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Comparative Evaluation of Ceftriaxone Efficacy Against Escherichia coli: A Study of Three Commercial Brands Using Minimal Inhibitory Concentration

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ABSTRACT:

Objective: This study compares the efficacy of three commercially available ceftriaxone brands in Libya (from Tunisia, Spain, and India) against Escherichia coli using minimal inhibitory concentration (MIC) assays.

Methods: A susceptible strain of E. coli was tested following CLSI protocols. MIC values were determined using serial two-fold dilutions of ceftriaxone in Mueller-Hinton broth. Experiments were conducted in triplicate under controlled laboratory conditions. Results: The Spanish and Indian brands exhibited lower MIC values (0.1172–0.2344 mcg/mL), indicating higher efficacy, while the Tunisian brand showed reduced efficacy with MIC values (2.7581 mcg/mL) exceeding standard benchmarks.

Conclusions: These findings underscore the variability in the efficacy of ceftriaxone brands, emphasizing the need for stringent quality control and standardized testing.

Keywords: E. coli, MIC, ceftriaxone, UTI, ENT infections.

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INTRODUCTION

Ceftriaxone is a third-generation, broad-spectrum cephalosporin antibiotic with a long half-life (8 hours). It belongs to the beta-lactam class of antibiotics and inhibits bacterial cell wall synthesis, leading to cell lysis and a bactericidal effect (Katzung, 2012; Tripathi, 2019). Ceftriaxone, administered intravenously or intramuscularly, is effective against a wide range of Gram-positive and Gram-negative bacteria and is therefore used to treat various infections, including respiratory, skin, soft tissue, urinary tract (UTI), and ear, nose, and throat (ENT) infections caused by susceptible pathogens(Brogden & Ward, 1988; Richards, Heel, Brogden, Speight, & Avery, 1984) . Adverse effects may include hypersensitivities, hypoprothrombinemia, and bleeding(Shanbhag, 2015) .Ceftriaxone is a recommended first-line treatment for E. coli infections(Dezfulian, 1993). E. coli is a common cause of many bacterial infections, such as cholecystitis, bacteremia, cholangitis, urinary tract infections (UTIs), traveler's diarrhea, neonatal meningitis, and pneumonia(Soussy, 1985).

The study aims to determine the effectiveness of these three brands against E. coli by measuring the MIC to obtain good prognosis in treating infections caused by E. coli and avoiding bacterial resistance. The significance of the study is to help physicians prescribe effective drugs, give a clear idea to the community about the effectiveness of these brands, and prevent drug resistance by using effective antibiotics.

Although there are many different brands of ceftriaxone in our country (Libya), which have been expected to have the same effectiveness against E. coli, there is an increase in reports from the community that these brands don’t have the same effectiveness. However, there haven’t been enough findings on whether these brands might have different effectiveness or not.

MATERIALS AND METHODS

This study was conducted in the Microbiology Laboratory of Zliten Teaching Hospital between July 13 and August 1, 2022. Three ceftriaxone brands, commonly prescribed in Libya, were purchased from a private Zliten medicine market (Zliten Pharmacy). Brands from Tunisia, Spain, and India were selected to compare their efficacy in vitro. A susceptible strain of E. coli (confirmed via the Phoenix system) was used to measure the MIC of each brand according to CLSI protocols. Antibiotic stock solutions were freshly prepared by dissolving the drug powder in 10 ml of water for injection (1000 mg/10 ml). A two-fold serial dilution method was used to achieve a final concentration of 10 mcg/ml. Ten labeled test tubes were used for dilutions as follows: (1:1), (1:2), (1:4), (1:8), (1:16), (1:32), (1:64), (1:128), (1:256), (1:512), along with positive and negative controls. E. coli suspensions were added to all tubes except the negative control. Samples were incubated at 37°C for 24 hours, and bacterial growth was assessed by visual turbidity. MIC calculations were then performed, and the experiment was repeated three times for each brand.

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RESULTS

The study evaluated the efficacy of three ceftriaxone brands—Spanish, Tunisian, and Indian—against *Escherichia coli* using minimum inhibitory concentration (MIC) assays. The findings are presented in **Table 1**, **Table 2**, and **Figure 1**.

As shown in Table 1 the various dilutions tested for each brand and the corresponding turbidity observed in the medium. These dilutions indicate the ability of the antibiotic to inhibit bacterial growth, with higher dilutions reflecting greater efficacy of the brand.

Table 1: Dilutions at Which Turbidity Appeared

	Experiment 1	**Experiment 2**	**Experiment 3**
Spanish	(1:32)	(1:64)	(1:64)
Tunisian	(1:2)	(1:2)	(1:64)
Indian	(1:32)	(1:4)	(1:32)

As shown in Table 2 the MIC values for each brand are based on the results of three experiments. These values represent the minimum concentration of the antibiotic required to inhibit bacterial growth, reflecting the antibiotic's efficiency. The data include the lowest concentration that inhibited growth and the highest concentration that allowed growth, helping to determine the brands' effectiveness.

Table 2: MIC of Three Brands of Ceftriaxone.

Brands	**Exp.NO.**	**Lowest conc. Inhibit bacterial growth (mcg/ml)**	**Highest conc. allows bacterial growth (mcg/ml)**	**MIC (mcg/ml)**
Spanish	1	0.3125	0.1563	0.2344
	2	0.1563	0.0782	0.1172
	3	0.1563	0.0782	0.1172
Tunisian	1	5	2.5	3.75
	2	5	2.5	3.75

	3	0.1563	0.0782	0.1172
Indian	1	0.3125	0.1563	0.2344
	2	2.5	1.25	1.875
	3	0.3125	0.1563	0.2344

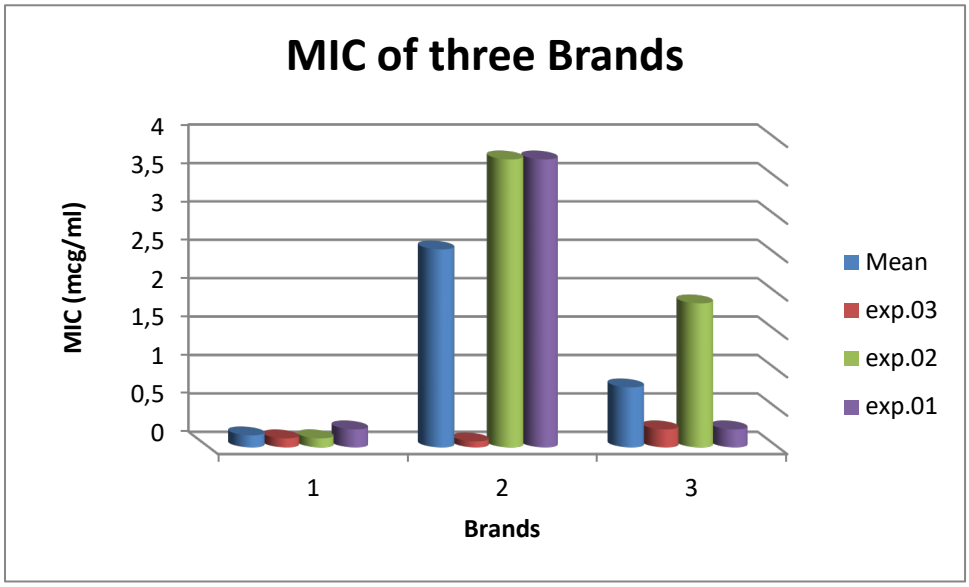

Figure 1: The Mean MIC for the Three Brands (1 = Spanish, 2= Tunisian, 3= Indian) [Include a clear bar graph representing this data]

As shown in Figure 1 the mean MIC values for each brand are based on the results of the three experiments. Each bar represents the average MIC for a specific brand. The figure visually highlights the differences in antibiotic efficacy among the three brands, with lower MIC values indicating higher efficacy.

DISCUSSION

Our study highlights significant differences in the efficacy of three ceftriaxone brands tested in inhibiting Escherichia coli growth. The evaluation focused on determining the minimum inhibitory concentration (MIC), defined as the lowest antibiotic concentration (mcg/mL) that prevents visible bacterial growth after a standardized incubation period. The MIC serves as a critical benchmark for assessing antibiotic potency, where a lower MIC value correlates with higher antimicrobial effectiveness. The Spanish and Indian ceftriaxone brands demonstrated mean MIC values of 0.1563 mcg/mL and 0.7813 mcg/mL, respectively. These values fall within the established Clinical and

Laboratory Standards Institute (CLSI) breakpoint for ceftriaxone against E. coli (<1 mcg/mL), indicating optimal efficacy. These findings are consistent with previous studies that have validated ceftriaxone as an effective agent against Gram-negative pathogens like E. coli, which is frequently implicated in urinary tract infections (UTIs), neonatal meningitis, and sepsis. The Spanish brand showed superior activity with the lowest mean MIC, reflecting its high quality and potency. In contrast, the Tunisian (UNIMED) ceftriaxone exhibited a mean MIC of 2.7581 mcg/mL, exceeding the CLSI standard range for susceptibility. This diminished efficacy raises concerns regarding potential factors such as manufacturing variability, differences in raw material quality, formulation, or production standards, and storage conditions. Exposure to temperature fluctuations or prolonged storage under suboptimal conditions could degrade the active compound. Additionally, the specific batch (NO. 79) used in the study may have suffered from manufacturing inconsistencies, leading to reduced potency. The positive control's turbidity confirmed bacterial growth in untreated conditions, affirming the viability of the test strain. The absence of turbidity in the negative control validated the sterility of the media and ensured the integrity of experimental procedures. These controls reinforce the reliability of the observed MIC differences across the tested brands.

Our findings are congruent with earlier research, such as(Thapa & Mahat, 2010) , which documented variability in the antimicrobial efficacy of generic ceftriaxone brands. While the Spanish and Indian brands aligned with expected performance, the Tunisian brand's elevated MIC highlights the need for regulatory oversight. The presence of substandard or poorly stored antibiotics can contribute to therapeutic failures and drive the emergence of antimicrobial resistance (AMR). Notably, ceftriaxone remains a critical treatment for E. coli infections, especially in resource-limited settings where resistance to other antibiotics like fluoroquinolones and carbapenems is rising. Therefore, ensuring the quality of ceftriaxone is vital to maintaining its clinical utility.

Future studies should include additional bacterial isolates and compare ceftriaxone efficacy against other pathogens, such as Klebsiella pneumoniae and Pseudomonas aeruginosa, to provide a more comprehensive analysis. Repeating the study with multiple batches from each brand could help identify inconsistencies related to manufacturing or distribution. Pharmacokinetic and pharmacodynamic studies would provide insight into in vivo efficacy and determine whether differences in MIC translate to clinical outcomes. Evaluating the chemical stability of ceftriaxone under various storage conditions could confirm the role of environmental factors in efficacy reduction. This study underscores the critical need for stringent quality control of ceftriaxone formulations to prevent the distribution of suboptimal drugs. The reduced efficacy of the Tunisian brand raises important concerns about manufacturing practices and the impact of storage conditions. By addressing these issues, healthcare providers can ensure the continued effectiveness of ceftriaxone in combating E. coli and other Gram-negative bacterial infections.

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CONCLUSION

The Spanish and Indian ceftriaxone brands demonstrated superior efficacy against E. coli compared to the Tunisian brand. These results emphasize the need for regular monitoring and quality assurance of antibiotics to prevent antimicrobial resistance and ensure effective treatment.

Advice to Policy Makers

Policymakers must prioritize the enforcement of stringent quality assurance systems to ensure that all antibiotics, including ceftriaxone, meet international standards. This includes routine testing of imported and locally produced drugs for potency and stability. Supply chain monitoring should be enhanced to prevent improper storage and handling, as temperature fluctuations can degrade antibiotic efficacy. Ensuring proper cold chain logistics is essential to maintaining drug quality.

Regulatory frameworks must mandate detailed labeling that includes storage instructions, batch numbers, and expiration dates. Investing in local manufacturing under strict oversight can reduce reliance on imports and improve quality control. Collaboration between regulatory bodies, pharmaceutical companies, healthcare providers, and researchers is critical to address issues like counterfeit drugs, substandard products, and antimicrobial resistance.

A robust antimicrobial resistance surveillance program should be implemented to track resistance patterns and inform policy decisions. Healthcare providers should receive training to identify potential antibiotic failures and report them promptly. Public awareness campaigns should educate communities on the importance of using high-quality antibiotics and the risks associated with substandard drugs. These measures can ensure the availability of effective antibiotics, protect public health, and mitigate the growing threat of antimicrobial resistance.A

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