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# Evaluation of the price-efficacy relationship for multiple brands of ciprofloxacin and gentamicin in Kabul: a cross-sectional study

Ahmad Zia Noori<sup>1</sup>, Hashmatullah Yousufi<sup>1\*</sup> and Haji Mohammad Naimi<sup>1</sup>

## Abstract

**Background** The quality of consumer products constitutes a prominent issue on a global scale. The proliferation of counterfeit pharmaceuticals poses a significant challenge not only in developing and underdeveloped nations but also represents a considerable concern in developed countries. In Kabul, a major issue is the availability of multiple brands of antibiotics with fluctuating prices. To ascertain the quality and correlation of pricing with the efficacy of antibiotics, an evaluation of their effectiveness is deemed both essential and significant. Ciprofloxacin and Gentamicin are widely utilized antibiotics for treating infections induced by specific strains of Gram-negative and Gram-positive bacteria. The aim of this study was to investigate the relationship between brand price and the efficacy of these antibiotics.

**Methods** A total of 40 ciprofloxacin 500 mg tablet brands and 15 gentamicin 80 mg ampule brands were procured from pharmacies in Kabul across eight countries. Ten samples from each brands were assessed for efficacy through MIC and MBC assays against *Staphylococcus aureus* (ATCC 29213), following Clinical and Laboratory Standards Institute protocols. Efficacy data were obtained by inoculating *S. aureus* suspensions in Mueller-Hinton medium with various concentrations of each antibiotic, incubated at 35–37°C for 24 h. Following MIC determination, inoculated cultures were plated on Mueller-Hinton agar and incubated at 35–37°C for 24 h for colony enumeration. Statistical analysis was conducted using ANOVA, Student's t-test, and Pearson correlation via SPSS version 26, with p-values of  $\leq 0.05$  considered significant.

**Results** The prices of Ciprofloxacin tablets ranged from 25 to 275 Afghanis (mean = 99.60), while Gentamicin prices varied from 3 to 15 Afghanis (mean = 8.37). Of the 40 ciprofloxacin brands, 6 (15%) were unregistered, and from 15 gentamicin brands, 3 (20%) were unregistered. There was no significant difference in Gentamicin efficacy against *S. aureus*. However, a significant difference was noted in Ciprofloxacin efficacy against *S. aureus* ( $p < 0.01$ ).

**Conclusions** The results of this study highlight the critical need for stringent quality control and regulatory oversight, especially for unregistered antibiotics, due to the significant variations observed in Ciprofloxacin efficacy ( $p < 0.01$ ).

\*Correspondence:  
Hashmatullah Yousufi  
yousufhashmatullah@gmail.com

Full list of author information is available at the end of the article



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even though no such difference was noted with Gentamicin. Policymakers should implement regulations to ensure all antibiotic brands adhere to quality standards, while pharmacists and healthcare professionals should prioritize using registered, effective medications to safeguard public health.

**Keywords** Ciprofloxacin, Gentamicin, Afghanistan, Medicine, Pharmacy, Cost, Efficacy, *Staphylococcus aureus*, Minimal inhibitory concentration (MIC), Minimal bactericidal concentration (MBC), Clinical practice

## Background

Efficacy denotes the capacity of a pharmaceutical product to exert a favorable outcome or a therapeutic agent that can specifically interact with its target and modulate the functionality of that target [1]. The availability of high-quality medications is an essential part of efficient healthcare. If there is no assurance that medications meet the necessary standards for quality, safety, and efficacy, then healthcare services are clearly at risk [2]. Economic constraints, inadequate drug-regulatory frameworks, and insufficient oversight regarding manufacturing, distribution, and importation foster the expansion of the illicit medicine market [3, 4]. Substandard and counterfeit medications represent two primary challenges on a global scale, particularly within low-income and lower-middle-income nations. Counterfeit medications are intentionally and deceitfully misrepresented regarding their identity or origin; their quality is unpredictable as they may possess incorrect concentrations of active substances, contain inappropriate ingredients, or lack active constituents altogether [5]. The incidence of counterfeit pharmaceuticals appears to be increasing and has not been effectively countered by coordinated efforts among pharmaceutical corporations, governmental entities, or international organizations focused on trade, health, customs and excise, and counterfeiting. A significant portion of the data pertaining to the epidemiology of counterfeit pharmaceuticals is withheld by the pharmaceutical sector and governmental bodies. Pharmaceutical companies engage investigators to identify and assist in the dismantling of counterfeit operations; however, such actions predominantly occur in a clandestine manner [6]. It has been approximated that as much as 15% of all pharmaceuticals sold are counterfeit, with certain regions in Africa and Asia reporting figures exceeding 50% [7, 8, 9]. The FDA estimates that counterfeit medications constitute approximately 10% of the global pharmaceutical market. The frequency of investigations concerning potential counterfeit medications conducted by the FDA has escalated from roughly five per year during the 1990s to over 20 per year since the year 2000 [6].

## Method

The research involved the examination of 40 different brands of ciprofloxacin (500 mg tablet) and 15 different brands of gentamicin (80 mg ampule), which

were purchased from Kabul's medicine market, a major wholesale distributor of pharmaceuticals throughout the country.

Ten samples/ brand of ciprofloxacin and gentamicin were randomly selected for analysis to compare their efficacy with each other and with the respective standard. To ensure unbiased results, each brand was assigned a numerical code.

Susceptible strain of *Staphylococcus aureus* (*S. aureus*) (American Type Culture Collection 29213) was used to assess the comparative in-vitro antibacterial activity of each brand due to its known susceptibility to both gentamicin and ciprofloxacin. The minimal inhibitory concentration (MIC) and minimal bactericidal concentration (MBC) of each brand were measured according to the protocols established by the Clinical Laboratory Standards Institute (CLSI).

Stock culture of *S. aureus* (ATCC 29213) were cultured on Tryptose blood agar plates (Oxoid) and incubated at 37 °C for 18–24 h. After this incubation period, 1–2 isolated colonies of *S. aureus* were transferred into 5 mL of normal saline to prepare a bacterial suspension with a turbidity corresponding to 1 McFarland standard. A 10 µL aliquot of this suspension was then used to inoculate test tubes containing 2.5 mL of Muller Hinton broth (Difco) mixed with ciprofloxacin or gentamicin samples at varying concentrations. Ciprofloxacin concentrations ranged from 0.125 to 64 µg/mL, while gentamicin concentrations ranged from 0.07 to 40 µg/mL, based on the respective sample/brand. The cultures were incubated at 37 °C for 18–24 h.

Each brand was subjected to 10 sample replicates, and each sample underwent 10 technical replicates to ensure reliability and precision in the measurements. For ciprofloxacin, this resulted in a total of 400 MIC assays and 400 MBC assays. Similarly, for gentamicin, 150 MIC assays and 150 MBC assays were performed.

Positive control was not treated with ciprofloxacin or gentamicin, while negative control lacked the bacterial suspension. The concentration of ciprofloxacin and gentamicin that prevented visible bacterial growth was recorded as the minimal inhibitory concentration (MIC). Following this, 10 µL of the drug-inoculated *S. aureus* cultures that showed no visible growth were streaked onto Muller Hinton Agar (Oxoid) plates and incubated for an additional 24 h at 37 °C. After the second incubation, the plates were examined for the presence of

*S. aureus* colonies. The concentration of ciprofloxacin or gentamicin that resulted in no colony growth was recorded as the minimal bactericidal concentration (MBC).

The comparative efficacy of different drug brands against *Staphylococcus aureus* was evaluated by analyzing the average Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC) values for each brand. Statistical analysis was conducted using ANOVA (Analysis of Variance) to determine significant differences in efficacy among the brands. For this analysis, the statistical software SPSS version 26 was employed.

The association between the efficacy of the drugs and their respective prices was assessed using Pearson's correlation coefficient test. Additionally, differences in both price and efficacy between registered and non-registered drug brands were examined using the Student's t-test. A significance threshold of  $p \leq 0.05$  was applied throughout the study to determine statistical significance.

These rigorous testing protocols provided a robust dataset to compare the antimicrobial efficacy of the drug brands, explore potential relationships between efficacy and cost, and identify differences in performance and pricing based on the registration status of the brands.

## Results

In this study, 40 different brands of 500 mg ciprofloxacin tablets and 15 different brands of 80 mg gentamicin ampoules were collected from major pharmacies in Kabul to evaluate the relationship between price and efficacy. The price of ciprofloxacin samples ranged from 25 Afghanis (~0.40 USD) to 275 Afghanis (~4.43 USD), with an average price of 99.60 Afghanis, a median of 98 Afghanis, and a standard deviation of  $\pm 54.2$ .

The ciprofloxacin brands analyzed in this study were manufactured in various countries, with the majority produced in Pakistan (21 companies), followed by India

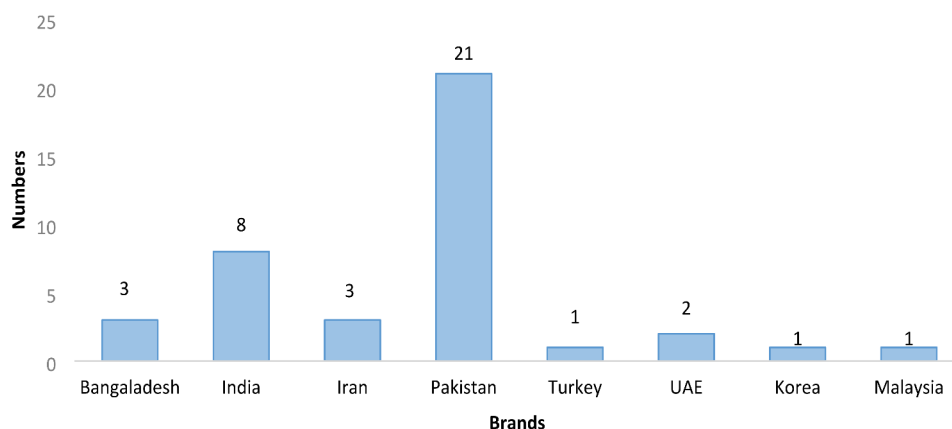
(8 companies), Iran (3 companies), Bangladesh (3 companies), the UAE (2 companies), Turkey (1 company), Korea (1 company), and Malaysia (1 company). Similarly, the gentamicin brands originated from several countries, primarily Pakistan (5 companies), along with Turkey (2 companies), China (2 companies), India (2 companies), Iran (2 companies), Germany (1 company), and Uzbekistan (1 company) (Figs. 1 and 2).

All ciprofloxacin and gentamicin samples adhered to international packaging standards. Each ciprofloxacin's tablet packet and gentamicin's ampoule was labeled with the manufacturer's name, batch number, manufacturing date, expiration date, and other production-related details.

Using an ANOVA test, the results showed that the average Minimum Inhibitory Concentration (MIC) for all ciprofloxacin samples against a sensitive wild-type strain of *S. aureus* was 2.97  $\mu\text{g/ml}$  (95% CI: 2.8241–3.1159). The MIC values among the samples ranged from 2 to 8  $\mu\text{g/ml}$ , with the differences being statistically significant ( $p < 0.001$ ) (Fig. 3). Similarly, the average Minimum Bactericidal Concentration (MBC) for ciprofloxacin against the same strain was 11.90  $\mu\text{g/ml}$  (95% CI: 11.32–12.48). The MBC values across samples ranged from 8 to 32  $\mu\text{g/ml}$ , and these differences were also statistically significant ( $p < 0.001$ ) (Fig. 4).

The Pearson correlation test conducted in this study revealed a weak correlation between price and efficacy among the various brands of ciprofloxacin. Specifically, an increase in price by one Afghani was associated with a decrease in MIC of approximately 0.245  $\mu\text{g/ml}$ , which was statistically significant ( $r = -0.245$ ,  $p = 0.01$ ) (Fig. 5). Similarly, an increase of one Afghani in price corresponded to a decrease in MBC of approximately 0.257  $\mu\text{g/ml}$ , also statistically significant ( $r = -0.257$ ,  $p = 0.01$ ) (Fig. 6).

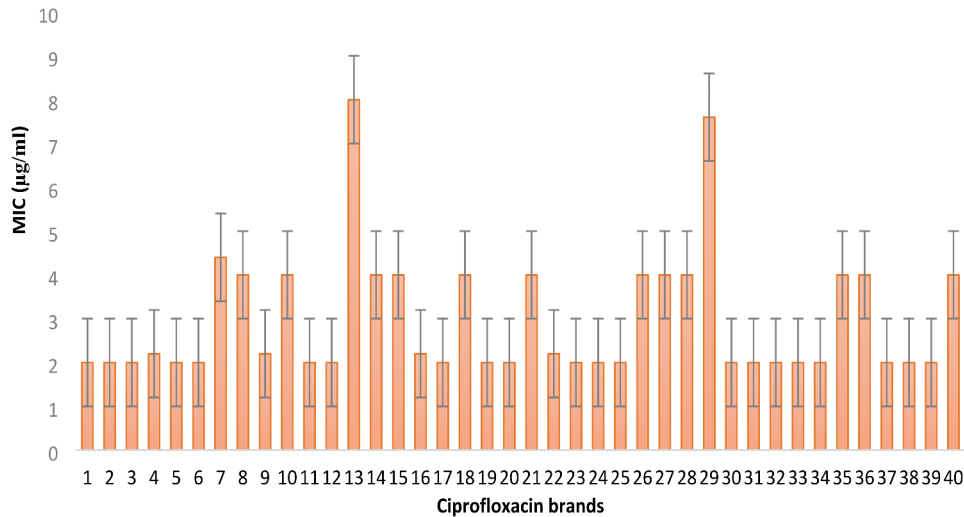
To obtain more precise insights, each ciprofloxacin brand was ranked based on their respective MIC and MBC values, from lowest to highest (1–40), and then



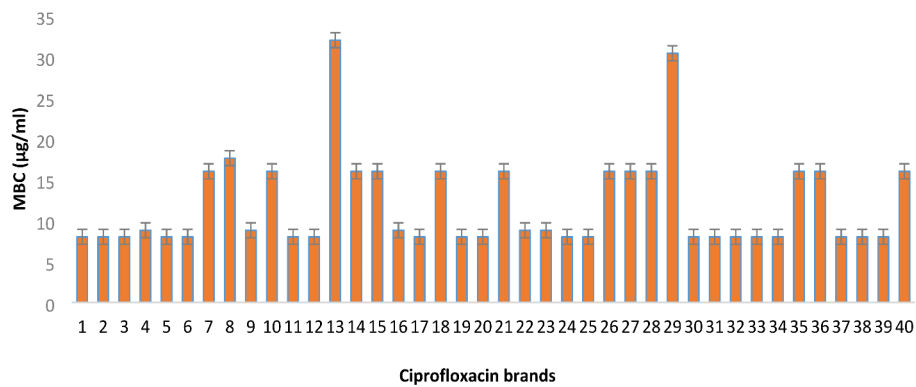
**Fig. 1** The number of tested ciprofloxacin brands and the countries where they manufactured. The X-axis represents the countries where the antibiotics were produced, while the Y-axis shows the number of ciprofloxacin brands tested from each country, with the exact numbers displayed above each bar



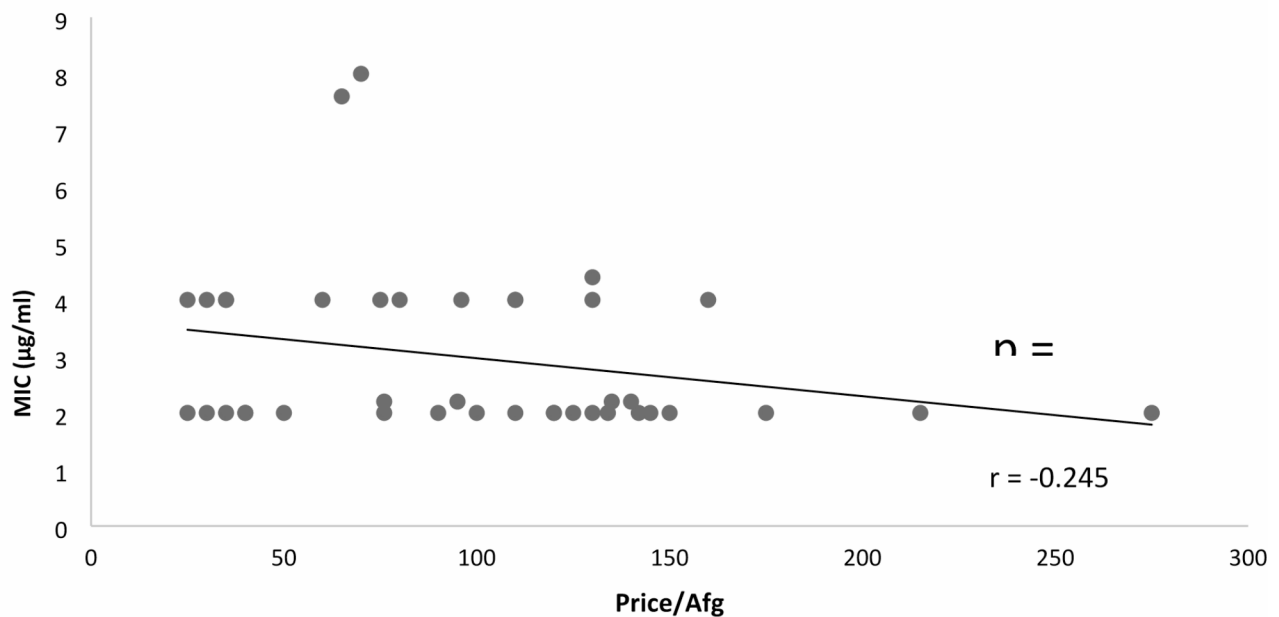
**Fig. 2** The number of tested gentamicin brands and the countries where they manufactured. The X-axis represents the countries where the antibiotics were produced, while the Y-axis shows the number of gentamicin brands tested from each country, with the exact numbers displayed above each bar



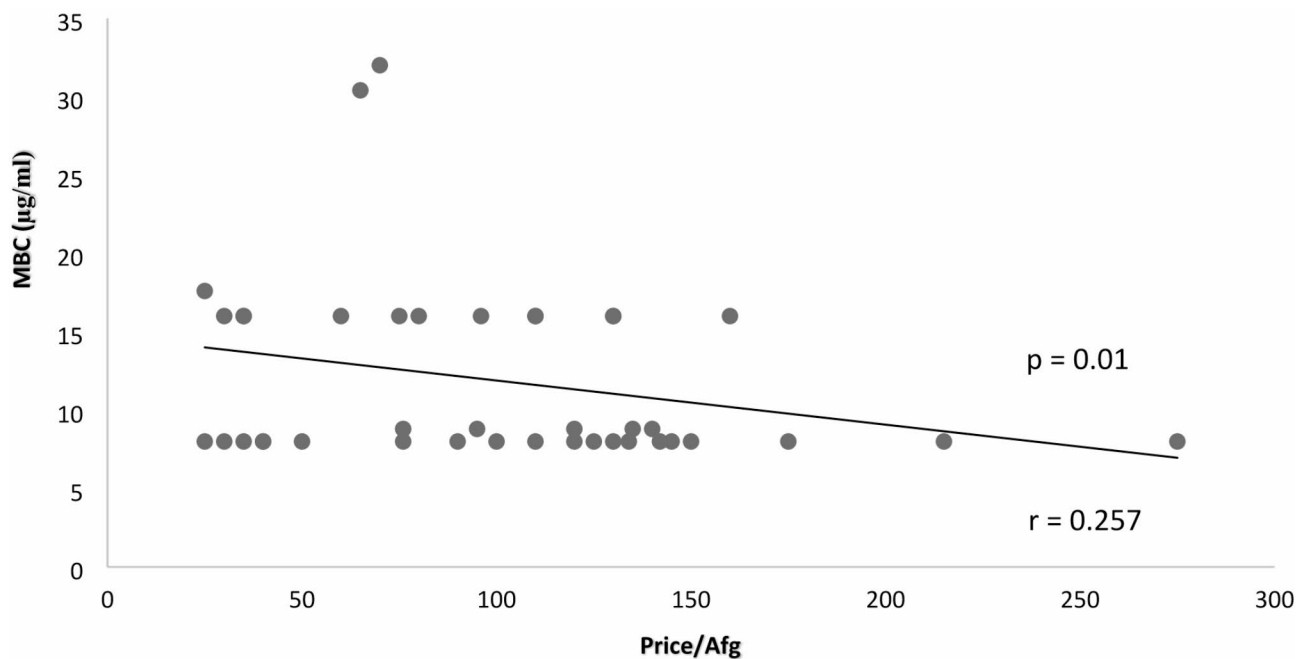
**Fig. 3** The graph illustrates the average Minimum Inhibitory Concentration (MIC) of different ciprofloxacin brands against *S. aureus* in µg/ml. The X-axis represents the various ciprofloxacin brands, while the Y-axis shows the average MIC for each brand, with error bars indicating the minimum and maximum values



**Fig. 4** The graph depicts the average Minimum Bactericidal Concentration (MBC) of various ciprofloxacin brands against *S. aureus* in µg/ml. The X-axis represents the different ciprofloxacin brands, while the Y-axis shows the average MBC for each brand, with error bars indicating the minimum and maximum values



**Fig. 5** The graph shows the relationship between price and the Minimum Inhibitory Concentration (MIC) of each brand. The X-axis represents the price, while the Y-axis indicates the average MIC per milliliter for each drug brand

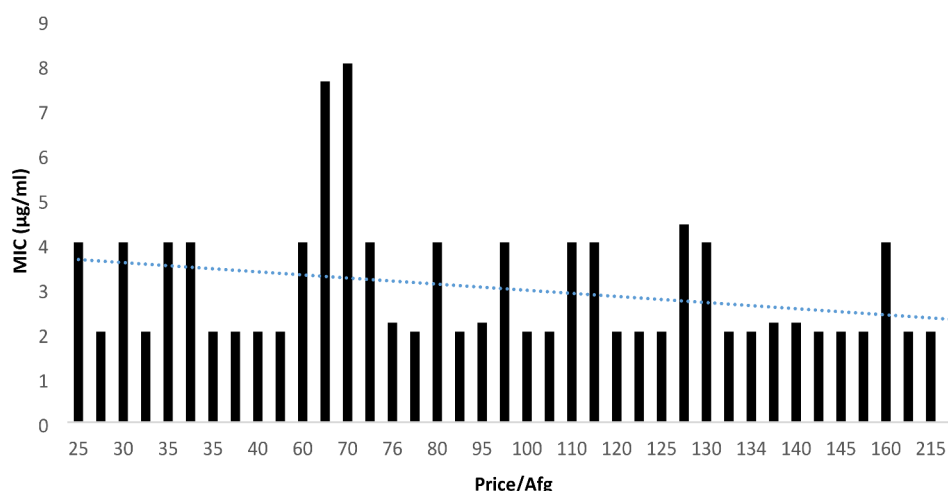


**Fig. 6** The graph shows the relationship between price and the Minimum Bactericidal Concentration (MBC) of each brand. The X-axis represents the price, while the Y-axis displays the average MBC per milliliter for each drug brand

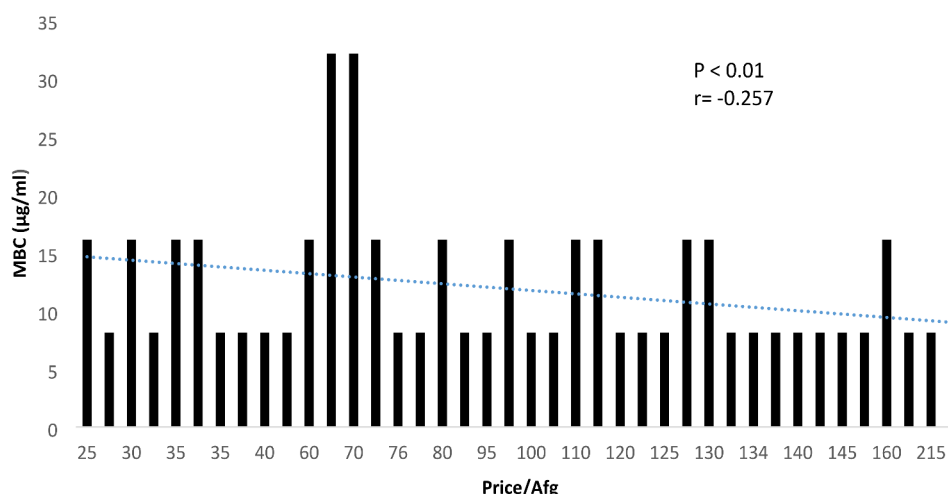
compared to price. The results reaffirmed a significant relationship between price and efficacy. An increase of one Afghani in price resulted in a decrease in MIC of approximately  $0.007 \mu\text{g/ml}$ , which was statistically significant ( $p < 0.01$ ) (Fig. 7). Similarly, an increase of one Afghani in price led to a decrease in MBC of

approximately  $0.028 \mu\text{g/ml}$ , also statistically significant ( $p < 0.01$ ) (Fig. 8).

As previously mentioned, our research included some unregistered brands. To analyze these, we separated registered brands from unregistered ones and compared their average price with the MIC and MBC using the Student's t-test. The data analysis showed that the average



**Fig. 7** This graph ranks different ciprofloxacin brands based on their MIC, from lowest to highest. The X-axis represents the Minimum Inhibitory Concentration (MIC) of each brand, while the Y-axis shows the price for each brand



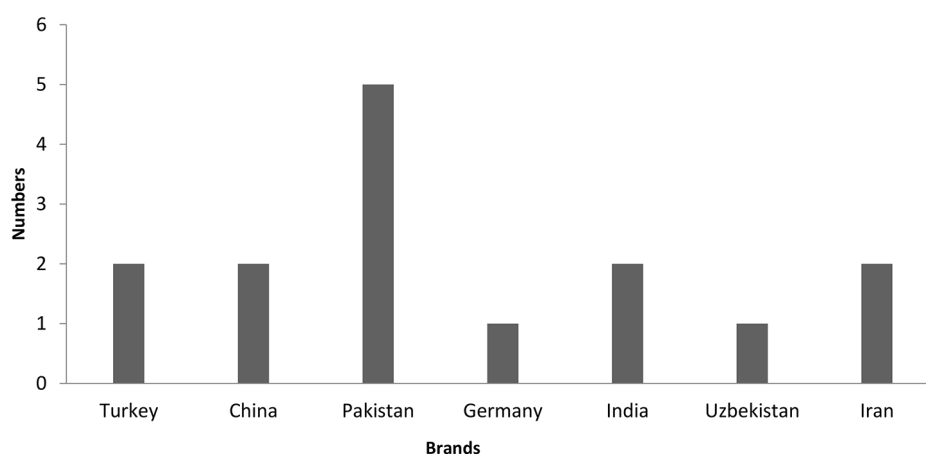
**Fig. 8** The graph ranks different ciprofloxacin brands based on their Minimum Bactericidal Concentration (MBC), from lowest to highest. The X-axis represents the MBC for each brand, while the Y-axis shows the price of each brand

MIC and MBC for registered brands were 2.8529 µg/ml and 11.39 µg/ml, respectively, while unregistered brands had an average MIC of 3.633 µg/ml and MBC of 14.80 µg/ml ( $p < 0.05$ ). Meanwhile, the average price for registered ciprofloxacin brands was 102.21 Afghani, compared to 84.83 Afghani for unregistered brands ( $p = 0.970$ ).

Additionally, this study tested 15 different brands of gentamicin for price versus efficacy, obtained from Kabul's main pharmacies. The price among these brands ranged from 3 Afghanis (~0.039 USD) to 15 Afghanis (~0.20 USD), with an average price of 8.37 Afghanis and a median of 8 Afghanis (STD  $\pm$  3.6). All 15 brands of gentamicin were imported from different countries (none manufactured in Afghanistan), with the majority from Pakistan (5 companies), Turkey (2 companies), China (2 companies), India (2 companies), Iran (2 companies), Germany (1 company), and Uzbekistan (1 company)

(Fig. 9). All gentamicin brands were packed according to international regulatory standards and labeled with details such as the manufacturer's name, manufacturing date, expiration date, batch number, importer's name, and other manufacturing specifications, except for one brand from China, which had poor packaging with no clear manufacturer name or manufacturing date.

Analysis using the One-Way ANOVA test showed that the average Minimum Inhibitory Concentration (MIC) and Average Minimum Bactericidal Concentration (MBC) for all brands against the ATCC strain of *S. aureus* were 0.33 µg/ml and 1.25 µg/ml, respectively (95% CI: 0.32 µg/ml–0.34 µg/ml for MIC and 95% CI: 1.25 µg/ml–1.25 µg/ml for MBC). The average MIC among brands ranged from 0.31 µg/ml to 0.63 µg/ml, and the average MBC among brands was 1.25 µg/ml, with no statistically significant differences (Tables 1 and 2).



**Fig. 9** The graph illustrates the number of gentamicin brands tested and their countries of manufacture. The X-axis represents the countries of manufacture, while the Y-axis indicates the number of brands obtained from each country

**Table 1** Shows the statistical significance of gentamicin brands based on minimum inhibitory concentration

P-Value	Maxi- mum MIC	Mini- mum MIC	Aver- age MIC	Code for each brand of antibiotic	Group code of brand
n.ss*	0.3125	0.3125	0.3125	Standard ATB	A
	0.3125	0.3125	0.3125	1, 2, 3, 4, 5, 7, 8, 9, 10, 11, 12, 13, 14, 15	B
n.ss*	0.625	0.625	0.625	6	C

\*n.ss = not statistically significant.

**Table 2** Displays the statistical significance of gentamicin brands based on the minimum bactericidal concentration (MBC)

(P-Value)	Maxi- mum MBC	Mini- mum MBC	Aver- age MBC	Code for each brand	Group code
n.ss*	1.2500	1.2500	1.2500	Standard ATB	A
	1.2500	1.2500	1.2500	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15	B

\*n.ss = not statistically significant

Using the Student's t-test, we separated registered brands from unregistered ones and compared the average MIC and MBC against prices. The results indicated that there were no statistically significant differences (Tables 3 and 4).

To compare the efficacy of different gentamicin brands versus price, a Pearson correlation test was employed. The results showed that a one Afghan increase in price was associated with a decrease in MIC of approximately 0.176 µg/ml, but there were no changes observed in MBC. Both results were not statistically significant ( $r = -0.176$ ,  $p > 0.05$ ) (Figs. 10 and 11).

## Discussion

Concerns have recently emerged about the efficacy and the price of antibiotics approved for use in humans. The focus of this study was to test efficacy of different brands of ciprofloxacin and gentamicin as they relate to price using the MIC and MBC tests for efficacy. Most of the brands included in our analyses were not studied before

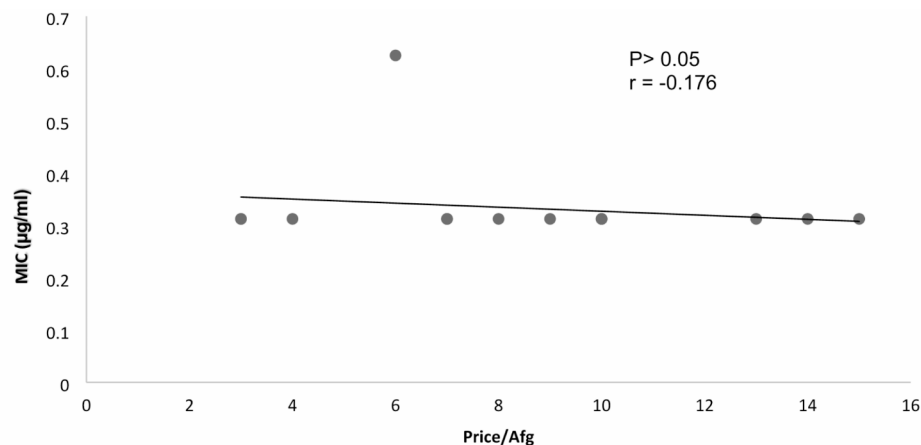
**Table 3** Displays the statistical significance of minimum inhibitory concentration (MIC) for registered and unregistered gentamicin brands in relation to price

(P-value)	Average MIC for unregistered brands	Average MIC for registered brands	MIC of unregistered brands		MIC of registered brands	
			maxi- mum	minimum	maximum	minimum
P = 0.381	0.34	0.33	1.25	0.31	0.63	0.31

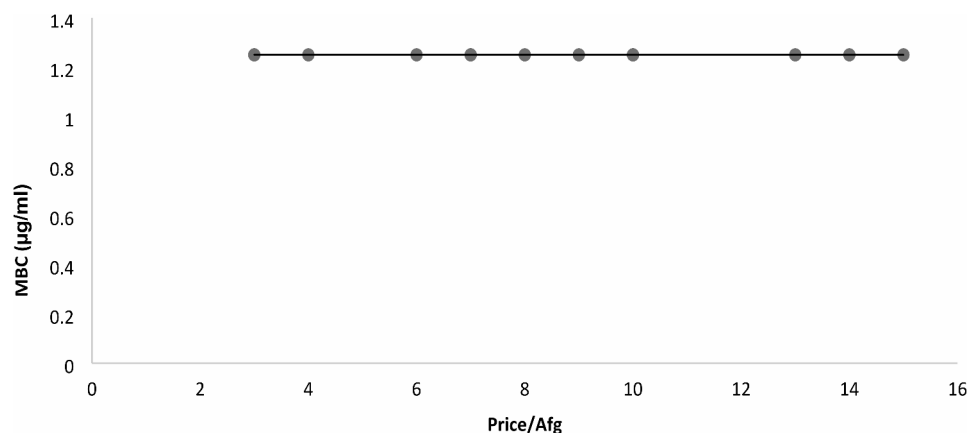
**Table 4** Displays the statistical significance of the minimum bactericidal concentration (MBC) for registered and unregistered gentamicin brands in relation to price

(P-value)	Average MBC of unregistered brands	Average MBC of registered brands	MBC of unregistered brands		MBC of registered brands	
			maxi- mum	minimum	maximum	minimum
n.ss*	1.25	1.25	1.25	1.25	1.25	1.25

\*n.ss = not statistically significant



**Fig. 10** The Minimum Inhibitory Concentration (MIC) of gentamicin brands versus price, showing no statistically significant correlation ( $r = -0.176$ ,  $p > 0.05$ )



**Fig. 11** The Minimum Bactericidal Concentration (MBC) of gentamicin brands versus price, showing no statistically significant relationship

and none were tested for efficacy using the MIC and MBC assays, in Afghanistan. In this study the impurities of samples and additional chemical tests which will be required to do so, are have not measured. The results of this study show that several brands of ciprofloxacin and gentamicin are available in Kabul pharmacy, which have different prices.

We selected a significance level of  $p < 0.05$  for our analysis, which is a commonly accepted threshold point in clinical research and medicine. By reducing the possibility of Type I errors and allowing for the discovery of statistically significant effects, this level achieves a crucial balance. It serves as a standard for determining whether observed results can be considered meaningful and not due to random chance. We additionally understand that confounding variables may have an effect on how the main variables in our study relate to one another. We addressed this by implementing a number of measures to lessen the impact of confounders. In order to control for known confounding variables and make sure that outside

influences are not biasing the results, we used randomization in our research. To assess the reliability of our results, we also performed sensitivity analyses, taking into account the potential for unmeasured confounders. We aimed to lower the possibility of confounding bias and improve the validity of our findings by implementing these measures.

Our study shows that there was a significant relationship between the price and efficacy of some brands in Kabul drugstores, compared to standard ciprofloxacin (with increase by one Afghani in prices, the efficacy also increased to the specified values mentioned in the results ( $P < 0.05$ ). The findings suggest that more expensive brands might have more therapeutic benefits, which could be attributed to factors like greater formulation, higher-quality ingredients, or more stringent production procedures. Our study's results are consistent with those of Miljković MD et al. (2022), who correlated drug price to efficacy measures, suggesting that more expensive cancer medications might be more effective [10].



Additionally, the study highlights the presence of unregistered medicines in the Afghan market. A relationship was found between the price and efficacy of registered and unregistered ciprofloxacin brands. Unregistered brands may have impurities or poor production methods that affect the product's overall effectiveness or alter the concentration of the active component. Furthermore, less stable formulations could result from poor supervision by regulators and quality control, which would reduce the efficacy of medicine. Use of unregistered antibiotic may have negative impacts on public health since inadequate treatments could promote the emergence of antibiotic resistance. From a regulatory perspective, the absence of supervision for unregistered brands might allow substandard or counterfeit products reach the market, causing a threat to public health. This emphasizes how crucial strict regulation and quality assurance are for all antimicrobial products, whether or not they are registered.

However, for gentamicin, no such relationship between price and efficacy was observed when comparing registered and unregistered brands. A number of factors contributing in this result. First one is the stability of gentamicin that highlights the complexity of drug efficacy, which may be influenced by factors other than cost, such as manufacturing practices. There may also be other reasons why there isn't a strong correlation between cost and effectiveness, such as the particular manufacturing method and quality control procedures.

The results of other research show that in developing countries the multiplicity of brands and price differences are directly related to the quality of the drug, meaning that in most low-priced drugs the amount of active ingredient is lower than that stated in the label, or There have been impurities in the drug that have had an impact on their effectiveness [4, 11].

Our study limitations are the inability to determine the quantities of active ingredients in the antibiotics under examination due to resource limitations. This limitation may have influenced the interpretation of the efficacy outcomes. The second limitation of our investigation is the absence of in vivo validation, which we recognize as a significant factor in evaluating the true therapeutic potential of the antibiotics assessed. Due to resource limitations and ethical considerations. In case of ciprofloxacin We anticipate that forthcoming research with sufficient resources and ethical approval will rectify this deficiency and provide a more complete appraisal of the antibiotics' effects. The third limitation of this study is the potential impact of batch-to-batch variability, despite the fact that ciprofloxacin was taken from a single batch. The efficacy of the medicine may be impacted by batch variations even with efforts to maintain a constant and optimal storage environment. Additionally, the excipients

in the formulations may have an effect on the effectiveness of ciprofloxacin; however, our ability to assess this effect was limited by inadequate information about the specific excipients used in each formulation. All of these aspects highlight the need for additional study to completely account for these factors.

## Conclusions

The results of this study highlight the critical need for stringent quality control and regulatory oversight, especially for unregistered antibiotics, due to the significant variations observed in Ciprofloxacin efficacy ( $p < 0.01$ ), even though no such difference was noted with Gentamicin. Policymakers should implement regulations to ensure all antibiotic brands adhere to quality standards, while pharmacists and healthcare professionals should prioritize using registered, effective medications to safeguard public health. In light of these findings, we advocate for additional chemical and clinical investigations concerning the various brands of both ciprofloxacin and gentamicin.

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## Author contributions

All authors contributed to the conception and design, while data collection and analysis were specifically performed by AZ Noori, H Yousufi, and HM Naimi. The initial draft of the manuscript was made by AZ Noori. All authors reviewed and provided feedback on earlier versions and ultimately approved the final manuscript.

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This study was conducted out with no funding.

## Data availability

No datasets were generated or analysed during the current study.

## Declarations

### Ethics approval and consent to participate

Not applicable.

### Competing interests

The authors declare no competing interests.

### Consent for publication

Not applicable.

### Author details

<sup>1</sup>Department of Microbiology, Faculty of Pharmacy, Kabul University, Kabul, Afghanistan

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