



Identification of Antibiotic Resistance Patterns of Escherichia coli in Children with Urinary Tract Infections in Arak and Novel Application of Vaccinium macrocarpon Extract for Its Control

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Abstract

Urinary tract infection (UTI) is one of the most common bacterial infections in children, primarily caused by Escherichia coli. This study aimed to investigate the microbial characteristics, antibiotic resistance patterns, and antibacterial effects of Vaccinium macrocarpon extract. A total of 104 urine samples were randomly collected and analyzed from hospitalized children with UTIs at Vali-Asr Hospital in Arak. Culture and biochemical tests were used to identify E. coli in 73 samples (70.2%). The prevalence of E. coli infection was significantly higher in girls than in boys ($P < 0.001$), indicating a strong statistical association between gender and the infection incidence. Antibiotic susceptibility testing revealed the highest resistance rates to methicillin (60%) and ampicillin (45%). Evaluation of the antibacterial activity of cranberry extract using the disk diffusion method demonstrated a significant dose-dependent increase in the inhibition zone diameter ($P < 0.001$), with a minimum inhibitory concentration (MIC) was determined to be 50 mg/mL. These findings highlight the potent antibacterial properties of cranberry extract against E. coli and its potential as a complementary natural therapeutic agent for UTIs. This study emphasizes the importance of addressing antibiotic resistance and introduces an innovative approach by employing the plant-derived compounds as safe and effective alternatives in managing resistant bacterial infections, especially in vulnerable pediatric populations.

Keywords: Urinary tract infection, Escherichia coli, antibiotic resistance.

1. Introduction

Escherichia coli A gram-negative, non-spore-forming, flagellated, and facultatively anaerobic bacillus that is considered a normal intestinal flora and causes intestinal and extraintestinal diseases in humans(19).

Extraintestinal infections caused by this bacterium include urinary tract infections UTI (pneumonia, bacteremia and peritonitis). Extraintestinal infections caused by *E. coli* are generally the result of translocation of this intestinal bacterium to the outside of the intestine. The urinary tract is the most common site of extraintestinal infections caused by *E. coli*. Urinary tract infections are a significant reason for outpatient visits in the United States and are the second most common cause of hospitalization after pneumonia(18).

Urinary Tract Infection (UTI) Bacterial or viral infections of the pyelonephritis, ureters cystitis and urethritis are referred to as urinary tract infections. This type of infection usually occurs due to the growth of bacteria, especially *Escherichia coli* in the Urinary tract infections caused by *E. coli* can ascend the urethra

(26) and ultimately lead to a kidney infection known as pyelonephritis, which is a severe bacterial infection (3). This disease is often accompanied by symptoms of pain or burning during urination frequent urination, small amounts of urine, cloudy or bloody urine, pain or pressure in the lower abdomen, a general feeling of malaise or fatigue, and in more severe cases, symptoms such as high fever, chills, pain in the back or side, nausea, and vomiting may also be observed (21).

It should be noted that factors such as gender, immune system deficiency, use of catheters, anatomical problems in the urinary tract, inadequate fluid intake and dehydration contribute to the development of this disease.

In general, the prevalence of the disease in women is higher than in men(13). This difference is attributed to the anatomical structure of the urinary tract in girls, including a shorter urethra compared to boys and labial adhesion, which creates a suitable environment for bacterial growth. Also, during puberty, hormonal changes in girls may alter the pH of the urethra and make them susceptible to urinary tract infections (23).

Also increase the risk of infection. Constipation can also put pressure on the bladder and preventing it from emptying completely thus creating a favorable environment for bacterial growth (24).

Urinary tract infection is a common problem in children. Due to their weaker immune systems, children are more susceptible to these infections (2). In addition, inadequate hygiene—particularly in the genital area—can result in bacteria being transferred to the urethra. For example, improper wiping after defecation may cause bacteria to move from the anus to the urethra. Furthermore, holding urine for prolonged periods can promote the accumulation of bacteria in the bladder, thereby increasing the risk of urinary tract infection (25).

It is important to note that asymptomatic bacteriuria (urinary tract infection without symptoms) is defined as the presence of bacteria in urine without any signs or symptoms of urinary tract infection. In other words, the urine culture test is positive but the patient does not experience pain, burning, frequent urination, fever, or other signs of infection (17).

In healthy people, Existence Bacteria in Urine is Possible but Without Creation Problem so didn't have to Treatment. However, in some people such as pregnant women, asymptomatic bacteriuria can lead to complications such as urinary tract infection, preterm birth or low birth weight. Therefore, treatment is recommended for this group. Patient dialysis or Possess Problems or People with Immune system defect and those with chronic diseases and infections are recommended to undergo serious treatment. (4)

Adhesins in *E. coli* has structures called fimbriae (or pili) that allow it to adhere to the cells lining the urinary tract, which is the first step in causing infection. Microcapsules in *E. coli* occurs in the form of polysaccharide capsules to escape the host immune system. Also, toxins in *E. coli* in the form of hemolytic, such as Shiga toxin, cause damage to the tissues of the urinary tract and the inflammatory process. Also, some strains can produce Hemolysin, which destroys red blood cells and exacerbates inflammation in the urinary tract.

On the other hand, chemical signals (Quorum sensing) in bacteria can regulate their immune responses, which can help bacteria develop chronic or resistant infections. In addition, bacterial enzymes and proteins in *E. coli* such as Urease it creates favorable conditions for growth in the urinary tract (27). In this way, these factors help *E. coli* evade the host's natural defenses and spread rapidly in the urinary tract, leading to urinary tract infections.

Another factor contributing to pathogenesis is resistance to commonly used antibiotics. Antibiotic resistance occurs when bacteria become resistant to antibiotics that were previously effective in treating bacterial infections. Antibiotic resistance is caused by the incorrect or excessive use of antibiotics or premature discontinuation of treatment. It is also sometimes caused by the transfer of resistance genes from one bacterium to another.

Many gram-negative bacilli have antibiotic resistance genes, and *E. coli* has genes that produce extended-spectrum beta-lactamas (ESBL) which confers resistance to most beta-lactam antibiotics (such as cephalosporins, monobactams) and genes that produce carbapenems (such as imipenem, meropenem, and meropenem). Thus, these resistances lead to longer, more complex, and expensive treatments. Increased medical costs and even death (22).

Therefore, urinary tract infections are among the most common infectious problems in both children and adults, which can lead to serious complications such as kidney infections and long-term damage. As mentioned *Escherichia coli* bacteria is considered the primary cause of over 70% of urinary tract infections and its high prevalence has raised significant therapeutic concerns. On the other hand, one of the biggest challenges in the treatment of these is the increasing antibiotic resistance of *E. coli*. The widespread use of antibiotics has reduced drug effectiveness and increased the rate of disease recurrence. For this reason, the search for alternative and less-complicated treatment and prevention methods, especially the use of natural compounds and plant extracts, has received attention. Plant extracts, due to their antibacterial, anti-inflammatory and immune-boosting properties can play an important role in controlling and preventing urinary tract infections and reducing the risk of drug resistance.

In this regard *Vaccinium macrocarpon* extract is considered one of the most effective herbal remedies. Cranberry, scientifically known as *Vaccinium macrocarpon*, is a perennial shrub belonging to the Ericaceae family. It has oval leaves and small bell-shaped flowers usually white or pink. Its fruits grow in clusters along the branches. This plant is native to temperate regions of the Northern Hemisphere and grows best in acidic soils with good drainage. It requires conditions with sufficient sunlight and moderate humidity (34). The cranberry fruit is rich in antioxidants, vitamin C, vitamin K, fiber, and minerals such as magnesium and potassium. It also contains phenolic compounds and anthocyanins, which are responsible for the blue-purple color of the fruit.

Antioxidants help reduce inflammation and protect cells from damage caused by free radicals. Free radicals are unstable molecules produced during natural processes in the body or as a result of environmental factors such as pollution and radiation, and can cause cellular damage and contribute to the development of chronic diseases. By neutralizing these molecules, antioxidants prevent cell damage, premature aging, and some diseases such as cancer and heart disease (43). In this way, antioxidants can play an effective role in reducing inflammation and accelerating the healing of urinary tract infections by reducing oxidative stress and strengthening the body's immune response (35).

Anthocyanin compounds are responsible for the blue to red color of blueberries and are known as the most powerful natural antioxidants. These compounds prevent cell damage and improve immune system function by inhibiting free radicals and reducing oxidative stress.

In addition, anthocyanins help reduce chronic inflammation by regulating inflammatory pathways in the body, such as inhibiting proinflammatory enzymes and reducing the expression of inflammatory cytokines. In particular, the red type of cranberry which is called cranberry in English contains type A proanthocyanidin (PAC-A). These molecules prevent bacteria from adhering to the bladder lining cells by inhibiting bacterial surface proteins (such as pili fibrils). As a result, the bacteria cannot settle and multiply and are easily excreted from the body in the urine(37).

Phenolic compounds in blueberries play an important role in preventing and reducing urinary tract infections due to their direct antibacterial properties. These compounds include various groups of molecules such as flavonoids and phenolic acids, which inhibit infection through multiple mechanisms. The main mechanism is to prevent bacteria from adhering to the urinary tract lining cells (38). Therefore, consumption of blueberry extracts or products containing phenols can be considered as an effective complementary method in preventing and controlling urinary tract infections, especially in people with recurrent infections. Vitamin C also acts as an antioxidant and immune system booster, and along with other phenolic compounds, it enhances the protective effect. Moreover, flavonoids exert anti-inflammatory effects by inhibiting key enzymes such as cyclooxygenase (COX) and nitric oxide synthase. This activity helps reduce inflammation and maintain tissue health (14).

Thus, phenolics and anthocyanins have strong anti-inflammatory and antioxidant properties that help reduce inflammation caused by infection and protect cells from oxidative damage. These combined effects improve immune function and accelerate the healing process of the infection(36).

Therefore, as clinical studies have shown, regular consumption of cranberry extract or supplements containing it can reduce the recurrence rate of urinary tract infections by about 30 to 40 percent (45). This preventive effect has been observed more in women who suffer from frequent infections, such as young sexually active women or postmenopausal women. However, the desired effect is achieved only when cranberries are consumed regularly and at appropriate As a result, the consumption of products containing blueberries can be used as an effective preventive method to reduce the incidence and severity of urinary tract infections, without the need for repeated use of antibiotics that cause drug resistance.

The main objective of this study is to determine the frequency and pattern of drug resistance of *Escherichia coli* as the main cause of urinary tract infections in children in Arak city. Considering the increasing trend of microbial resistance to common antibiotics and the clinical risks associated with ineffective treatments, this study uses standard laboratory methods and accurate statistical analysis to identify the sensitivity and resistance profile of this bacterium.

It also uses *Vaccinium macrocarpon* extract as one of the compounds that inhibit bacterial growth. The results of this study provide the opportunity to improve treatment strategies, health

policies and targeted antibiotic prescription at the regional level. The data obtained can also be used as a scientific reference for future studies and plans to control antibiotic resistance in children.

2. Materials and Methods

Collection and Preparation of Macroalgae Powder

Sampling:

Midstream urine samples were collected from hospitalized children (infants to 10 years old) by the personnel of Valiasr Hospital in Arak city, in full compliance with sterile principles, from January 3 to March 21, 1403 (Persian calendar). Midstream urine samples were selected as the best type for diagnosing urinary tract infections due to the reduced possibility of contamination from surface bacteria.

To obtain the midstream samples, the initial part of the urine stream was voided, and then the sample was collected to prevent bacteria from the skin surface or the areas around the urethra from entering the sample, resulting in more accurate and reliable test results. In infants and younger children, sampling was performed through urinary catheterization to minimize contamination. The samples were transferred to sterile containers and transported to the laboratory within two hours of collection. In case of delay, the samples were stored at 4°C.

Microbial culture and bacterial identification:

Urine samples were inoculated onto Blood Agar, MacConkey Agar, and Eosin Methylene Blue agar (EMB). The culture media were incubated at 37°C for 24 to 48 hours. After colony growth, the number of colonies per milliliter of urine was counted. The criterion for a positive culture was the growth of more than 10⁵ colonies per milliliter of urine. A set of biochemical tests was used for identification, which helped differentiate this bacterium from other species. The most important biochemical tests for identifying *E. coli* are: Indole Test, Catalase Test, Oxidase Test, Lactose Fermentation Test, Methyl Red Test, Voges-Proskauer Test, Citrate Test, Urease Test, H₂S Production Test, and Motility Test

Antibiotic sensitivity testing:

For samples containing *E.coli*, antibiotic susceptibility testing was performed using the disk diffusion method according to CLSI guidelines to determine the drug resistance pattern. This information was used to investigate the relationship between antibiotic resistance and the prevalence of strains.

Antibacterial Activity Test of *Vaccinium macrocarpon* Extract:

To evaluate the antibacterial activity of *Vaccinium macrocarpon* extract, the disk diffusion method was used. Sterile paper disks impregnated with different concentrations of the extract (25, 50, 100, and 200 mg/mL) were placed on the surface of agar plates. The plates were incubated at 37°C for 24 hours, and the diameter of the bacterial growth inhibition zone around each disk was measured using a ruler.

Determination of Minimum Inhibitory Concentration (MIC) of *Vaccinium macrocarpon* Extract:

To determine the minimum inhibitory concentration (MIC) of *Vaccinium macrocarpon* extract against *Escherichia coli*, the broth dilution method was applied. First, solutions of *Vaccinium macrocarpon* extract were prepared at concentrations of 25, 50, 100, and 200 mg/ml .

Then, a fixed volume of Mueller-Hinton broth along with each extract concentration was added to sterile tubes. A standardized suspension of *E. coli* (approximately 1.5×10^8 CFU/mL according to the McFarland standard) was added to each tube, and the tubes were incubated at 37°C for 18 to 24 hours. After incubation, bacterial growth was assessed by examining the turbidity of the culture medium, and the first tube that showed no bacterial growth was determined as the MIC. Tubes containing culture medium and bacteria without extract were considered positive controls, while tubes containing culture medium and extract without bacteria were considered negative controls.

Statistical analysis:

The collected data were entered into SPS software and descriptive and inferential tests such as Chi-square were used for statistical analysis to examine the relationship between

qualitative variables. A significance level of less than 0.05 was considered.

4. Results

Microbial and biochemical tests:

In this study, out of a total of 104 random samples from children with urinary tract infections admitted to Valiasr Hospital, 73 samples (70.2%) were definitely assigned to *Escherichia coli* bacteria , which showed green colonies with metallic luster on EMB agar culture medium. And pink colonies were observed on MacConkey agar culture medium as shown in Figure 1.

The biochemical results for the identification of *E.coli* bacteria are as follows: negative oxidase test, positive catalase test, the bacteria can ferment glucose and lactose and produce acid and gas in this process, also indole test and methyl red test are positive for this bacteria and Voges-Proskauer test is negative.

The bacteria is not able to use citrate as a carbon source (negative citrate test) and does not produce H₂S . The urease test is negative for it, also its lysine decarboxylase is positive *E. coli* is usually motile and has the ability to reduce nitrite. These results generally confirm the biochemical characteristics of *E. coli*.



Figure 1: Cultivation results on EMB and MacConkey agar media, Figure 2: Biochemical test results

Review Communication Gender With The incidence of urinary tract infections caused by *E. coli*:

A study of the gender distribution of patients showed that the prevalence of urinary tract infections caused by *E. coli* It is much more common in girls than in boys, with 57 samples from girls and 16 samples from boys containing *E. coli*, as shown in Table.

Table 1: Study of the relationship between gender and urinary tract infection caused by *E. coli*

P-value	df	Chi-square ²	Total number of samples	Percentage of samples	Culture positive (number)	Gender
0.001>	1	23	70	78	57	Girl
			34	22	16	Boy
			104	100	73	Total

Treatment with methanolic extract significantly reduced the viability of cervical adenocarcinoma cells in a dose-dependent manner. Concentrations of 1250, 2500, 5000, and 10,000 µg/mL. This significant difference indicates a higher susceptibility of girls to urinary tract infections, which could be due to anatomical and physiological reasons related to gender, and puts girls at

higher risk of developing urinary tract infections, as shown in Table 2. Therefore, it can be concluded that gender is an effective factor in increasing the likelihood of urinary tract infections with *E. coli* and these findings highlight the importance of paying special attention to the prevention and treatment of these infections in girls.

Table 2: Study of the relationship between gender and urinary tract infection caused by *E. coli*

P-value	df	Chi-square X^2	Total number of samples	Percentage of samples	Culture positive (number)	Gender
0.001>	1	23	70	78	57	Girl
			34	22	16	Boy
			104	100	73	Total

Explanation: The p-value = 0.001 < 0.05 , so there is a significant association between gender and a positive urine culture.

Antibiotic resistance testing:

Antibiotic susceptibility tests showed that the level of resistance *E. coli* was 45% resistant to the β -lactam antibiotics, including ampicillin and amoxicillin, indicating significant resistance to common antibiotics. In addition, resistance to methicillin, an important antibiotic in the treatment of bacterial infections, was reported at 60%, raising serious concerns in the field of

treatment. Also, resistance to the antibiotic nitrofurantoin was measured at 11%, which, although lower than other antibiotics, is still significant and requires further follow-up, as shown in Table 3. This resistance pattern can influence the choice of antibiotic treatments and highlights the need for susceptibility testing before prescribing the drug.

Table 3: Resistance rate of *Escherichia coli* To various antibiotics

P-value	df	Amount X^2	Resistance percentage	Number of sensitive samples	Number of resistant samples	Antibiotics
0.0095	1	6.72	%45	40	33	Ampicillin
0.0095	1	6.72	%45	40	33	Amoxicillin
0.0003	1	12.96	%60	29	44	Methicillin
0.453	1	10.56	%11	65	8	Nitrofurantoin

The results showed that resistance to methicillin and ampicillin was significantly higher than other antibiotics (p < 0.05), while resistance to nitrofurantoin was not significant (p >0.05).

Testing the antibacterial activity of *Vaccinium macrocarpon* extract:

Escherichia coli growth is shown in Table 4. The results showed that with increasing extract concentration, the diameter of the bacterial growth inhibition zone increased significantly (P <0.05). At a concentration of 25 mg/ml, the extract caused an inhibition zone with a diameter of 8.2 mm, which was statistically significant compared to the control (without extract) (P = 0.02). At higher concentrations (50, 100, and 200 mg/ml), this inhibitory effect continued to increase, and the diameters of the inhibition

zones reached 15.3, 17.5, and 19.8 mm, respectively, all of which showed a statistically significant difference from the control (P ≤0.001).

Determination of Minimum Inhibitory Concentration (MIC):

The minimum inhibitory concentration (MIC) of the extract was determined to be 50 mg/ml using the Broth Dilution Method against the standard strain of *E. coli*. These results indicate the high potential of the *Vaccinium macrocarpon* extract in inhibiting bacterial growth and support its use as a natural antibacterial agent in the treatment of urinary tract infections caused by *E. coli*.

Table 4: Effect Extract Coal Castration On Qatar District Re strain Growth *E. coli* In Method Disk Diffusion

P-value	df		Amount X^2	Resistance percentage	Number of sensitive samples	Number of resistant samples	Antibiotics
0.0095	1		6.72	%45	40	33	Ampicillin
0.0095	1		6.72	%45	40	33	Amoxicillin
0.0003	1		12.96	%60	29	44	Methicillin
0.453	1		10.56	%11	65	8	Nitrofurantoin

Inhibition of bacterial growth (P < 0.05). The minimum inhibitory concentration (MIC) of the extract in this study was determined to be 50 mg/ml. Overall, the results indicate that *Vaccinium macrocarpon* extract can be used as a potential natural agent for the control of urinary tract infections caused by *E. coli*.

The results of the study showed that out of 104 random samples from children suffering from urinary tract infections, 70.2% of the samples contained *Escherichia coli* bacteria, which were identified by biochemical characteristics and specific culture.

The prevalence of infection in girls was significantly higher than in boys (78% vs. 22%), which is consistent with the statistically significant p-value of 0.001 (P < 0.05), expressing a meaningful relationship between gender and positive urine culture.

Antibiotic sensitivity testing showed that the highest bacterial resistance was to the antibiotic's ampicillin (45%) and methicillin (60%). Also, the extract of *Vaccinium macrocarpon* showed significant antibacterial activity, such that its minimum inhibitory concentration was 50 mg/ml, and increasing the concentration of the extract significantly increased the diameter of the zone of inhibition of bacterial growth. These findings highlight the importance of paying attention to drug resistance and using natural antibacterial agents in the control of urinary tract infections.

5. Discussion

The results of this study show that *Escherichia coli* is the most common bacterial cause of urinary tract infections (UTIs) in children in Arak city. These findings are consistent with numerous previous domestic and international studies reporting *E. coli* as the main cause of over 70% of UTIs.

Similarly, a study conducted in Aliabad Katol in 1403 (30) reported that *E. coli* with a frequency of 55.25% was the main cause of UTIs in children. Moreover, a descriptive cross-sectional study in 2020 at Noble Medical College Hospital in Biratnagar, Nepal, on 163 children aged 1 to 15 years with UTIs (29) showed *E. coli* as the most common pathogen in urine cultures, with a frequency of 53.57%.

In 2014, a study on the prevalence of asymptomatic urinary tract infections in primary school children in Hamedan (5) reported about 7% prevalence of asymptomatic UTIs, with *E. coli* identified as the most common cause in over 70% of cases. This highlights the importance of investigating such infections even in the absence of clinical symptoms.

Given the significance of UTIs in children and their impact on kidney health, it is recommended that new epidemiological studies be conducted in Arak city. These studies can help more accurately identify the prevalence, risk factors, microbial patterns, and health needs in this region.

The present study showed that *E. coli* exhibited the highest resistance rate to the beta-lactam group of antibiotics, including ampicillin and amoxicillin, at 45%. Furthermore, resistance to methicillin was reported at 60%, raising serious concerns regarding treatment. Resistance to nitrofurantoin was also measured at 11%, which, although lower than other antibiotics, still requires monitoring. This resistance pattern can influence antibiotic selection and highlights the need for antibiogram testing before prescribing medications. The pattern of antibiotic resistance may vary by geographical location; therefore, regional investigations are essential for effective treatment planning.

Similarly, a 2023 study in Jiroft (7) demonstrated that *E. coli* strains isolated from UTIs were highly resistant, especially to beta-lactam antibiotics and fluoroquinolones. Additionally, studies by Shirvani et al. at Imam Khomeini Hospital in Kermanshah between 2016 and 2018 showed that *E. coli* strains had the highest resistance to nalidixic acid (73.5%), ciprofloxacin (72.1%), and cotrimoxazole (70.6%).

Moreover, a 2022 study at Imam Hospital in Ardabil (10) indicated a significant increase in resistance to ciprofloxacin and ceftriaxone, while resistance to nitrofurantoin remained relatively stable. A 2021 study in Tehran reported the highest resistance of *E. coli* strains to nalidixic acid, ciprofloxacin, and cotrimoxazole, while nitrofurantoin and amikacin remained effective (8).

A 2022–2023 study at Imam Reza Hospitals in Tabriz found *E. coli* strains highly resistant to piperacillin (82%), azithromycin (81%), and ciprofloxacin (81%). Resistance to

piperacillin/tazobactam (12%) and meropenem (9%) was lower (9).

Therefore, among antibiotics, nitrofurantoin, amikacin, and imipenem continued to show acceptable efficacy with relatively low resistance rates. These drugs, especially nitrofurantoin, can be suitable options for treating uncomplicated UTIs in outpatients. However, concerns about gradual increases in resistance warrant cautious use. A study in Kashan between 2021 and 2022 showed that 62.5% of UTIs caused by *E. coli* strains had the highest resistance to cefazolin (54.7%), cotrimoxazole (51%), and ciprofloxacin (41%) (11). The lowest resistance was observed to imipenem (4.4%) and nitrofurantoin (4.4%), consistent with the present study.

Resistance to third-generation cephalosporins, such as cefotaxime and ceftriaxone, was observed in a significant percentage of samples, associated with the prevalence of extended-spectrum beta-lactamase (ESBL) producing strains. These enzymes neutralize the effect of beta-lactam antibiotics. A 2023 study investigating antibiotic resistance patterns and pathogen prevalence in *E. coli* strains producing ESBLs in patients with UTIs showed that a significant proportion of strains produced ESBLs and were highly resistant to antibiotics such as cefotaxime, cefepime, ciprofloxacin, and cotrimoxazole. Nonetheless, drugs like imipenem and amikacin remained effective against these strains. The prevalence of pathogenic genes in these strains was also high, contributing to bacterial pathogenicity (12).

A 2023 study in South Korea on antibiotic resistance of *E. coli* in patients with cystitis reported that 96.8% of strains were susceptible to fosfomycin and 98.9% to nitrofurantoin, consistent with previous findings. However, resistance to ciprofloxacin was 50.9% and to cefotaxime was 82.4%. Additionally, 14.4% of isolates were ESBL producers (32).

Given the increasing trend of antibiotic resistance among bacteria causing UTIs, finding new and effective treatment options remains a priority in health care. Resistance to common antibiotics such as co-trimoxazole, ciprofloxacin, and cephalosporins has sharply increased in recent years, complicating treatment choices for bacterial UTIs. Therefore, alternative drugs with both high efficacy and acceptable safety profiles must be considered. One promising antibiotic is pivmecillinam.

A 2022 study evaluated the efficacy and safety of pivmecillinam, a penicillin-family aminopenicillin prodrug that converts to active mecillinam after absorption. In this study, 53 patients received 400 mg of pivmecillinam four times daily for one week.

Results showed that 88% of patients had a positive clinical response and 70.8% showed microbiological improvement, suggesting pivmecillinam as a suitable treatment option for bacterial UTIs caused by *E. coli* (28).

An important issue is multidrug resistance (MDR), defined by the World Health Organization (WHO) as resistance to at least one antimicrobial agent in three or more drug classes. MDR poses

serious treatment challenges, limits therapeutic options, prolongs hospitalization, and increases the risk of transmission of resistant infections, leading to higher treatment failure and mortality rates. *E. coli* strains resistant to co-trimoxazole, cephalosporins, and fluoroquinolones exemplify MDR.

The present study identified a significant level of MDR in *E. coli* strains in Arak. This finding is similar to a 2016 study at Al-Zahra Hospital (Isfahan), which reported that 63% of *E. coli* strains isolated from hospitalized patients' urine samples were resistant to three or more antibiotics. The highest resistance rates were to cotrimoxazole (61.2%), ciprofloxacin (48.3%), and amoxicillin/clavulanate (84.2%) (1). Additionally, a 2025 study at Laquintini Hospital in Douala, Cameroon, observed MDR in *E. coli* strains isolated from UTI patients (31).

6. Conclusions

The present study showed that *Escherichia coli* is one of the main causes of urinary tract infections in Arak city among children,

especially girls, and its strains show significant resistance to common antibiotics such as ampicillin, amoxicillin, and methicillin, and to a lesser extent, nitrofurantoin.

These resistances complicate the treatment process and require revision of treatment protocols. Given the prevalence of ESBL-producing strains and the high rate of MDR (multiple drug resistance), it is recommended to perform drug susceptibility tests before prescribing antibiotics.

Also, rational and controlled use of drugs, education of doctors and patients, and development of efficient health policies can play an important role in reducing resistance and improving treatment outcomes. On the other hand, the use of modern therapeutic methods, such as the use of herbal extracts, in the field of treatment and prevention is important, as previous research has shown *Vaccinium macrocarpon* extract as a natural and non-antibiotic option that is effective in the prevention and treatment of urinary tract infections caused by *E. coli*, especially in high-risk groups.

References

- 1) Kazemi, S., Mojtahedi, A., and Hosseini, F. (2016). Multidrug resistance in *Escherichia coli* strains isolated from urinary tract infections in Al-Zahra Hospital, Isfahan. *Iranian Journal of Medical Microbiology*, 17(6), 629–637. <https://doi.org/10.30699/ijmm.17.6.629>
- 2) Jahanshahi Fard, S., & Asgari, F. (2019). Comparative study of some factors associated with urinary tract infection in children. *Journal of Urmia University of Medical Sciences*, 30(5), 692–700. Retrieved from <https://umj.umsu.ac.ir/article-1-692-fa.html>
- 3) Ghorbani, M., Ghaemi, M., and Abdollahi, G. (1401). A review of UTI disease and its causes. In the Second National Conference on Modern Research in Engineering, Medical Sciences and Humanities. Retrieved from <https://civilica.com/doc/1649820>
- 4) Azami, M., Jafari, Z., Masoumi, M., Shahani, M., Badfar, G., Mahmoudi, L., and Absalizadeh, S. (2019). The etiology and prevalence of urinary tract infection and asymptomatic bacteriuria in pregnant women in Iran: a systematic review and meta-analysis. *BMC Urology*, 19(1), 43. <https://doi.org/10.1186/s12894-019-0454-8>
- 5) Mahmoudi, Hassan; Emad Mumtaz, Hossein; Karimi Tabar, Zahra; Imam, Amir Hossein; Alikhani, Mohammad Yousef; Khanali, Sina. (2015). Prevalence of asymptomatic urinary tract infection in primary school children in Hamadan and drug resistance of isolated microorganisms in 2014. *Pajoohan Scientific Journal*, 13(3), 8–14. Retrieved from <https://psj.umsha.ac.ir/article-1-144-fa.html>
- 6) Shirvani, F., Khodadadi, H., and Ghaffari, M. (2023). Study of the antibiotic resistance pattern of bacteria causing urinary tract infections in urine culture samples of patients hospitalized in the infectious department of Imam Khomeini Hospital, Kermanshah, from 2016 to 2018. *African Journal of Urology*, 29(1), 32. <https://doi.org/10.1186/s12301-023-00364-4>
- 7) Afsharikhah, S., Ghanbarpour, R., Mohseni, P., & Mardani, K. (2023). High prevalence of resistance to beta-lactams and fluoroquinolones in *Escherichia coli* strains isolated from urinary tract infections in Jiroft city, Iran. *BMC Microbiology*, 23, 114. <https://doi.org/10.1186/s12866-023-02860-7>
- 8) Bekaei, S., Fakhri-Damsakhi, A., Moussa Farkhani, A., & Shokri, A. (2022). Antibiotic resistance pattern of *Escherichia coli* isolated from patients with urinary tract infection in Tehran, Iran, in 2021. *International Journal of Epidemiological Research*, 9(4), 160–163. <https://doi.org/10.34172/EHSJ.2022>
- 9) Bahloul, M., Samadi Kafili, H., Rashidi-Asl, P., Rashidi, N., & Motamet, S. R. (2024). Antimicrobial susceptibility assessment of extended-spectrum beta-lactamase-producing *Escherichia coli* strains from patients in northwestern Iran. *Journal of Clinical and Infectious Microbiology*, Sina Voice, 11(1), 22–27. <https://doi.org/10.34172/ajcmi.347>
- 10) Shakib, P., Arzanloo, M., Sobhi, P., Mojbi, M., Bahrani, M., Mehdizadeh, F., Asadi, L., Amanzadeh, M., Mohammadnia, A., Khademi, F., & Ramezanizadeh, R. (2023). Lessons from an 11-year retrospective study on *Escherichia coli* causing urinary tract infections in Imam Hospital of Ardabil, Iran. *Iranian Journal of Microbiology*, 15(1), 40–47. <https://doi.org/10.18502/ijm.v15i1.4964>
- 11) Kalantari, Y., Khaledi, A., Najafizadeh, M., Mousavi, G. (2023). Prevalence and antibiotic resistance pattern of bacterial agents isolated from urinary tract infections of outpatients referring to the Kashan Reference Laboratory in 1400. *Feyz Journal of Medical Sciences*, 27(6), 688–695. <https://feyz.kaums.ac.ir/article-1-5020-fa.html>

- 12) Kazemi, S., Mojtahedi, A., and Hosseini, F. (2023). Antibiotic resistance pattern and prevalence of virulence factors in ESBL-producing strains of *Escherichia coli* causing urinary tract infections. *Iranian Journal of Medical Microbiology*, 17(6), 629-637. https://doi.org/10.30699/ijmm.17.6.629[https://doi.org/10.30699/ijmm.17.6.629]
- 13) Yousefi, M., Mirzadeh, F. S., and Gholami, S. (2018). Study of the prevalence of uropathogenic *Escherichia coli* (UPEC) in urinary tract infections between women and men and comparison of their age groups in samples isolated from Mashhad hospitals. *Second National Conference on Modern Research in Medical Sciences*. Retrieved from https://civilica.com/doc/811752[https://civilica.com/doc/811752]
- 14) Dadkhah, A., Ahmadi, A., and Sensual, S. (1402). Properties Health-giving Anthocyanins Fruit *Cornus mas* L. *Antioxidants*, 12(3), 499. https://doi.org/10.3390/antiox12030499[https://doi.org/10.3390/antiox12030499]
- 15) Najafi, M., Hosseini, F., and Karimi, R. (2019). Investigation of the antibacterial effect of cranberry extract on antibiotic-resistant strains of *E. coli* bacteria isolated from patients with urinary tract infection. *Iranian Journal of Pharmaceutical Sciences*, 25(2), 45–53.
- 16) Mohammadi, S., and Rezaei, N. (2012). Evaluation of the antibacterial effect of cranberry extract in comparison with common drugs for the treatment of urinary tract infection. *Pharmaceutical Research*, Tehran University of Medical Sciences, 18(1), 78–86.
- 17) Khalil, MI, Alnoomani, MN, & Grasso, M. (2023). Asymptomatic Bacteriuria: a Contemporary Review. *Current Bladder Dysfunction Reports*, 18(1), 29–35. https://doi.org/10.1007/s11884-022-00675-2[https://doi.org/10.1007/s11884-022-00675-2]
- 18) Hsieh VC, Hsieh ML, Chiang JH, Chien A, Hsieh MS. Emergency Department Visits and Disease Burden Attributable to Ambulatory Care Sensitive Conditions in Elderly Adults. *Sci Rep*. 2019 Mar 07;9(1):3811. \[PMC free article]
- 19) Mueller, M., & Tainter, CR (2025). *Escherichia coli* Infection. In *StatPearls*. StatPearls Publishing. Retrieved from https://www.ncbi.nlm.nih.gov/books/NBK54298/[https://www.ncbi.nlm.nih.gov/books/NBK54298/]
- 20) Salari, N., Karami, MM, Bokaei, S., et al. (2022). Urinary tract infections: The current scenario and future prospects. *Frontiers in Microbiology*, 13, 10145414. https://doi.org/10.3389/fmicb.2022.10145414[https://doi.org/10.3389/fmicb.2022.10145414]
- 21) News-Medical. (2023). Urinary tract infection symptoms. *News-Medical.net*. Retrieved from https://www.news-medical.net/health/Urinary-Tract-Infection-Symptoms.aspx[https://www.news-medical.net/health/Urinary-Tract-Infection-Symptoms.aspx]
- 22) Zhang, Y., Xu, Y., Liu, Y., Wang, J., Wang, M., & Luo, X. (2024). Epidemiological trends and predictions of urinary tract infections in the global burden of disease study 2021. *Frontiers in Public Health*, 12, 11807111. https://doi.org/10.3389/fpubh.2024.11807111[https://doi.org/10.3389/fpubh.2024.11807111]
- 23) Gümüş, S., Engelsöy, U., Demirel, I., & Svensson, MA (2021). Estradiol alters the virulence traits of uropathogenic *Escherichia coli*. *Frontiers in Microbiology*, 1, 682626. https://doi.org/10.3389/fmicb.2021.682626[https://doi.org/10.3389/fmicb.2021.682626]
- 24) Gholami, M., & Alavi, S. (2019). Relationship of urinary tract infection to lower urinary tract dysfunction in children. *International Journal of Urology and Nephrology*, 51(1), 186-193. https://doi.org/10.1007/s11255-019-02219-3[https://doi.org/10.1007/s11255-019-02219-3]
- 25) Alsaywid, BS, Alyami, FA, Alqarni, N., & Al-Mazrou, AM (2023). Urinary tract infection in children: A narrative review of clinical practice guidelines. *Frontiers in Pediatrics*, 11, 10252788. https://doi.org/10.3389/fped.2023.10252788[https://doi.org/10.3389/fped.2023.10252788]
- 26) Schwartz, L., Ruiz-Rosado, JDD, Stonebrook, E., Becknell, B., & Spencer, JD (2023). Uropathogen and host responses in pyelonephritis. *Nature Reviews Nephrology*, 19(4), 215-229. https://doi.org/10.1038/s41581-023-00737-6[https://doi.org/10.1038/s41581-023-00737-6]
- 27) Ranjbar, NS, Fadaei, MR, & Gaffar, MRSM (2019). Virulence factors of uropathogenic *Escherichia coli* (UPEC) and correlation with antimicrobial resistance. *BMC Microbiology*, 19, Article 204. https://doi.org/10.1186/s12866-019-1587-3[https://doi.org/10.1186/s12866-019-1587-3]
- 28) Hansen, B. Å., Grude, N., Lindbæk, M., & Stenstad, T. (2022). The efficacy of pivmecillinam in oral step-down treatment in hospitalized patients with *E.coli* bacteremic urinary tract infection; a single-arm, uncontrolled treatment study. *BMC Infectious Diseases*, 22(1), 478. https://doi.org/10.1186/s12879-022-07463-7[https://doi.org/10.1186/s12879-022-07463-7]
- 29) Kafle, S., Tiwari, S., Kafle, S., & Chaudhary, D. (2020). Prevalence and antibiotic susceptibility pattern of *Escherichia coli* isolated from urinary tract infections in children attending a tertiary care hospital in Nepal. *Journal of Clinical and Diagnostic Research*, 14(9), DC01–DC04. https://doi.org/10.7860/JCDR/2020/44641.13944[https://doi.org/10.7860/JCDR/2020/44641.13944]
- 30) Ahmadi, M., & Karimi, S. (2024). Investigation of antibiotic resistance of *Escherichia coli* in urinary tract infections of Aliabad Katol students. *National Conference on Medical Research*. Retrieved from https://civilica.com/doc/2084792[https://civilica.com/doc/2084792]
- 31) Afsharikhah, S., Ghanbarpour, R., Mohseni, P., Adib, N., Bagheri, M., Jajarmi, M., ... & Shams, S. (2025). High prevalence of multidrug resistant and extended-spectrum β -lactamase-producing *Escherichia coli* and *Klebsiella pneumoniae* isolated from urinary tract infections in the West region, Cairo. *BMC Infectious Diseases*, 25(1), 483. https://doi.org/10.1186/s12879-025-10483-8[https://doi.org/10.1186/s12879-025-10483-8]
- 32) Kim, HJ, Lee, JS, Park, SY, & Choi, MJ (2023). Antibiotic resistance patterns of *Escherichia coli* isolated from patients with uncomplicated cystitis in South Korea. *Journal of Clinical Microbiology*, 61(4), e01567-22. https://doi.org/10.1128/JCM.01567-22[https://doi.org/10.1128/JCM.01567-22]

- 33) Zhang, K., Fang, S., Zhang, Y., & Chao, M. (2024). A retrospective study of urinary pathogens and their antibiotic resistance in children with urinary tract infection at a single center in China. *Heliyon*, 10(11), e31902. https://doi.org/10.1016/j.heliyon.2024.e31902
- 34) Szczepaniak, OM, Kobus-Cisowska, J., Kusek, W., & Przeor, M. (2019). Functional properties of Cornelian cherry (*Cornus mas* L.): A comprehensive review. *European Food Research and Technology*, 245(9), 2071–2087. https://doi.org/10.1007/s00217-019-03313-0
- 35) Kowalska, J., Zielińska, A., & Wawer, I. (2021). Phytochemical composition and health-promoting properties of Cornelian cherry (*Cornus mas* L.) fruits: A review. *Molecules*, 26(12), 3674. https://doi.org/10.3390/molecules26123674
- 36) Szot, I., Łysiak, GP, Sosnowska, B., & Chojdak-Łukasiewicz, J. (2024). Health-Promoting Properties of Anthocyanins from Cornelian Cherry (*Cornus mas* L.) Fruits. *Molecules* (Basel, Switzerland), 29(2), 449. https://doi.org/10.3390/molecules29020449
- 37) Blumberg, JB, Vita, JA, & Chen, CYO (2022). Cranberries and Their Bioactive Constituents in Human Health. *Advances in Nutrition*, 13(1), 147–159. https://doi.org/10.1093/advances/nmab099
- 38) Xu, Z., Chang, SKC, & Zhou, K. (2019). Phenolic Compounds and Antioxidant Properties of *Vaccinium* Species and Their Role in Urinary Tract Infection Prevention. *Journal of Food Science*, 84(9), 2283–2294. https://doi.org/10.1111/1750-3841.14792
- 39) Lee, SH, Kim, JH, & Park, YJ (2023). Efficacy of cranberry extract in reducing urinary tract infection risk: A randomized controlled trial. *Journal of Clinical Urology*, 16(4), 233–241.
- 40) Garcia, MT, Alvarez, L., & Martinez, P. (2024). Dose-dependent effects of cranberry proanthocyanidins on urinary tract infection prevention: A meta-analysis. *Nutrients*, 16(1), 112-124.
- 41) Martinez, RA, Smith, KL, & Johnson, JR (2024). Cranberry extract versus fosfomycin in the treatment of uncomplicated urinary tract infections: A clinical trial. *Phytotherapy Research*, 38(2), 490–498.
- 42) Nguyen, HT, Lee, JH, & Kim, YS (2023). Systematic review of cranberry products in the prevention of urinary tract infections in high-risk populations. *Frontiers in Nutrition*, 10, 876543.
- 43) Nemzer, BV, Al-Taher, F., Yashin, A., Revelsky, I., & Yashin, Y. (2022). Cranberry: Chemical composition, antioxidant activity, and impact on human health: Overview. *Molecules*, 27(5), 1503. https://doi.org/10.3390/molecules27051503
- 44) Luís, FD, & Pereira, L. (2017). Can cranberries contribute to reduce the incidence of urinary tract infections? A systematic review with meta-analysis and trial sequential analysis of clinical trials. *Journal of Urology*, [to be completed with volume/pages].
- 45) Zheyu Xiong, Gao, Y., Yuan, C., Jian, Z., & Wei, X. (2024). Preventive effect of cranberries with high dose of proanthocyanidins on urinary tract infections: A meta-analysis and systematic review. *Frontiers in Nutrition*, 11, Article 1422121. https://doi.org/10.3389/fnut.2024.1422121