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Original article

Comparative *In Vitro* Quality Evaluation of Six Commercial Ciprofloxacin 500 mg Tablet Brands Marketed in Libya

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Abstract
Ciprofloxacin hydrochloride is a widely prescribed fluoroquinolone antibiotic in Libya, with several generic formulations representative of the broader Libyan pharmaceutical market. As generic substitution is common, evaluating pharmaceutical quality and in vitro performance is essential to verify compliance with pharmacopeial standards and therapeutic equivalence. Six commercially available brands of ciprofloxacin hydrochloride 500 mg tablets (Sarf, Ciprofloxacin (Combitic), Ladinin, Ciproquin, Quinox, Ciprofloxacin (Bristol), coded as A–F respectively, were evaluated using pharmacopeial quality control tests, including identification, weight variation, hardness, friability, disintegration, and dissolution. Dissolution testing was performed using USP Apparatus II, and drug release was quantified by UV spectrophotometry at 276 nm using a validated calibration curve (R^2 = 0.9945). Dissolution profiles were analyzed using kinetic models and model-independent parameters. All brands complied with pharmacopeial requirements for weight variation, friability, and disintegration. Tablet hardness ranged from 5.33 to 10.98 kg/cm^2, with higher hardness associated with prolonged disintegration. Only four brands met the USP acceptance criterion of ≥75% drug release at 45 min, while two brands B and D showed slower dissolution behavior. Five products followed the Higuchi model, indicating diffusion-controlled release, whereas one followed first-order kinetics. Similarity analysis showed that three brands (A, C and E) were dissolution-equivalent to the reference product Brand F (Ciprofloxacin Bristol, UK) (f_2 = 62.25–74.47), while brands (B and D) exhibited non-equivalent profiles (f_2 = 47.1 and 48.77). Differences were also observed in DE (68.49–79.34%) and MDT (5.43–10.30 min). All products met pharmacopeial requirements for physical quality; however, variations in dissolution performance were observed among the evaluated brands. Routine post-marketing dissolution surveillance is recommended to monitor product quality and support the assessment of generic ciprofloxacin hydrochloride tablet interchangeability.
Keywords. Ciprofloxacin Hydrochloride, Quality Control, Dissolution Profile, Generic Tablets.

Introduction

Ciprofloxacin hydrochloride is a broad-spectrum fluoroquinolone antibiotic widely used for the treatment of respiratory, urinary tract, gastrointestinal, and other bacterial infections [1]. Developed by Bayer, it received approval from the United States Food and Drug Administration in 1987 and was marketed under the trade name Cipro® [2]. Owing to its broad spectrum of activity, favourable safety profile, and low cost, it remains listed on the World Health Organization Model List of Essential Medicines [3]. The active ingredient used in most commercial tablet formulations is ciprofloxacin hydrochloride monohydrate, chemically 1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-3-quinolinecarboxylic acid, with the molecular formula $C_{17}H_{18}FN_3O_3 \cdot HCl \cdot H_2O$ and a molecular weight of 385.82 g/mol (Figure 1) [4].

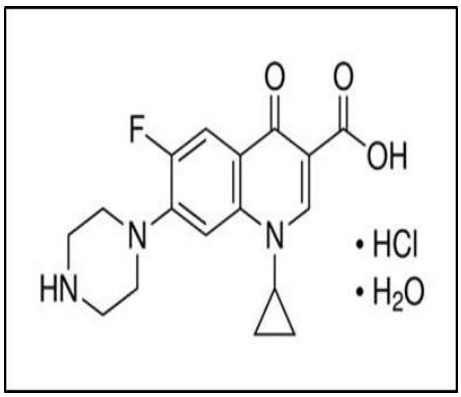

Figure 1. Chemical Structure of Ciprofloxacin Hydrochloride Monohydrate

Ciprofloxacin hydrochloride has been variably classified within the Biopharmaceutics Classification System (BCS), with some studies reporting Class IV behavior (low solubility and low permeability) depending on the pH of the test medium [5,6]. Consequently, drug dissolution is an important factor influencing the performance of its oral formulations.
The availability of generic medicines has improved access to essential drugs; however, products containing the same active pharmaceutical ingredient and strength may differ in formulation composition and manufacturing characteristics. Biopharmaceutical equivalence requires compliance with established standards for identity, strength, quality, and purity, while bioequivalence concerns comparable drug exposure under specified conditions [7,8]. Therefore, routine quality

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assessment of marketed generic products remains important, particularly in settings where independent post-marketing evaluation is limited. For immediate-release tablets, dissolution testing provides critical information about drug release from the dosage form. Comparative dissolution profiles can be evaluated using model-independent parameters such as the difference factor (f_1), similarity factor (f_2), dissolution efficiency (DE), and mean dissolution time (MDT). In addition, kinetic models such as zero-order, first-order, Higuchi, and Hixson–Crowell models can provide information about the pattern and possible mechanism of drug release [9,10].

A previous study reported differences in the pharmaceutical quality and dissolution performance of commercially available ciprofloxacin tablets, with dissolution being an important parameter for distinguishing between products [11]. Such differences highlight the need for continued evaluation of marketed formulations to ensure consistent pharmaceutical quality. In Libya, several brands of ciprofloxacin hydrochloride 500 mg tablets are commercially available, whereas comparative independent data on their pharmaceutical quality and dissolution performance are limited. Therefore, this study aimed to evaluate six commercial brands of ciprofloxacin hydrochloride 500 mg tablets marketed in Tripoli, Libya, using selected pharmacopeial quality-control tests. Dissolution profiles were further characterized using kinetic models and model-independent parameters to compare the *in vitro* release performance of the evaluated products.

Materials

Instrumentation

The following instruments were used: a calibrated analytical balance (Mettler Toledo AL104, precision 0.1 mg); a friabilator (PTF 20E/20ER, Pharma Test, Germany); a hardness tester (PTB 311E, Pharma Test, Germany); a USP disintegration apparatus (PTZ AUTO 1, Pharma Test, Germany); a USP dissolution apparatus (PT-DT70, Pharma Test, Germany); and a UV spectrophotometer (UV-1800, Shimadzu Corp).

Chemicals and Reagents

A ciprofloxacin hydrochloride analytical reference standard (purity ≥ 99%), was obtained from the Faculty of Pharmacy, University of Tripoli. Analytical grade hydrochloric acid and distilled water prepared in the laboratory were used throughout the experiments.

Sample Collection

Six commercial brands of ciprofloxacin hydrochloride tablets, each labelled to contain 500 mg of ciprofloxacin hydrochloride, were included in this study. Samples were purchased randomly from licensed retail and wholesale pharmacies located in the central commercial district of Tripoli, Libya. To maintain product confidentiality, the brands were coded A–F throughout the study. All samples were tested before their respective expiration dates.

Methods

Pharmaceutical formulations were evaluated using appropriate analytical and quality control methods to assess their compliance with established pharmacopeial requirements. All tests were performed in accordance with the relevant procedures and acceptance criteria specified in the United States Pharmacopeia (USP) and British Pharmacopoeia (BP).

Weight Uniformity Test

This test was performed in accordance with the relevant USP–NF compendial procedure. Twenty tablets from each of the six brands were randomly selected, dedusted, and weighed individually using an analytical balance. The mean tablet weight and standard deviation (SD) were calculated for each brand. The percentage deviation of each individual tablet weight from the corresponding mean weight was determined using the following equation [12,13]:

$$\text{Weight variation (\%)} = [(Iw - Aw) / Aw] \times 100 \quad \text{Eq. (1)}$$

where Iw is the individual weight of the tablet and Aw is the average weight of the tablets.

The results were assessed against the applicable pharmacopeial acceptance limits based on the average tablet weight. The compendial weight variation limits specified by the USP and IP/BP are presented in (Table 1).

Table 1. Weight Variation Limits Defined by The USP and IP/BP

IP/BP	Limit	USP
80 mg or less	10%	130mg or less
More than 80mg or less than 250mg	7.5%	130mg to 324mg
250mg or more	5%	More than 324mg

Hardness Test

Tablet hardness was determined using a Pharma Test hardness tester. Ten tablets were randomly selected from each of the six brands and tested individually. The breaking force required to fracture each tablet was measured by applying diametrical pressure until the tablet broke. The force required to break each tablet was recorded as the tablet breaking force and expressed in kg/cm^2. The tablet breaking force values were evaluated as a physical quality attribute in accordance with the principles described in USP [14].

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Friability

Friability was evaluated using a Pharma Test Friabilator. Twenty tablets from each brand were randomly selected, accurately weighed, and placed in the friabilator. The apparatus was operated at a rotational speed of 25 rpm for 4 minutes, corresponding to 100 revolutions. Upon completion of the test, the tablets were carefully removed and dedusted to eliminate loose surface particles before being reweighed. The percentage friability, representing the percentage weight loss during the test, was calculated using the following equation:

$$Friability\ (\%) = [\ (I_w - F_w) / I_w] \times 100 \qquad \text{Eq. (2)}$$

Where, I_w = Total Initial weight of tablets; and F_w = Total final weight of tablets.
The sample meets USP-NF acceptance criteria if total weight loss does not exceed 1% of the initial weight [1].

Disintegration test

Disintegration testing was performed using a Pharma Test disintegration apparatus. Six tablets from each brand were tested individually using 900 mL of distilled water maintained at 37 ± 2°C. The disintegration time was recorded for each tablet. For film-coated tablets, complete disintegration was required within 30 min, with all particles passing through the specified screen. Any remaining residue was required to consist of a soft mass with no palpably firm core [1,15].

Calibration Curve

A calibration curve for ciprofloxacin hydrochloride was prepared using a series of standard solutions at known concentrations ranging from 6 to 14 µg/mL. The absorbance of each standard solution was measured at a wavelength of 276 nm using a UV–visible spectrophotometer, with the dissolution medium 0.1 N hydrochloric acid (HCl) solution, used as the blank. The measured absorbance values were plotted against the corresponding drug concentrations, and linear regression analysis was performed to obtain the calibration equation. The linearity of the calibration curve was assessed using the coefficient of determination (R^2). The resulting regression equation was used to determine the ciprofloxacin hydrochloride concentration in the dissolution samples.

Dissolution Test

Dissolution testing was performed using the USP Dissolution Apparatus II (paddle method) in accordance with United States Pharmacopoeia protocol [16]. Each vessel contained 900 mL of the dissolution medium 0.1 N HCl, maintained at 37 ± 0.5 °C, and the paddle speed was set at 50 rpm. At predetermined sampling times of 5, 15, 30, 45, 60, and 90 min, 5.0 mL of dissolution medium was withdrawn from each vessel and immediately replaced with an equal volume of fresh dissolution medium to maintain a constant dissolution volume.
The collected aliquots were filtered and diluted to an appropriate concentration using the dissolution medium before spectrophotometric analysis, 1 mL of each dissolution sample was transferred to a 100 mL volumetric flask and diluted to volume with the dissolution medium. The absorbance of the resulting solutions was measured at 276 nm using a UV–visible spectrophotometer. Ciprofloxacin hydrochloride concentrations were calculated from the calibration curve, and the percentage of drug released at each sampling time was determined, taking into account the dilution factor and replacement of the dissolution medium, using the following equation:

$$\%\ Release = (Concentration \times Dilution\ factor \times Dissolution\ volume) / Label\ claim \times 100 \qquad \text{Eq. (3)}$$

Dissolution profiles for the six brands were constructed by plotting the cumulative percentage of ciprofloxacin hydrochloride released against dissolution time. According to the United States Pharmacopeia (USP), tablets satisfy the dissolution requirement if not less than 75% (Q) of the labelled amount dissolves within 45 minutes. Similarly, the British Pharmacopoeia (BP) stipulates that the product complies with the test if drug dissolution is not less than 80% within the same timeframe [17,18].

Data Analysis and Statistical Processing

The coded data were entered and analyzed using Microsoft Excel 2016. Descriptive statistics were utilized to summarize the data, with results expressed as mean ± standard deviation (SD). Microsoft Excel was further used to construct the calibration curve of the working standards and to plot the time-dependent *in vitro* drug release profiles.

Model-Dependent Dissolution Profile Comparison

To evaluate the mechanisms and kinetics of drug release, the *in vitro* release data of the formulations were fitted to various mathematical kinetic models, including zero-order, first-order, Higuchi, and Hixson–Crowell models [19]. The corresponding equations are defined as follows:
Zero-Order Model: Describes systems where release rate is independent of concentration

$$Q = k_0 \cdot t \qquad \text{Eq. (4)}$$

First-Order Model: Relates release rate to the amount of drug remaining

$$\log Q_t = \log Q_0 - (K_1 . t / 2.303) \qquad \text{Eq. (5)}$$

Higuchi Model: Based on Fickian diffusion, proportional to the square root of time

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$$Q = k_H \cdot \sqrt{t} \qquad \text{Eq. (6)}$$

Hixson–Crowell Model: Accounts for changes in surface area and particle/tablet volume over time

$$\sqrt[3]{100 - Q} = \sqrt[3]{100} - K_{HC} \cdot t \qquad \text{Eq. (7)}$$

Where k_0, K_1, k_H, and K_{HC} represent the zero-order, first-order, Higuchi, and Hixson–Crowell rate constants, respectively, and Q is the percentage of drug released at time t. The model yielding the highest coefficient of determination (R^2) value was selected as the best-fit model describing the drug release kinetics.

Model-Independent Dissolution Profile Comparison

Dissolution profiles were compared using the area under the dissolution curve (AUC), dissolution efficiency (DE), mean dissolution time (MDT), and the model-independent difference factor (f_1) and similarity factor (f_2) [20]. AUC was calculated using the trapezoidal rule. Dissolution efficiency was expressed as the percentage of the area under the dissolution curve relative to the area corresponding to 100% drug release over the same time interval. MDT was calculated as the mean time required for drug release, based on the dissolution profile. The f_1 factor represents the percentage difference between the reference and test profiles, while f_2 measures their similarity. The factors were calculated as follows:

$$f_1 = \{[\Sigma^n_{t=1} | R_t - T_t |] / \Sigma^n_{t=1} R_t\} \times 100 \qquad \text{Eq. (8)}$$

$$f_2 = 50 \times \log \{[1 + (1/n) (\Sigma^n_{t=1} (R_t - T_t)^2)]^{-0.5} \times 100\} \qquad \text{Eq. (9)}$$

where (R_t) and (T_t) represent the percentage of drug released from the reference and test products, respectively, at time (t), and (n) is the number of experimental data. Values of (f_1) between 0 and 15 and (f_2) between 50 and 100 indicate similar dissolution profiles [21].

Dissolution Efficiency (DE%) is defined as the area under the dissolution curve up to a time point t, expressed as a percentage of the area of the rectangle described by 100% dissolution at the same time [22,23]. It was calculated using the trapezoidal rule according to the following equation:

$$DE = \frac{\int_0^t y.dt}{y\ 100.\ t} \times 100 \qquad \text{Eq. (10)}$$

Where y is the percentage of drug dissolved at time t, $\int_0^t ydt$ is the area under the dissolution curve from time 0 to t, y_{100} is the maximum drug release (100%), and t is the total time of the dissolution test (90 minutes).

Mean Dissolution Time (MDT), which represents the average time required for the drug to dissolve out of the dosage form, was calculated using the following equation [21]:

$$MDT = \sum [t_{mid.i} . \Delta Q_i] / Q_\infty \qquad \text{Eq. (11)}$$

Where $t_{mid,i}$ is the intermediate time of the sampling intervals, ΔQ_i is the amount of active pharmaceutical ingredient (API) dissolved in each interval, and Q_∞ is the maximum amount of API dissolved.

Results and discussion

Physical Characteristics of Tablets

(Table 2) summarizes the six commercial brands of ciprofloxacin hydrochloride 500 mg tablets included in this study, these brands represent different manufacturers and countries of origin available in the Libyan market. The tablet samples exhibit uniform and acceptable physical appearance. All brands (A – F) were white, film-coated, oblong-shaped tablets with concave, smooth surfaces and no evidence of physical defects. The products differed in tablet identification features, particularly the presence of score lines and embossed markings. Five brands (B, C, D, E and F) were scored, whereas Brand A lacked a score line, which may reduce the reliability of manual tablet splitting when required for dose adjustment or ease of swallowing [24, 25]. Three brands (C, E, and F) carried distinctive embossed markings, which facilitate product identification and help distinguish genuine products from potential counterfeits [26], whereas Brands A, B, and D had no embossed identification. These characteristics are important for product recognition and patient use but are independent of the pharmacopeial quality attributes evaluated in this study.

Table 2. Description of the Commercial Ciprofloxacin 500 mg Tablet Samples Included in the Study

Brand code	Trade Name	Manufacturer	Country of Origin	Score line	Monogram
A	Sarf	Julphar	U.A.E	-	-
B	Ciprofloxacin	Combitic	India	+	-
C	Ladinin	Pharmathen	Greece	+	5
D	Ciproquin	Uni pharma	A.R.E	+	-
E	Quinox	Tabuk Co.	Saudi Arabia	+	QUINOX 500
F	Ciprofloxacin	Bristol Laboratories Ltd	UK	+	CPR500/BL

+ indicates presence, while – indicates absence

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Physical Quality Tests

The physicochemical quality attributes of the six commercial ciprofloxacin hydrochloride 500 mg tablet brands are presented in (Table 3). These tests were performed to evaluate compliance with pharmacopeial specifications and to assess manufacturing consistency among the investigated products.

Table 3. Summary of the Physical Quality Control Tests of Six Brands of Ciprofloxacin 500 mg Tablets

Brand code	Weight variation (%) n=20	Hardness (kg/cm^2) n=10	Friability (%) n=20	Disintegration Time (min) n=6
	Mean ± SD	Mean	Mean ± SD	Mean ± SD
A	1.71 ± 0.79	6.38	0.011 ± 0.08	3.07 ± 0.001
B	1.02 ± 0.89	8.85	0.015 ± 0.013	2.81 ± 0.007
C	1.01 ± 0.76	5.33	0.02 ± 0.009	1.55 ± 0.014
D	1.54 ± 0.81	10.98	0.008 ± 0.001	8.88 ± 0.0066
E	2.02 ± 0.78	6.48	0.012 ± 0.003	2.35 ± 0.0002
F	1.66 ± 0.75	5.85	0.02 ± 0.000	1.45 ± 0.0004

n: number of samples, SD: standard deviation

Weight Uniformity

Weight uniformity is an important quality control parameter that reflects consistency in tablet manufacturing and provides an indirect indication of dose uniformity, particularly for tablets in which the active pharmaceutical ingredient constitutes a substantial proportion of the formulation [27]. Consistent tablet weight reflects uniform die filling during compression and contributes to batch-to-batch reproducibility [28]. As shown in Table 3, all brands complied with the pharmacopeial requirements for weight variation. The highest percentage of mean % weight variation was observed for Brand E (2.02% ± 0.78), whereas Brand C exhibited the lowest mean % weight variation (1.01% ± 0.76). These values were well within the acceptance limits specified by both the United States Pharmacopeia and the British Pharmacopoeia, which require that for tablets weighing more than 324 mg, no more than two units may deviate from the mean weight by more than ±5%, and none may deviate by more than ±10%. The low variability observed among all brands indicates satisfactory weight uniformity.

Tablet Hardness

Tablet hardness reflects the mechanical strength of tablets and their ability to withstand handling, packaging, and transportation without breakage. It also influences friability, disintegration, and dissolution behavior [29]. As presented in (Table 3), Brand D exhibited the highest crushing strength (10.98 kg/cm^2), while Brand C showed the lowest hardness (5.33 kg/cm^2). The remaining brands demonstrated hardness values ranging from approximately 5.85 to 8.85 kg/cm^2. Although considerable variation in tablet breaking force was observed among the brands, all formulations demonstrated sufficient mechanical strength to withstand handling during manufacturing, packaging, and transportation [30]. The higher hardness observed for Brand D may explain its comparatively longer disintegration time, whereas lower hardness values may facilitate faster tablet disintegration. Variations in hardness among manufacturers are likely attributable to differences in formulation composition, compression force, granulation technique, and manufacturing conditions [31].

Friability

Friability measures the resistance of tablets to abrasion and mechanical stress encountered during manufacturing, packaging, transportation, and routine handling. According to the USP, conventional tablets should exhibit a weight loss of not more than 1% after friability testing.

As shown in (Table 3), all investigated brands exhibited extremely low friability values (0.008–0.02%), which were substantially below the USP acceptance limit of 1% [1]. These findings indicate adequate mechanical integrity and sufficient resistance to abrasion without compromising structural stability.

Disintegration Time

Disintegration is the process by which tablets break down into smaller particles upon contact with the liquid medium and represents a critical step preceding drug dissolution and absorption in immediate-release dosage forms [32]. Rapid tablet disintegration facilitates drug release and contributes to optimal therapeutic performance.

The disintegration times of all investigated brands complied with both USP and British Pharmacopoeia specifications for film-coated tablets, which require complete disintegration within 30 minutes [33]. As shown in (Table 3), Brand D exhibited the longest disintegration time (8.88 min), whereas Brand F showed the shortest time (1.45 min). All products disintegrated well within pharmacopeial limits, indicating satisfactory tablet performance. The relatively prolonged disintegration of Brand D is consistent with its higher hardness, demonstrating the well-established relationship between tablet mechanical strength and disintegration behaviour.

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Calibration Curve

Quantification of ciprofloxacin released during dissolution testing was performed by UV spectrophotometry against a standard calibration curve constructed over the concentration range 6–14 µg/mL (Figure 2). The curve was linear across this range (absorbance = 0.1438 × concentration - 0.0017; R^2 = 0.9945), indicating a strong coefficient of determination.

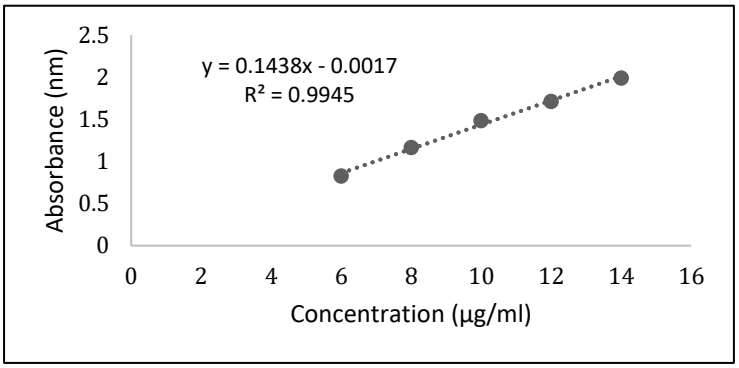

Figure 2. Standard Calibration Curve of Ciprofloxacin Hydrochloride

Dissolution Test

The *in vitro* dissolution profile of the six brands, expressed as mean percentage ciprofloxacin release ± SD (n = 6) over 90 minutes, is presented in Table 4 and Figure 3. The USP-NF standard specifies that tablets meet this test if not less than 75% (Q) of the labelled content is released within 45 minutes. According to the BP standard, a tablet complies with this test if the drug is released not less than 80% (Q) at 45 minutes [1]. The observation window resolves the six brands into two distinct groups. Using the stricter BP criterion (≥80% at 45 min), Brands A, C, E, and F crossed the threshold (82.05%, 80.14%, 80.01%, and 84.48%, respectively); the same four brands also satisfied the USP criterion (≥75%) and continued to increase thereafter, reaching 80.61-89.59% by 90 minutes. Brands B and D, in contrast, never reached the 80% criterion at any tested time point: Brand B plateaued at 71.57-74.39% and Brand D at 72.85-75.29% between 30 and 90 minutes. Brand D also showed the slowest onset of release, with only 48.84% dissolved at 5 minutes compared to 60.44-68.25% for the other five brands, reflecting true release retardation rather than a mere delay.

This pattern is consistent with the physical quality-control results in (Table 3). Brands D and B recorded the two highest tablet hardness values, while the four brands that met the Q-value criterion (A, C, E, F) all had hardness values of 6.48 kg/cm^2 or below. Harder and slower-disintegrating tablets tended to show slower drug release, suggesting that tablet hardness may serve as a useful, though not definitive, indicator of dissolution behaviour among these brands.

Table 4. In Vitro Dissolution Profile (% Drug Released) of Six Commercial Brands (A–F) of Ciprofloxacin Hydrochloride 500 mg Tablets.

Time (min)	% Drug Release					
	Brand A	Brand B	Brand C	Brand D	Brand E	Brand F
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
5	62.04 ± 0.100	60.44 ± 0.055	63.03 ± 0.083	48.84 ± 0.113	68.25 ± 0.117	61.34 ± 0.081
15	79.19 ± 0.100	63.30 ± 0.062	74.63 ± 0.057	72.29 ± 0.196	74.11 ± 0.103	77.09 ± 0.064
30	79.38 ± 0.052	71.57± 0.058	78.47 ± 0.031	72.85 ± 0.014	77.34 ± 0.045	79.05 ± 0.052
45	82.05 ± 0.085	72.06 ± 0.038	80.14 ± 0.085	73.42 ± 0.009	80.01 ± 0.025	84.48 ± 0.049
60	82.23 ± 0.108	73.28 ± 0.031	81.39 ± 0.020	74.33 ± 0.031	80.42 ± 0.032	85.34 ± 0.048
90	82.64 ± 0.072	74.39 ± 0.049	85.94 ± 0.090	75.29 ± 0.041	80.61 ± 0.031	89.59 ± 0.075

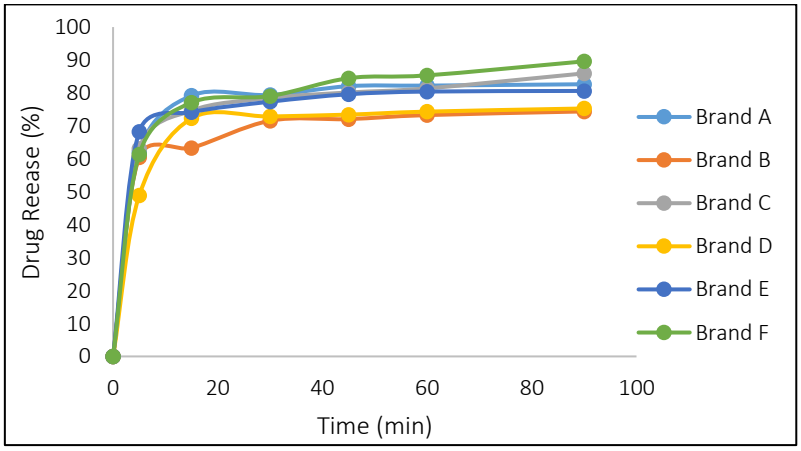

Figure 3. In Vitro Dissolution Profiles of Six Brands of Ciprofloxacin Hydrochloride Tablets in 0.1N HCl

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Dissolution profile comparison by model-dependent parameters

To characterise the mechanism underlying drug release, the mean dissolution data for each brand were fitted to four release-kinetics models: zero-order, first-order, Higuchi, and Hixson–Crowell. The coefficient of determination (R^2) for each model and brand is summarized in (Table 5).

The Higuchi model gave the best fit for five of the six brands (A, B, C, D and E), with R^2 ranging from 0.5739 (Brand D) to 0.8907 (Brand C), indicating that drug release from these five brands was predominantly diffusion-controlled. This is consistent with rapid matrix wetting and solute diffusion out of the disintegrating tablet, rather than a simple concentration- or surface-area-dependent process. Brand F was the exception, best described by first-order kinetics (R^2 = 0.8979, compared with R^2 = 0.8742 for its Higuchi fit), suggesting a release rate proportional to the amount of drug remaining in the tablet, a pattern that may reflect the formulation's relatively fast disintegration (Table 3).

Table 5. Kinetics of Drug Release for Six Brands of Ciprofloxacin Tablets

Brand Code	Zero-order (R^2)	First-order (R^2)	Higuchi (R^2)	Hixson–Crowell (R^2)
A	0.4752	0.5402	0.6371	0.5172
B	0.7507	0.7791	0.8742	0.7695
C	0.7724	0.8843	0.8907	0.8502
D	0.4168	0.4606	0.5739	0.4447
E	0.721	0.7647	0.8711	0.7506
F	0.7498	0.8979	0.8742	0.8537

Comparisons of dissolution profiles by independent model parameters

To directly test dissolution equivalence between brands, the model-independent difference factor (*f1*) and similarity factor (*f2*) were calculated for each test brand against Brand F, which showed the highest overall release and was used as the reference product for this comparison (Table 6). According to the FDA [34] and EMA [35] guidelines, two dissolution profiles are considered similar when $f1 \leq 15$ and $f2 \geq 50$; f2 values of 50 –100 correspond to an average difference of 10 percentage points or less across all sampling times. Brands A, C and E met both criteria, with *f1* values of 3.28-6.37 and *f2* values of 62.25-74.47, indicating that their dissolution profiles are statistically and practically similar to that of Brand F. Conversely, Brands B and D produced f_2 values below 50 (47.10 and 48.77, respectively), indicating that their dissolution profiles were considered non-equivalent to the reference product according to regulatory criteria. This *f2*-based classification is consistent with the Q-value shortfall and the lower dissolution plateau identified for Brands B and D in the Dissolution Test subsection above.

To further characterize dissolution behaviour, two additional model-independent parameters, Dissolution Efficiency (DE) and Mean Dissolution Time (MDT) were determined. As summarized in Table 6, Brand F achieved the highest overall dissolution efficiency (DE = 79.34%), closely matched by Brand A (77.40%), Brand C (76.72%), and Brand E (75.75%), aligning with their favourable *f2* equivalence classifications. Conversely, Brands B and D exhibited lower overall dissolution efficiencies of 68.49% and 69.62%, respectively. Formulations with lower MDT values (e.g., Brand E: 5.43 min; Brand A: 5.70 min) released the bulk of their drug content more rapidly, whereas brands with higher MDT values (e.g., Brand F: 10.30 min) exhibited more gradual, prolonged release. The reduced DE % values and lower dissolution plateaus for Brands B and D are consistent with their non-equivalent *f2* status relative to the reference product.

Table 6. Comparisons of Dissolution Profile by Model Independent Parameters.

Brand Code	Difference Factor (f_1)	Similarity Factor (f_2)	DE (%)	MDT (min)
A	3.28	72.59	77.40	5.70
B	12.97	47.1	68.49	7.14
C	3.5	74.47	76.72	9.65
D	12.55	48.77	69.62	6.78
E	6.37	62.25	75.75	5.43
F (Ref)	0	100	79.34	10.30

Conclusion

This study provides a comprehensive post-marketing quality evaluation of six available ciprofloxacin hydrochloride 500 mg tablet brands marketed in Libya. Although all investigated products complied with pharmacopeial requirements for the evaluated physicochemical quality attributes, differences in dissolution behaviour were identified among the formulations. These findings demonstrate that satisfactory physical quality alone is insufficient to establish biopharmaceutical equivalence, as products meeting conventional quality-control specifications may still exhibit differences in drug release characteristics.

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The combined application of dissolution profile comparison, release-kinetic modelling, and model-independent similarity analysis provided a more comprehensive assessment of product performance than routine physicochemical tests alone. This approach identified variations in dissolution equivalence that would not have been detected by conventional quality-control testing. The results highlight the importance of incorporating dissolution profile evaluation into routine post-marketing surveillance programs. Such an evaluation would support both quality assurance and interchangeability assessment of multisource ciprofloxacin products. Further studies, including comparative bioavailability or bioequivalence investigations, are recommended to determine whether the observed *in vitro* differences have clinical relevance.

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Conflicts of Interest
The authors declare no conflicts of interest

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