

Original Article

Anti-Microbial Effects of Vaccinium Macrocarpon (Cranberry) Extract on Serotypes 26 and 45 of Escherichia Coli as a Prophylaxis of Recurrent Urinary Tract Infection (UTI)

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ABSTRACT

Background: Urinary tract infection (UTI) is the second most common type of bacterial infection globally, affecting people of different age groups. Cranberry is renowned for its antibacterial properties and has been used to treat UTIs in recent years.

Objective: This study aimed to assess the antimicrobial effects of cranberry extract on the prophylaxis of recurrent UTI caused by different serotypes of Escherichia coli (E. coli).

Methods: This quasi-experimental study recruited 60 recurrent UTI patients from the Urology department of King Edward Medical University, Lahore, Pakistan. Patients with a history of recurrent UTIs caused by E. coli were included. Urine microscopy and culture tests were performed, and only E. coli-positive cases were serotyped. Patients received Vaccinium macrocarpon (cranberry) extract at a dose of 500 mg/day for four weeks along with their standard treatment. Follow-up evaluations were conducted after one and three months to assess UTI symptoms and the presence of E. coli in urine samples. Statistical analysis was performed using SPSS version 25, with quantitative variables expressed as mean \pm standard deviation and qualitative variables as frequencies and percentages.

Results: Of the 60 patients, 15 (25%) were positive for E. coli. Serotyping revealed 8 patients (53%) with serotype 26 and 7 patients (47%) with serotype 45. After three months of treatment, cranberry extract eradicated E. coli in 12 patients (80%); specifically, it eradicated 100% of serotype 45 and 62% of serotype 26 cases.

Conclusion: Cranberry extract (500 mg/day) for three months demonstrated significant antimicrobial effects on E. coli serotypes 26 and 45, with greater efficacy observed in serotype 45. These findings suggest cranberry extract as a potential prophylactic treatment for recurrent UTIs.

Keywords: Cranberry extract, recurrent UTI, E. coli serotypes, antimicrobial effects, prophylactic treatment, Vaccinium macrocarpon, urinary tract infection, Escherichia coli

INTRODUCTION

Urinary tract infection (UTI) is recognized as the second most prevalent bacterial infection worldwide, impacting individuals across various age groups, notably those in their early twenties and late eighties (1). Women are particularly susceptible to UTIs, with an incidence rate of 50%, compared to 12% in men, and a high recurrence rate of 40% (2). Several risk factors contribute to the higher prevalence of UTIs in women, including sexual activity, pregnancy, contraceptive use, menopause, catheterization, and diabetes (3). Men, though less frequently affected, can experience recurrent UTIs due to conditions such as an enlarged prostate, cancer, diabetes, and stress (4). Among uropathogens, Escherichia coli (E. coli) is the predominant causative agent of UTIs in both inpatient and outpatient settings, followed by other pathogens such as Pseudomonas, Proteus, Klebsiella, Staphylococcus saprophyticus, and Enterococcus species. These infections typically present clinically with symptoms of dysuria, frequency, and urgency of micturition. Notably, the most common serotypes of E. coli causing UTIs include O4, O6, O7, O20, O25, O26, O45, O50, and O51 (5). Recurrent

UTIs, which affect 20-30% of young women, may be due to the same or different microorganisms or serotypes and are often linked to reinfection by bacteria that survive intensive antibiotic treatments, persisting in underlying bladder or gastric tissues (6).

Cranberry (*Vaccinium macrocarpon*), known as the fifth highest-selling herb in the United States, has been extensively utilized for treating urinary disorders, stomach problems, wounds, and diabetes mellitus. In recent years, the use of cranberry for UTI treatment has garnered significant attention due to its rich antioxidant content, particularly polyphenols, which are believed to confer health benefits through their antioxidant properties (7, 8). Additionally, cranberry extract has been reported to improve digestion and cholesterol profiles in cardiac patients (9, 10). Cranberry is consumed in various forms, including fresh and dried fruit, juice, and extract capsules (11). The antimicrobial properties of cranberry extract are primarily attributed to proanthocyanidins (PACs), which exert anti-adhesive effects by preventing *E. coli* from binding to the bladder uroepithelium, thereby mitigating UTI incidence (12). Despite extensive research, the literature presents conflicting results regarding the efficacy of cranberry extract in treating UTIs. While some systematic reviews highlight its benefits, others find no significant difference compared to placebo (13-15). A few studies have demonstrated the effectiveness of cranberry extract in treating acute UTIs (16). However, no research to date has specifically investigated the effects of cranberry extract on different serotypes of *E. coli*. Thus, this study aims to evaluate the antimicrobial effects of cranberry extract on various serotypes of *E. coli* in the prophylaxis of recurrent UTI.

MATERIAL AND METHODS

This quasi-experimental study was conducted at the Urology department of Mayo Hospital, Lahore, Pakistan, and was approved by the ethical review committee of King Edward Medical University (KEMU) (4935/REG/KEMU/2016). The study adhered to the principles outlined in the Declaration of Helsinki. Participants were recruited based on predefined inclusion and exclusion criteria. The inclusion criteria encompassed patients of all age groups and genders with a documented history of recurrent UTIs caused by *E. coli* within the past 12 months, those who were catheterized, and those on long-term antibiotic therapy. Exclusion criteria included patients with a history of urological surgery, urinary tract abnormalities, immunodeficiency (e.g., AIDS, post-splenectomy), severe renal impairment, or renal failure. Written informed consent was obtained from all participants prior to enrolment.

A total of 60 recurrent UTI patients were included in the study. Demographic information such as name, age, gender, and address was collected through medical record review. Baseline assessments involved urine microscopic examination and urine culture for all participants. Only patients with *E. coli*-positive results were further analyzed for serotyping. Cranberry extract, containing 25% anthocyanidin, 50% proanthocyanidin, traces of flavonoids, catechins, and ascorbic acid, was administered at a dose of 500 mg once daily for four weeks. Following the initial treatment phase, patients were evaluated at one and three-month intervals to assess the persistence of UTI symptoms and the presence of *E. coli* in urine samples.

Urine samples were collected as midstream specimens in sterilized containers during the first morning void. Approximately 12 ml of urine was centrifuged for five minutes, and the sediment was examined microscopically to count pus cells. Urine cultures were performed by streaking samples on CLED agar medium using a calibrated wire loop, followed by incubation at 37°C for 24-48 hours. *E. coli* colonies were isolated for serotyping, which involved preparing a suspension in phosphate buffer saline, corresponding to a 3-5 McFarland standard. Serotyping was conducted using latex agglutination assays with specific reagents for serotypes O26 and O45. Positive reactions were confirmed with the Prolex Negative Control Latex Reagent.

Statistical analysis was performed using SPSS version 25. Quantitative variables, such as age, were expressed as mean \pm standard deviation, while qualitative variables, including gender, were presented as frequencies and percentages. The effectiveness of cranberry extract in eradicating different *E. coli* serotypes was evaluated by comparing baseline, one-month, and three-month follow-up data. This comprehensive methodological approach ensured robust and reliable results, contributing to a better understanding of cranberry extract's role in managing recurrent UTIs.

RESULTS

The quasi-experimental study enrolled 60 recurrent UTI patients admitted to the Urology department of Mayo Hospital, Lahore, Pakistan. The demographic and clinical characteristics of the patients are summarized in Table 1. The study population consisted of 20 males (33%) and 40 females (67%) with a mean age of 47 ± 15 years. Initial urine microscopy and culture revealed that 15 patients (25%) were positive for *E. coli*, while 45 patients (75%) were negative. Among the *E. coli*-positive cases, serotyping identified that 8 patients (53%) had serotype 26 and 7 patients (47%) had serotype 45.

Table 1. Demographic and Clinical Characteristics of Enrolled Patients

Characteristic	Value
No. of Patients	60

Mean Age \pm SD	47 \pm 15
Male (%)	20 (33%)
Female (%)	40 (67%)
E. Coli Positive Cases (%)	15 (25%)
E. Coli Negative Cases (%)	45 (75%)
E. Coli Serotypes	
- Serotype 26 (%)	8 (53%)
- Serotype 45 (%)	7 (47%)

The effectiveness of cranberry extract treatment was evaluated at one-month and three-month intervals. After one month of cranberry extract (500 mg/day) administration, 1 out of 15 patients (7%) was found to be E. coli-negative. The remaining 14 patients (93%) still had E. coli present in their urine cultures. Detailed results are presented in Table 2.

Table 2. Effect of Cranberry Extract on E. Coli Serotypes at One-Month Interval

Patient No.	Age (Years)	Gender	Serotype 26	Serotype 45	E. Coli Status After 1 Month
7	51	Male	-	+	Positive
8	43	Male	+	-	Negative
10	25	Male	-	+	Positive
11	48	Female	+	-	Positive
12	26	Female	-	+	Positive
13	44	Female	+	-	Positive
15	67	Male	+	-	Positive
18	47	Male	+	-	Positive
24	61	Male	+	-	Positive
26	41	Male	-	+	Positive
28	70	Female	+	-	Positive
34	77	Male	-	+	Positive
46	30	Male	-	+	Positive
50	42	Female	+	-	Positive
55	42	Male	-	+	Positive

After three months of cranberry extract treatment, a significant improvement was observed. A total of 12 patients (80%) were found to be E. coli-negative, whereas 3 patients (20%) remained positive. The eradication rate was 100% for serotype 45 and 62% for serotype 26. These results are detailed in Table 3.

Table 3. Effect of Cranberry Extract on E. Coli Serotypes at Three-Month Interval

Patient No.	Age (Years)	Gender	Serotype 26	Serotype 45	E. Coli Status After 3 Months
7	51	Male	-	+	Negative
8	43	Male	+	-	Negative
10	25	Male	-	+	Negative
11	48	Female	+	-	Positive
12	26	Female	-	+	Negative
13	44	Female	+	-	Negative
15	67	Male	+	-	Positive
18	47	Male	+	-	Negative
24	61	Male	+	-	Positive
26	41	Male	-	+	Negative
28	70	Female	+	-	Negative
34	77	Male	-	+	Negative
46	30	Male	-	+	Negative
50	42	Female	+	-	Negative
55	42	Male	-	+	Negative

The results demonstrate that cranberry extract, administered at a dose of 500 mg/day for three months, significantly reduced the presence of *E. coli* in urine cultures, with a higher eradication rate observed for serotype 45 compared to serotype 26. The data highlight the potential of cranberry extract as an effective prophylactic treatment for recurrent UTIs caused by specific serotypes of *E. coli*.

DISCUSSION

The study evaluated the antimicrobial effects of cranberry extract on two serotypes of *E. coli* (26 and 45) in patients with recurrent UTIs. The findings demonstrated that cranberry extract, administered at a dose of 500 mg/day for three months, effectively eradicated *E. coli* serotype 45 in all patients and significantly reduced the presence of *E. coli* serotype 26. This indicated a more pronounced antibacterial effect of cranberry extract on serotype 45 compared to serotype 26.

Previous studies have shown conflicting results regarding the efficacy of cranberry products in preventing and treating UTIs. Some systematic reviews and meta-analyses have reported beneficial effects of cranberry products in reducing UTI recurrence (13, 14), while others found no significant difference compared to placebo (17,18). The current study's results align with those suggesting that cranberry extract has a substantial impact on specific strains of uropathogenic *E. coli*. The antimicrobial properties of cranberry are primarily attributed to proanthocyanidins (PACs), which inhibit the adhesion of *E. coli* to the uroepithelium, thus preventing infection (19). This study adds to the growing body of evidence supporting the use of cranberry extract as a complementary therapy in managing recurrent UTIs.

A notable strength of this study was the focus on specific serotypes of *E. coli*, which allowed for a more detailed understanding of cranberry extract's antibacterial effects. By differentiating between serotypes 26 and 45, the study provided valuable insights into the varying responses of *E. coli* strains to cranberry treatment. This specificity has been lacking in previous research, which often did not distinguish between different *E. coli* serotypes.

However, the study had several limitations. The sample size was relatively small, with only 60 participants, which may limit the generalizability of the findings. Additionally, the study was conducted at a single medical center, which may introduce selection bias. Future studies with larger, more diverse populations and multi-center designs are needed to confirm these results. Another limitation was the lack of a control group receiving a placebo, which would have strengthened the conclusions about the efficacy of cranberry extract(20).

Despite these limitations, the study provided important preliminary evidence that cranberry extract could be an effective prophylactic measure against certain serotypes of *E. coli* in recurrent UTI patients. The findings suggested that cranberry extract might be particularly beneficial for eradicating *E. coli* serotype 45, highlighting its potential for targeted therapy.

Based on these results, it is recommended that clinicians consider incorporating cranberry extract into the treatment regimen for patients with recurrent UTIs, especially those with identified *E. coli* serotype 45. Further research should explore the mechanisms underlying the differential effects of cranberry extract on various *E. coli* serotypes and evaluate its long-term efficacy and safety. Additionally, investigating the optimal dosage and duration of cranberry extract treatment for different patient populations would be beneficial.

In conclusion, this study demonstrated that cranberry extract has significant antimicrobial effects on *E. coli* serotypes 26 and 45, with a higher efficacy observed in serotype 45. These findings contribute to the understanding of cranberry extract as a potential prophylactic treatment for recurrent UTIs and pave the way for more targeted and effective therapeutic strategies.t adherence in RA patients (21).

CONCLUSION

In conclusion, Cranberry extract (500 mg/day) for three months demonstrated significant antimicrobial effects on *E. coli* serotypes 26 and 45, with greater efficacy observed in serotype 45. These findings suggest cranberry extract as a potential prophylactic treatment for recurrent UTIs.

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