were punched into the agar and filled with 100 μL of ciprofloxacin solution (5 μg/mL^{-1}) prepared from the test products. Plates were incubated at 37 °C for 24 h, and the inhibition zones were measured in millimeters (mm). For the Kirby-Bauer disc diffusion method, sterile discs (6 mm) were impregnated with 5 μg of ciprofloxacin and placed on Mueller-Hinton agar plates inoculated with the test bacteria. After incubation at 37 °C for 24 h, inhibition zones were recorded in millimeters.

Statistical analysis

All results were expressed as mean ± standard deviation (SD). The dissolution test results were analyzed using one-way analysis of variance (ANOVA), followed by a Post Hoc t-test for pairwise comparisons. A P-value of <0.05 was considered statistically significant.

Results

All tested products met USP and BP standards for weight variation (<5 %), assay (95–105 %), disintegration (within 15 min for non-coated tablets), and dissolution (≥80 % in 30 min) as shown in Table 2. Among the tested products, Brand D exhibited the shortest disintegration time (8.6 min), the highest dissolution rate (94.4 %), and the highest assay value (102.8 %), indicating superior quality. Conversely, Brand A had the longest disintegration time (14.1 min), and Brand B showed the lowest dissolution rate (81.7 %) and lowest assay value (95.1 %).

Table 2. Quality findings of the four tested products of ciprofloxacin HCl.

Product	Weight variation[a] (%)	Hardness[b] (Kg/cm^{-2})	Friability[c] (%)	Disintegration[d] (min)	Dissolution[e] (% after 30 min)	Assay[f] (%)
A	<5 %	10.9 ± 0.3	0.61 ± 0.02	14.1 ± 0.1	89.1 ± 0.1	97.2 ± 0.2
B	<5 %	12.1 ± 0.08	0.25 ± 0.05	13.0 ± 0.2	81.7 ± 0.4	95.1 ± 0.3
C	<5 %	11.8 ± 0.2	0.39 ± 0.03	11.2 ± 0.3	84.8 ± 0.6	96.3 ± 0.1
D	<5 %	9.7 ± 0.4	0.68 ± 0.01	8.6 ± 0.6	94.4 ± 0.1	102.8 ± 0.5

Results are expressed as a mean ± SD.
[a] n = 20.
[b] n = 10.
[c] Tablets equivalent to 6.5 g.
[d] n = 3.
[e] n = 3.
[f] n = 5.

Regarding antimicrobial activity, all brands exhibited inhibition against *E. coli* and *S. aureus*, as shown in Table 3. Brand D demonstrated the largest inhibition zones against both *E. coli* (18.3 mm) and *S. aureus* (15.7 mm), suggesting the strongest antibacterial effect. In contrast, Brand B exhibited the smallest inhibition zones (14.6 mm for *E. coli* and 12.6 mm for *S. aureus*).

Discussion

The results are summarized in Table 2. The uniformity of weight, assay, disintegration, and dissolution are official tests used to assess tablet quality, while hardness and friability are considered non-official tests (Flatie Alemu et al., 2024). Weight variation serves as an indicator of uniform mixing, compression force, and machine settings. All tested products adhered to pharmacopoeial standards for weight uniformity. For tablets exceeding 324 mg, the specifications permit no more than two units to exceed a 5 % weight variation from the mean. Similarly, according to the European Pharmacopoeia, tablets must not exceed 115 % or fall below 85 % of the average weight. As shown in Table 2, the observed deviations remained within this limit, further supporting content uniformity. All tested products complied with USP assay specifications, which require the ciprofloxacin HCl content to be no less than 110 %, while the BP specifies a range of 95 %–105 %. The results confirmed that all brands contained the required quantity of ciprofloxacin hydrochloride, indicating they are not counterfeit or lacking active pharmaceutical ingredients (APIs). Compliance with these specifications reflects effective powder flow, mixing, and granulation, along with proper identification of the drug (Omar Khudhur et al., 2024; Wang et al., 2022). The hardness test evaluates tablet resistance to fracture during handling and transportation. Tablet hardness also influences friability and disintegration-harder tablets are generally less friable and take longer to disintegrate. All tested brands exhibited acceptable hardness values when assessed using a Monsanto Hardness Tester. The minimum acceptable hardness requirement for tablets is 4 kg (Treeno, 2024). However, some brands showed marginally lower hardness, possibly due to poor storage conditions and humidity exposure. The friability test determines the tablet's ability to withstand mechanical stress. The pharmacopoeial limit for friability is less than 1 % weight loss during the test. All brands complied with this requirement, indicating satisfactory tablet coating and compression force during manufacturing. Disintegration is the first step in drug release from a conventional tablet and depends on the disintegrant properties and compression force (Liu et al., 2023). All brands met pharmacopoeial disintegration criteria. Per the British Pharmacopoeia (BP), non-coated tablets must disintegrate within 15 min and film-coated tablets within 30 min, whereas the United States Pharmacopoeia (USP) mandates disintegration within 30 min for both tablet types. Regarding dissolution, According to BP and USP standards, at least 80 % of the labeled ciprofloxacin must dissolve within 30 min (Parshuramkar et al., 2023). All brands met this requirement, confirming acceptable drug release profiles. As shown in Table 3, all tested products demonstrated greater antibacterial activity against *Escherichia coli* (a Gram-negative bacterium) compared to *Staphylococcus aureus* (a Gram-positive bacterium). This activity is attributed to the release of ciprofloxacin from the matrix of each tested sample (Uhljar et al., 2021). Among the products, Brand D exhibited the highest antibacterial activity. *Staphylococcus aureus* showed resistance to ciprofloxacin in Products A, B, and C, while it was intermediately susceptible to Product D. In contrast, *Escherichia coli* was resistant to Product B and intermediately susceptible to Products A, C, and D, as detailed in Table 3 (Ali et al., 2010).

Table 3. Inhibition zones of the tested products of ciprofloxacin HCl.

Product	*E. Coli* Inhibition Zone (mm)	*S. aureus* Inhibition Zone (mm)
A	15.1 ± 0.3	12.9 ± 1.3
B	14.6 ± 1.8	12.6 ± 0.8
C	16.1 ± 1.4	13.8 ± 1.5
D	18.3 ± 1.6	15.7 ± 1.2

Zone of Inhibition (mm) ± SD, n = 3. Sensitivity of Pathogens against Ciprofloxacin is classified as follows: Resistant (R) ≤15 mm, Intermediate Resistant (IR) 16–20 mm, Sensitive (S) ≥21 mm.

Conclusion

This study demonstrates that Yemeni ciprofloxacin tablets meet key pharmacopoeial standards and exhibit comparable quality to non-Yemeni brands. Further research, including bioequivalence and clinical efficacy studies, is recommended to validate their therapeutic interchangeability.

Funding

This study did not receive any external funding.

Ethics information

Ethics Information is not applicable to this study.

Author contribution

Tareq Maqlam was responsible for conceptualization, methodology, data curation, and writing the original draft, while Abdullah H. Maad contributed to validation, formal analysis, and writing – review and editing.

Conflict of interest

The authors declare that there are no conflicts of interest.

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