International Journal of Chemical and Biochemical Sciences
(ISSN 2226-9614)

Journal Home page: www.iscientific.org/Journal.html

Evaluation of Fosfomycin in-vitro susceptibility among gram negative isolates from urine culture in a tertiary care hospital in Lucknow

Sandeepika Dubey[1*], Areena Hoda Siddiqui[2], Meenakshi Sharma[3]

[1,2] Integral Institute of Medical Sciences Research, Department of Microbiology, Lucknow, Uttar Pradesh, India.

[3]Autonomous State Medical college, Lakhimpur Kheri, Uttar Pradesh, India.

Abstract

The rise of bacteria that are Multidrug- resistant or Extended Drug Resistant (MDR or XDR) and the lack of novel antibiotics have wreaked havoc on patient treatment options. Fosfomycin has just recently come to light because of the development of resistance to existing drugs. This study aims to evaluate the Fosfomycin susceptibility of Gram- negative isolates in vitro. A prospective study done in the Department of Microbiology, Integral Institute of Medical Sciences of Research, Lucknow, over a period of six months from April 2023 to September 2023. A total of 1328 urine samples were processed in microbiology lab and after identification of urinary isolates, antibiotic susceptibility testing was performed, and results were interpreted following the Clinical and Laboratory Standards Institute guidelines (CLSI). Fosfomycin sensitivity was tested by the Kirby-Bauer disc diffusion method. 353 of the 1328 processed urine samples showed a growth of pathogens. 184 (52.1%) of the isolates were Gram-negative, while 169 (47.8%) were Gram-positive. Fosfomycin (7%) and Nitrofurantoin (13%) showed lower rates of resistance among these isolates. Relatively higher rates of resistance were observed for Doripenem (17%), Meropenem (17%), Imipenem (18%), Amikacin (18%), Gentamicin (27.9%). Norfloxacin, Aztreonam, Cefepime, Ciprofloxacin and Levofloxacin and Cotrimoxazole showed a high resistance rate of 46.2%, 48.8%, 50%, 60.4%, 61% and 70% respectively. Fosfomycin's low resistance (7%) to the antibiotic indicates that it works well as a urinary antibiotic. Uropathogenic Enterobacteriaceae isolates exhibited an excellent level of in vitro susceptibility to Fosfomycin. These in vitro results highlight the unexplored possibilities of Fosfomycin as a superior therapeutic option for the treatment of UTIs, and it has a good chance of expanding into a safe and effective oral alternative treatment that can be used in inpatient as well as outpatient settings.

Keywords: Gram-Negative bacteria, Fosfomycin, Urinary Tract Infections.

Full length article **Corresponding Author*, e-mail: sandipika.02@gmail.com Doi # https://doi.org/10.62877/71-IJCBS-24-25-19-71

1. Introduction

Fosfomycin (Phosphomycin) was presented as a novel antibacterial agent in 1969. It is classified as a bactericidal antibiotic with antibacterial action against both Gram-negative and Gram-positive bacteria [1]. Long used as a highly efficient antibacterial medicine, for the treatment of urinary tract infections (UTIs), it was largely superseded by new antibiotics like -β lactams and fluoroquinolones when they were developed. There have been reports of an abrupt rise of resistant pathogens over the past 10 years, including those that produce extended spectrum -β lactamases (ESBLs) or multi-drug resistant (MDR) pathogens (defined as being resistant to at least one agent from three or more antimicrobial groups) [2,3]. Given the circumstances, reassessing the older well-known antibiotics seems like a preferable course of action rather than limiting the accessibility of new antimicrobial medications. Fosfomycin inhibits the synthesis of bacterial cell wall by inactivating the enzyme UDP-N-acetylglucosamine-3-enol-pyruvyltransferase (MurA). Excellent tissue penetration, reduced adhesion to the urogenital mucosa, and high levels of unaltered excretion in the urine are all characteristics of this substance [4,5]. According to the results of previously published studies, this antibiotic is a suitable choice for the treatment of uncomplicated UTIs due to its benefits of administration as a single dose per day, a favorable safety profile, no impact on the anaerobic gut flora, and availability during pregnancy [4-9]. UTIs caused by *Escherichia coli*, *Enterococcus faecalis*, *Klebsiella*, *Citrobacter*, and *Enterobacter* spp. as well as *E. coli* have been successfully treated with Fosfomycin tromethamine (FOF), a stable salt of Fosfomycin [4,5,8-11]. In the last five years, interest in the usage of Fosfomycin has increased due to all the above-mentioned data.

The Infectious Diseases Society of America (IDSA) and European Society for Clinical Microbiology and Infectious Diseases (ESCMID) guidelines recommend Fosfomycin, nitrofurantoin, and trimethoprim-sulfamethoxazole (TMP-SMX) as first-line agents to treat acute uncomplicated UTIs in adult females, with fluoroquinolones, amoxicillin-clavulanate, and other beta-lactams reserved as second-line agents [12]. The goal of this study was to determine the in-vitro susceptibility of Fosfomycin among gram negative isolates from urine culture in a tertiary care hospital Lucknow.

2. Material and Methods

2.1. Study Design

This cross-sectional study covered 6 months, from May 2023 to October 2023, at a tertiary care hospital affiliated with a medical college in Lucknow.

2.2. Ethical Consideration

Written approval (Letter No. IEC/ IIMSR/ 2023/ 52/ IEC/ 16-05-2023) was given by the Institutional Ethics Committee. Everyone who was suspected of having a UTI in OPD or IPD was added to the study after giving their informed consent. A fact sheet detailing the salient characteristics of UTI was distributed to research participants.

2.3. Inclusion Criteria

All urine samples collected from IPD and OPD patients was sent to the microbiology laboratory of the IIMSR Hospital in Lucknow for bacteriological analysis.

2.4. Exclusion Criteria

The patients who decline to consent to participate in the study, either on their own behalf or through their guardians.

2.5. Sample Collection

Urine samples were collected midstream using large-mouthed plastic containers that were universally available. After patients with catheterization have been properly cleaned, urine is collected from the port site. Prior to the collection of samples, patients gave their informed consent. Direct delivery of urine samples for bacteriological analysis was made to the microbiology lab. Samples were kept between 4 and 8°C in case of a delay.

2.6. Laboratory Methods

Using a semi-quantitative approach, the urine specimens were inoculated onto Cysteine lactose electrolyte agar (CLED) agar. After an overnight incubation at 37˚C for 18 to 24 hours, the culture plates were examined. The number of colonies and the organisms' growth were recorded. We considered in our analysis the isolates that were taken from samples that had considerable bacteriuria ($\geq 10^5$ colony forming units (CFU)/mL colony count). The Gram stain, Oxidase test, Catalase test, and colony morphology were often used to identify isolates. Other biochemical tests, such as the indole (I) test, methyl red (MR) test, voges-proskauer (VP) test, citrate utilization test, urease test, triple sugar iron (TSI) test, nitrate reduction test, fermentation test of carbohydrates (sugar), Hugh and Leifson oxidative fermentative test were used to confirm the isolates as per standard operating procedures. The Kirby-Bauer disc diffusion method was used to test the antibiotic susceptibility of a panel of drugs using an inoculum on Muller Hinton agar (MHA) that was matched to 0.5 McFarland's standard. The following antibiotics were used against Gram-negative isolates: ampicillin/sulbactam (10/10 µg), piperacillin tazobactum (100/10 µg), amikacin (30 µg), gentamicin (10µg), cotrimoxazole (1.25/23.75µg), cefepime (30µg) aztreonam (30µg), ciprofloxacin (5µg), imipenem (10µg), doripenem (10µg), meropenem (10µg), norfloxacin (10µg), nitrofurantoin (300µg) and Fosfomycin (200µg) supplement with 50µg of glucose-6-phosphate. The Clinical and Laboratory Standards Institute 2022 recommendations were followed in interpreting the zones of inhibition on MHA plates [13]. Zone sizes greater than 16 mm were classified as susceptible (S), 13–15mm as intermediate (I), and less than 12 mm as resistant (R). *Escherichia coli* (ATCC 25922) was utilized for quality control.

2.7. Detection of Extended Spectrum Beta Lactamase:

ESBL detection was done by combined disc test using ceftazidime (30 µg) and ceftazidime-clavulanic acid discs (30/10 µg).

2.8. Interpretation

A difference between the zone diameter of an antimicrobial agent tested in combination with clavulanate and the agent when tested alone of > 5 mm indicates the presence of ESBL [13].

2.9. Statistical Analysis

Statistical analysis of the data collected for the study was done using the Fisher's exact test using IBM SPSS statistics 20 (SPSS version 20.0). Any parameter that yielded a "P" value of less than 0.05 was considered statistically significant.

3. Results

A microbiology department of tertiary care hospital received 1328 urine samples in total during the study period for testing for antibiotic susceptibility and bacterial culture from suspected UTI cases. Out of these 1328 urine samples that were processed, 353 samples showed signs of pathogen growth. 184 out of 353 that is (52.1%) were gram negative isolates, majority of the isolates were from inpatients (n=113, 61.4%). Most patients with UTIs came from the obstetrics, medicine, emergency, and medicine wards (29.3%, 20.6%, and 19%, respectively). Female patients' percentage was more than half of the total patients (n = 130, 70.6%), followed by male patients (n = 54, 29.3%). Patients in the 16–30 age group made up 37% of the patient population, while patients in the 31–45 age group made up 19.5%. *E. coli* predominated the list of 184 gram-negative isolates with 73.3%, followed by *Klebsiella* species (16.3%) as shown in (Figure 1).

3.1. Antibiotic Susceptibility Pattern of Gram Negative Uropathogens

Lower rates of resistance were seen for Fosfomycin (7%) and Nitrofurantoin (13%) among 184 gram-negative isolates. The rates of resistance to Doripenem (17%), Meropenem (17%), Imipenem (18%), Amikacin (18%) and Gentamicin (27.9%) were all comparatively higher.

The high resistance rates to Norfloxacin, Aztreonam, Cefepime, Ciprofloxacin, Levofloxacin and Cotrimoxazole were 46.2%, 48.8%, 50%, 60.4%, 61% and 70% respectively. All antibiotics, except Fosfomycin, were in routine clinical use in our hospital. In our institution, all antibiotics were routinely used for clinical purposes, except for Fosfomycin. Fosfomycin is a good urinary antibiotic, as evidenced by the limited resistance (7%) to it (**Figure 2)**. ESBL was produced by 44.5% (n = 82) of the isolates overall, the majority of which were E. coli (n = 76).

3.2. Antibiotic susceptibility pattern of all first line antibiotics in common susceptible isolates and isolates producing β-lactamase (ESBL).

Fosfomycin (in *E. coli* 96.6% and in *E. coli* ESBL 92.1%) and Nitrofurantoin (88.1% in *E. coli* and 85.5% in *E. coli* ESBL) showed relatively higher activeness against both common susceptible and β-lactamase producing isolates (ESBL) in comparison to all other tested first line antibiotics which had a much lower ($p < 0.0001$) sensitivity rate compared to the isolates that produced β-lactamase **(Table 1)**.

4. Discussion

In healthcare settings, UTI is most common complaint presenting to OPD/IPD. For effective treatment, the patients frequently have silent bacteriuria and non-specific complaints, which need to be confirmed in a lab. The current state of UTI therapy choices is restricted due to the evolution of resistance to commonly used antibiotics. For this reason, there is a growing need to create and implement novel antimicrobials. All the same, there aren't many novel antibiotics being developed right now. Here, an earlier antibiotic called Fosfomycin has found its use again in the management of UTI [14]. All age groups and genders are affected by UTI, which are the most common illness. Males were not as common among UTI patients as females were in the current study. 52.3 % of the 353 urine isolates in the current study were gram negative bacilli, and 95.1 % of the isolates were Enterobacteriaceae, out of 184-gram negative isolates. It was shown that *E. coli* was the most prevalent pathogen in the current study. The Enterobacteriaceae family is a prominent cause of UTI, accounting for 64% of cases, with *E. coli* (50%) being the most common species in the family reported by Srivastava *et al.* from Lucknow [15]. Several reasons contribute to *E. coli* prevalence as the most common uropathogen, such as its most common intestinal flora and virulence factors, adhesins that allow entry into the urethra through type-I and P fimbriae [16]. *Klebsiella* spp. were present in 16.3% of the samples in this study. Comparable numbers of *Klebsiella* spp. were noted by other observers [17-21]. In the population, non-fermenters made up 4.89%. Similar findings have previously been reported by a few numbers of authors [17-22]. In the present study, we compared *in vitro* activity of Fosfomycin with other antibiotics commonly used for treating UTI to evaluate its utility among the 184 isolates. Lower rates of resistance were observed for Fosfomycin (7%), and nitrofurantoin (13%) similar finding reported by Sreenivasan *et al.* from Puducherry found low resistance to Fosfomycin 13.3% [23]. Norfloxacin, Aztreonam, Cefepime, Ciprofloxacin, Levofloxacin and Cotrimoxazole showed a high resistance rate of 46.2%, 48.8%, 50%, 60.4% and 61% and 70% respectively (**Figure 2**). Doripenem (17%), Meropenem (17%), Imipenem (18%), Amikacin (18%), and Gentamicin (27.9%) all had relatively lower rates of resistance. Other studies showed similarly high rates of resistance to oral antibiotics [24-25]. Amoxyclav, cotrimoxazole, ampicillin, nitrofurantoin, and norfloxacin were reported to have decreased in vitro activity in a study conducted in North India by Patwardhan and Singh.[24] In a recent study conducted in South India, Sardar et al. discovered that out of 170 uropathogenic *E. coli* isolates, 84.8%, 83.6%, and 79% were resistant to amoxicillin, cefixime, and norfloxacin, while imipenem and methenamine mandelate showed 100% sensitivity on these antibiotics [25]. We compared the susceptibility of susceptible bacterial isolates and bacterial isolates exhibiting multiple resistance (ESBL) to commonly used first-line antibiotics (Fosfomycin, nitrofurantoin, ampicillin-sulbactam, co-trimoxazole, ciprofloxacin, cefepime) to assess the viability of using oral antibiotics (particularly Fosfomycin trometamol) in the treatment of urinary tract infections brought on by multiple resistant pathogens. Several investigations have found that the prevalence of ESBL-producing isolates in UTI ranges from 21.8% to 64.8% [17,26-28]. ESBL enzymes were detected to be produced by 44.5% (n = 82) of the isolates in this study. A similar study was published by Khan et al., which showed that 44% of the isolates of gram-negative bacteria developed ESBL. 35.13% of *E. coli* isolates developed ESBLs after 2.7% of Klebsiella spp. [27]. There could be a regional variance since hospitals in various areas may use different antibiotics and use different infection control strategies. Fosfomycin exhibits significant antibacterial effectiveness against ESBL-producing uropathogens and strains that were resistant to other regularly used antibiotics, which is a noteworthy finding of our investigation. It was only resistant in 8.5% of our isolates. Of the 82 (44.5%) ESBL-producing isolates, 92.1% (n=76) of the strains of *E. coli* that were ESBL showed Fosfomycin sensitivity (Table 1). Our study's observation of the higher sensitivity of Fosfomycin is consistent with the results of multiple other recent investigations [24-26,29]. Uropathogen susceptibility to oral antibiotics and Fosfomycin was examined by Patwardhan and Singh in a recent study conducted at apex tertiary care centers of India. Fosfomycin sensitivity was present in 2730 (98.1%) of the 2783 non-repeating Enterobacteriaceae urine isolates from patients of both sexes and all ages. 91.9% of metallo β lactamase-producing isolates and 96.5% of ESBL-producing isolates showed high Fosfomycin susceptibility in vitro [24]. Our results suggest that Fosfomycin is a promising antibiotic in our country for the treatment of UTI. According to the guidelines of the Infectious Diseases Society of America (IDSA), co-trimoxazole and nitrofurantoin are the current recommended treatments for UTI in females. In our study cotrimoxazole sensitivity is reduced and similar observation reported by Ahmad et al. [30]. The recommended guidelines for UTI therapy need to be changed to prevent this side effect of the widespread use of Fosfomycin trometamol for UTIs.

5. Limitations

This study was conducted to assess the in vitro activity of Fosfomycin rather than to determine its therapeutic efficacy.

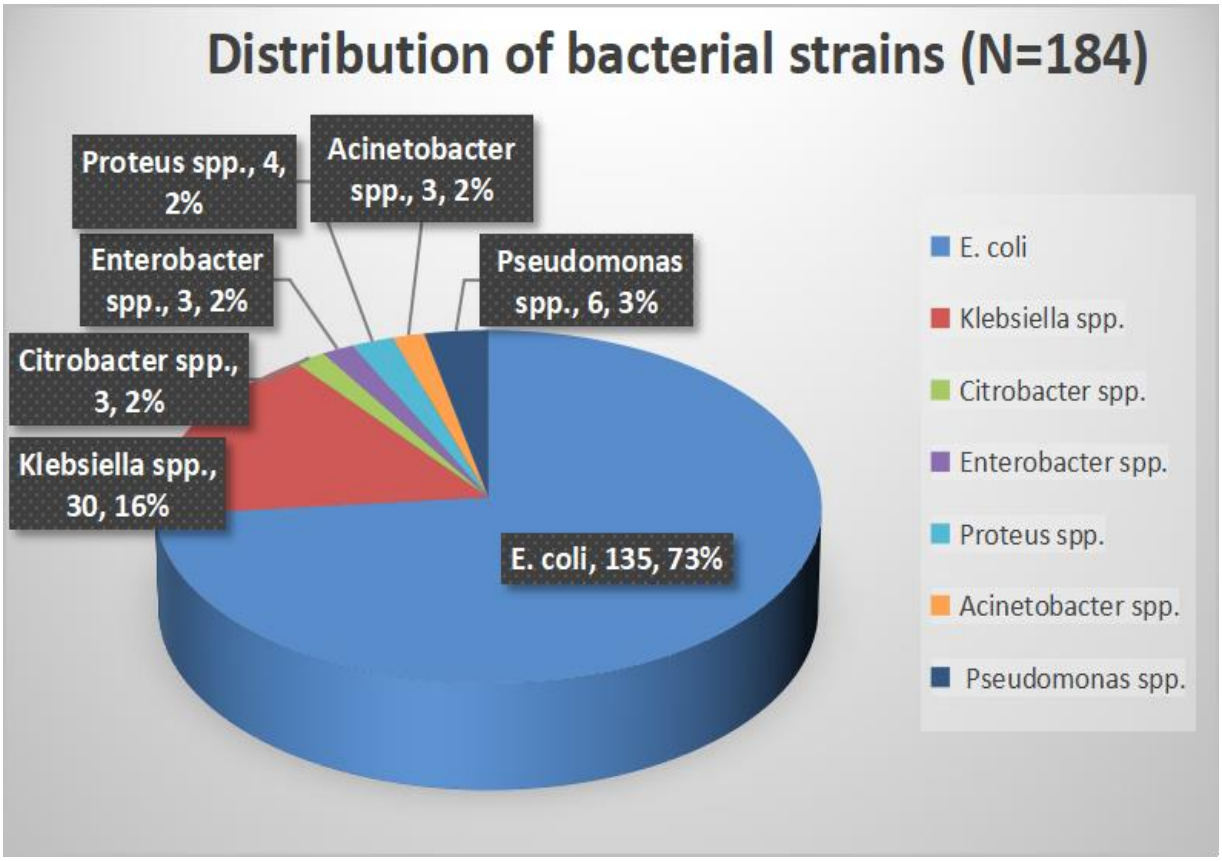

Figure 1: Bacteriological profile of gram negative uropathogens.

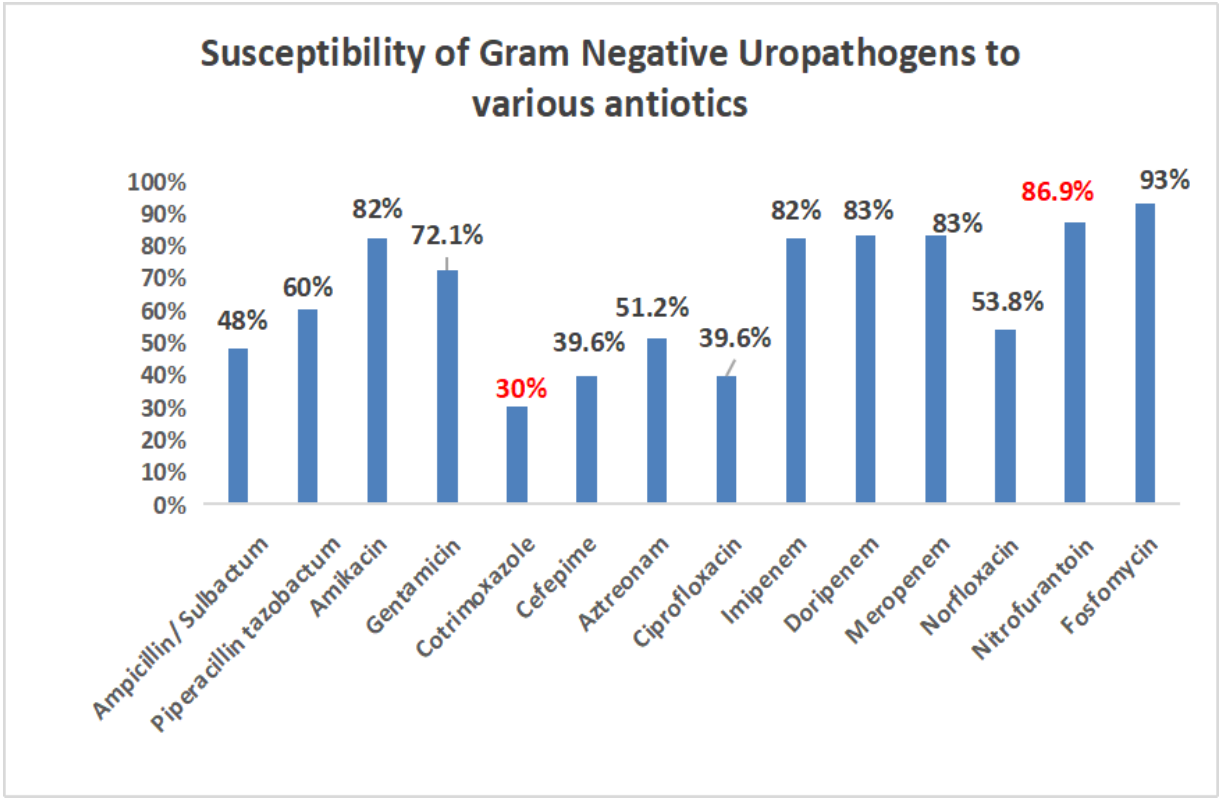

Figure 2: Susceptibility pattern of Gram negative uropathogens to various antibiotics.

Table 1: Comparing the susceptibility pattern of common susceptible isolates to chemotherapeutics and routinely used first-line antibiotics with isolates generating β-lactamase (ESBL).

Antibiotic	*E. coli* non-ESBL (n=59)	*E. coli* β- lactamase positive (ESBL)(n=76)
	Sensitivity %	Sensitivity %
Gentamicin	64.4%	59.2%
Amikacin	64.4%	77.6%
Cotrimoxazole	57.6%	38.2%
Cefepime	64.4%	15.8%
Aztreonam	61.0%	21.1%
Ciprofloxacin	49.1%	6.6%
Imipenem	86.4%	77.6%
Nitrofurantoin	88.1%	85.5%
Fosfomycin	96.6%	92.1%

Other than *E. Coli* and *K. pneumoniae*, very few isolates of Enterobacteriaceae were identified in the investigation.

6. Conclusions

In our investigation, the oral antibiotics that exhibited significant in vitro antibacterial activity against the Enterobacteriaceae isolates were Fosfomycin and nitrofurantoin. Most isolates that produced ESBLs and MDRs were Fosfomycin sensitive. Consequently, it may be a viable substitute for the first-line antibiotics that are currently available for treating UTI, particularly for a naive population where Fosfomycin use is nonexistent. Additional research is required to assess the different genotypic and phenotypic traits of Fosfomycin resistance in uropathogens in vitro.

Acknowledgments

We are grateful to Dr. Meenakshi Sharma and Prof. Areena Hoda Siddiqui for their revisions on this paper. The Manuscript Communication Number (MCN) for IU/R & D/2024 is MCN0002528.

Sources of Support and Funding

There was no financial support from any specific grant from funding agencies in the public, commercial, or not-for-profit sectors for this original article.

Conflicts of Interests

There are no conflicts of interest.

Statements and Declarations

This article has been reviewed and approved by all authors. This manuscript is unique, unpublished elsewhere, and not under consideration from any other publication.

References

[1] M. L. Grayson, S. M. Crowe, J. S. McCarthy, J. Mills, J. W. Mouton, S. R. Norrby, D. L. Paterson, M. A. Pfaller. (2010). Kucers' The Use of Antibiotics Sixth Edition: A Clinical Review of Antibacterial, Antifungal and Antiviral Drugs. CRC press.

[2] A. P. Magiorakos, A. Srinivasan, R. B. Carey, Y. Carmeli, M. E. Falagas, C. G. Giske, S. Harbarth, J. F. Hindler, G. Kahlmeter, B. Olsson-Liljequist, D. L. Paterson, D. L. Monnet. (2012). Multidrug-resistant, extensively drug-resistant, and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. Clinical microbiology and infection. 18 (3): e268-e281.

[3] M. Kaase, F. Szabados, A. Anders, S. G. Gatermann. (2014). Fosfomycin susceptibility in carbapenem-resistant Enterobacteriaceae from Germany. Journal of Clinical Microbiology. 52 (6): e1893-e1897.

[4] S. Auer, A. Wojna, M. Hell. (2010). Oral treatment options for ambulatory patients with urinary tract infections caused by extended-spectrum-β-lactamase-producing *E.coli*. Antimicrobial agents and chemotherapy. 54 (9): e4006-e4008.

[5] R. J. Chislett, G. White, T. Hills, D. P. J. Turner. (2010). Fosfomycin susceptibility among extended-spectrum-β-lactamase-producing Escherichia coli in Nottingham, UK. Journal of antimicrobial chemotherapy. 65 (5): e1076-e1077.

[6] B. J. Knottnerus, S. Nys, G. ter Riet, G. Donker, S. E. Geerlings, E. Stobberingh. (2008). Fosfomycin tromethamine as second agent for the treatment of acute, uncomplicated urinary tract infections in adult female patients in The Netherlands? Journal of antimicrobial chemotherapy. 62 (2): e356-e359.

[7] G. C. Schito. (2003). Why fosfomycin trometamol as first line therapy for uncomplicated UTI? International journal of antimicrobial agents. 22 (1): e79-e83.

[8] M. E. Falagas, E. K. Vouloumanou, A. G. Togias, M. Karadima, A. M. Kapaskelis, P. I. Rafailidis, S. Athanasiou. (2010). Fosfomycin versus other antibiotics for the treatment of cystitis: a meta-analysis of randomized controlled trials. Journal of Antimicrobial Chemotherapy. 65 (9): e1862-e1877.

[9] S. S. Patel, J. A. Balfour, H. M. Bryson. (1997). Fosfomycin tromethamine: a review of its antibacterial activity, pharmacokinetic properties and therapeutic efficacy as a single-dose oral treatment for acute uncomplicated lower urinary tract infections. Drugs. 53 (1): e637-e656.

[10] J. Oteo, V. Bautista, N. Lara, O. Cuevas, M. Arroyo, S. Fernández, Spanish ESBL-EARS-Net Study Group. (2010). Parallel increase in community use of Fosfomycin and resistance to Fosfomycin in extended-spectrum β-lactamase (ESBL)-producing Escherichia coli. Journal of Antimicrobial Chemotherapy. 65 (11): e2459-e2463.

[11] C. L. Lu, C. Y. Liu, Y. T. Huang, C. H. Liao, L. J. Teng, J. D. Turnidge, P. R. Hsueh. (2011). Antimicrobial susceptibilities of commonly encountered bacterial isolates to fosfomycin determined by agar dilution and disk diffusion methods. Antimicrobial agents and chemotherapy. 55 (9): e4295-e4301.

[12] K. Gupta, T. M. Hooton, K. G. Naber, B. Wullt, R. Colgan, L. G. Miller, G. J. Moran, L. E. Nicolle, R. Raz, A. J. Schaeffer, D. E. Soper. (2011). International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: a 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. Clinical infectious diseases. 52 (5): e103-e120.

[13] Clinical and Laboratory Standard Institute (CLSI). Performance standards for antimicrobial susceptibility testing. 33rd ed. CLSI supplements M100.USA.2023.

[14] E. M. Brown, D. Nathwani. (2005). Antibiotic cycling or rotation: a systematic review of the evidence of efficacy. Journal of antimicrobial chemotherapy. 55 (1): e6-e9.

[15] S. Srivastava, N. Singh, S. Sahai, M. Srivastava. (2018). Aerobic bacterial profile and antimicrobial resistance in bacterial isolates causing urinary tract infection in patients attending at integral institute of medical sciences and research hospital Lucknow. International Journal of Medical and Health Research. 4 (4): 140-146.

[16] R. Kucheria, P. Dasgupta, S. Sacks, M. Khan, N. Sheerin. (2005). Urinary tract infections: new insights into a common problem. Postgraduate medical journal. 81 (952): e83.

[17] A. Sultan, M. Rizvi, F. Khan, H. Sami, I. Shukla, H. M. Khan. (2015). Increasing antimicrobial resistance among uropathogens: Is fosfomycin the answer? Urology annals. 7 (1): e26-e30.

[18] G. Schmiemann, I. Gágyor, E. Hummers-Pradier, J. Bleidorn. (2012). Resistance profiles of urinary tract infections in general practice-an observational study. BMC urology. 12 (1): e1-e5.

[19] L. M. D. Shortliffe, J. D. McCue. (2002). Urinary tract infection at the age extremes: pediatrics and geriatrics. The American journal of medicine. 113 (1): e55-e66.

[20] R. Badhan, D. V. Singh, L. R. Badhan, A. Kaur. (2016). Evaluation of bacteriological profile and antibiotic sensitivity patterns in children with urinary tract infection: A prospective study from a tertiary care center. Indian journal of urology. 32 (1): e50-e56.

[21] A. Huttner, A. Kowalczyk, A. Turjeman, T. Babich, C. Brossier, N. Eliakim-Raz, S. Harbarth. (2018). Effect of 5-day nitrofurantoin vs single-dose fosfomycin on clinical resolution of uncomplicated lower urinary tract infection in women: a randomized clinical trial. Jama. 319 (17): e1781-e1789.

[22] G. V. Sanchez, R. N. Master, J. A. Karlowsky, J. M. Bordon. (2012). In vitro antimicrobial resistance of urinary Escherichia coli isolates among US outpatients from 2000 to 2010. Antimicrobial agents and chemotherapy. 56 (4): e2181-e2183.

[23] S. Sreenivasan, A. Kali, M. P. Charles, S. Kunigal. (2019). Evaluation of in vitro susceptibility of fosfomycin among Enterobacteriaceae isolates from urine cultures: A study from Puducherry. Journal of Laboratory Physicians. 11 (03): e249-e252.

[24] V. Patwardhan, S. Singh. (2017). Fosfomycin for the treatment of drug-resistant urinary tract infections: potential of an old drug not explored fully. International Urology and Nephrology. 49: 1637-1643.

[25] A. Sardar, S. R. Basireddy, A. Navaz, M. Singh, V. Kabra. (2017). Comparative evaluation of fosfomycin activity with other antimicrobial agents against E. coli isolates from urinary tract infections. Journal of clinical and diagnostic research: JCDR. 11 (2): DC26.

[26] E. R. Sabharwal, R. Sharma. (2015). Fosfomycin: an alternative therapy for the treatment of UTI amidst escalating antimicrobial resistance. Journal of Clinical and Diagnostic Research: JCDR. 9 (12): DC06.

[27] N. Khan, M. S. Khan. (2016). Prevalence of Antimicrobial Resistance in Bacterial Isolates Causing Urinary Tract infection in patients attending at IIMS&R Hospital, Lucknow. International journal of life sciences research. 2 (1): 1-8.

[28] S. Banerjee, M. Sengupta, T. K. Sarker. (2017). Fosfomycin susceptibility among multidrug-resistant, extended-spectrum beta-lactamase-producing,carbapenem-resistant uropathogens. Indian Journal of Urology. 33 (2): 149-154.

[29] M. R. Seo, S. J. Kim, Y. Kim, J. Kim, T. Y. Choi, J. O. Kang, H. Pai. (2014). Susceptibility of Escherichia coli from community-acquired urinary tract infection to fosfomycin, nitrofurantoin, and temocillin in Korea. Journal of Korean Medical Science. 29 (8): 1178.

[30] S. Ahmad, N. Jahan, S. S. Ahmad, N. Singh, R. Khatoon. (2021). A retrospective study of antimicrobial susceptibility pattern of aerobic microbial isolates from urine samples of patients attending a tertiary care hospital. Journal of Medical Science & Research. 9 (1): 5-10.