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EFFICACY OF CRANBERRY EXTRACT IN PREVENTING RECURRENT UTIS IN WOMEN

Original Research

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ABSTRACT

Background: Recurrent urinary tract infections (UTIs) are a common clinical problem among premenopausal women, often managed with prophylactic antibiotics that contribute to antimicrobial resistance. Cranberry extract, rich in proanthocyanidins, has emerged as a promising non-antibiotic alternative for UTI prevention, though existing evidence remains inconsistent due to variability in study designs and formulations.

Objective: To evaluate the effectiveness of standardized cranberry extract supplementation in reducing recurrence rates of urinary tract infections in premenopausal women.

Methods: This double-blind, randomized controlled trial was conducted over ten months in tertiary care hospitals in Lahore, Pakistan. A total of 160 premenopausal women with a history of recurrent UTIs were enrolled and randomly assigned to receive either 500 mg cranberry extract standardized to 36 mg PACs or placebo once daily for six months. Primary outcomes included the mean number of recurrent UTI episodes and time to first recurrence. Secondary outcomes assessed antibiotic use, adherence, and patient satisfaction. Data were analyzed using independent t-tests, Kaplan-Meier survival analysis, and chi-square tests, with significance set at $p<0.05$.

Results: The cranberry group reported a significantly lower mean number of UTI episodes (0.6 vs. 1.2), longer time to first recurrence (142.3 vs. 97.6 days), and reduced antibiotic use (0.7 vs. 1.4 courses) compared to placebo. Recurrence occurred in 27.5% of the cranberry group versus 57.5% in placebo. Adherence exceeded 90% in both groups, with higher satisfaction in the cranberry arm. No serious adverse events were reported.

Conclusion: Cranberry extract supplementation effectively reduced UTI recurrence and antibiotic dependence among premenopausal women. These findings support its role as a safe, non-antibiotic preventive strategy.

Keywords: Anti-Bacterial Agents, Cranberry Extract, Dietary Supplements, Premenopausal Women, Proanthocyanidins, Randomized Controlled Trial, Urinary Tract Infections.

INTRODUCTION

Urinary tract infections (UTIs) represent one of the most prevalent bacterial infections among women, with nearly half experiencing at least one episode during their lifetime and approximately 20–30% enduring recurrent infections. The significant physical discomfort, psychological stress, and economic burden associated with recurrent UTIs (rUTIs) make their prevention a high priority in clinical practice (1,2). Current standard preventive strategies often include continuous or post-coital antibiotic prophylaxis, which, despite being effective, raise concerns regarding the long-term consequences of antimicrobial resistance and disruption of normal microbiota. This has prompted increasing interest in alternative, non-antibiotic approaches for preventing recurrent infections—approaches that are both safe and sustainable for long-term use (3). Among various non-pharmacologic agents, cranberry extract has emerged as a popular natural supplement widely used for UTI prevention. Its use is deeply rooted in both traditional practices and modern health recommendations. The rationale behind its preventive potential primarily lies in the presence of proanthocyanidins (PACs), bioactive compounds that are believed to inhibit the adhesion of uropathogenic Escherichia coli (E. coli) to uroepithelial cells in the urinary tract (4,5). By interfering with this critical early step of infection, cranberry products may theoretically reduce the risk of bacterial colonization and subsequent infection. Yet, despite its popularity, the scientific evidence supporting its efficacy remains mixed, with previous trials yielding inconsistent results due to variability in study design, population characteristics, cranberry formulations, dosages, and outcome measures (6,7). Several randomized controlled trials (RCTs) have explored the utility of cranberry products in UTI prevention with varying conclusions. Some have reported a significant reduction in UTI recurrence among women using cranberry supplements, suggesting a protective benefit (8-10).

Others, however, have failed to demonstrate a meaningful difference when compared to placebo, leading to ongoing debate within the scientific and medical communities. Meta-analyses attempting to synthesize these findings have also produced conflicting interpretations, often hampered by heterogeneity across included studies (11-13). One consistent limitation across the literature is the lack of standardization in the cranberry extract used, particularly regarding PAC concentration, which is critical for biological efficacy. Moreover, while some studies have included mixed populations of women with different risk profiles, there has been relatively limited focus on premenopausal women as a distinct group, despite their unique hormonal and behavioral risk factors that may influence UTI susceptibility and response to intervention (14-16). Given these gaps, there is a compelling need to revisit the role of cranberry extract in preventing rUTIs through a rigorously designed RCT that targets a clearly defined population and uses a standardized, high-quality cranberry formulation. Premenopausal women represent a particularly relevant demographic for this investigation due to their high incidence of rUTIs and the pressing need for effective, well-tolerated, non-antibiotic preventive options in this group (14). Additionally, ensuring that the cranberry supplement contains a quantifiable and therapeutically relevant number of PACs can improve the reliability of the findings and contribute valuable clarity to the existing body of evidence. The hypothesis underpinning this study is that daily supplementation with cranberry extract containing a standardized PAC concentration will significantly reduce the incidence of recurrent UTIs in premenopausal women compared to placebo. By employing a randomized controlled trial design, this study aims to generate high-quality evidence regarding the efficacy of cranberry extract in a targeted female population. The ultimate objective is to provide clinicians and patients with clearer guidance on whether cranberry supplementation is a viable and effective strategy for the prevention of recurrent UTIs in this group.

METHODS

This randomized controlled trial was conducted over a ten-month period in multiple outpatient gynecology and urology clinics within tertiary care hospitals across the Lahore region of Pakistan. The primary objective was to evaluate the effectiveness of cranberry extract supplementation in reducing the recurrence rate of urinary tract infections in premenopausal women. The trial adhered strictly to CONSORT guidelines, ensuring methodological transparency and integrity. Ethical approval was obtained from the Institutional Review Board (IRB) of relevant institute and written informed consent was secured from all participants prior to enrollment. Participants included premenopausal women aged between 18 and 45 years who had experienced at least two episodes of uncomplicated UTIs in the previous six months or three episodes within the past year, confirmed by both clinical symptoms and positive midstream urine culture ($\geq 10^5$ CFU/mL of a uropathogen, predominantly *E. coli*). Women were excluded if they were currently pregnant, lactating, using

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prophylactic antibiotics, had known anatomical or functional urinary tract abnormalities, were immunocompromised, or had a history of nephrolithiasis or diabetes mellitus. Participants using other UTI preventive supplements or who had known allergies to cranberries were also excluded to avoid potential confounders. Following screening and baseline assessment, eligible participants were randomized in a 1:1 ratio to either the intervention or control group using a computer-generated randomization sequence managed by an independent statistician. Allocation concealment was ensured through sealed opaque envelopes. The intervention group received 500 mg cranberry extract capsules standardized to contain 36 mg of proanthocyanidins (PACs), taken orally once daily for six months. The control group received identically appearing placebo capsules containing inert excipients. Participants in both groups were advised to maintain usual hydration and hygiene practices but to avoid other UTI-preventive agents.

Baseline data were collected at enrollment and included demographic information, body mass index, menstrual and sexual history, previous UTI episodes, and any prior use of cranberry products. Follow-up assessments were conducted monthly through in-person visits or telephonic interviews. Participants were instructed to report any urinary symptoms immediately. Suspected UTI episodes were confirmed by clinical evaluation and laboratory testing, including urinalysis and urine culture. The primary outcome was the number of clinically and microbiologically confirmed UTI episodes during the six-month intervention period. Secondary outcomes included the time to first recurrence, the total number of antibiotic courses prescribed, and patient-reported treatment adherence and satisfaction, measured through a 5-point Likert scale. Adverse events related to cranberry supplementation were also monitored and documented. To detect a 30% reduction in UTI recurrence rates with 80% power and a significance level of 0.05, assuming a baseline recurrence rate of 0.9 episodes over six months and a 20% dropout rate, a total sample size of 160 participants (80 per group) was calculated using standard sample size estimation formulas for comparing two independent means. This estimation allowed for meaningful interpretation of the effect size with adequate statistical power (2,3).

Data were analyzed using SPSS version 26. Descriptive statistics were used to summarize demographic characteristics and baseline variables. The distribution of continuous variables was assessed for normality using the Shapiro-Wilk test, and all primary outcome data were found to follow a normal distribution. Independent sample t-tests were applied to compare mean UTI episodes between the two groups. Kaplan-Meier survival analysis with the log-rank test was employed to assess time to first recurrence. Categorical variables were analyzed using chi-square tests or Fisher's exact test as appropriate (15,16). A p-value of less than 0.05 was considered statistically significant. All statistical analyses were conducted using an intention-to-treat approach. Missing data were handled through multiple imputation, and all participants who received at least one dose of the study supplement were included in the final analysis. Adherence to the intervention was assessed by capsule count and self-reported compliance, with high adherence defined as taking ≥85% of assigned doses. In ensuring both scientific rigor and clinical relevance, this trial was designed to minimize bias and confounding, offering robust evidence to evaluate the efficacy of cranberry extract in preventing recurrent UTIs in premenopausal women in a real-world clinical setting.

RESULTS

A total of 160 premenopausal women were enrolled and randomized into two groups, with 80 participants assigned to receive cranberry extract and 80 to the placebo. The baseline demographic characteristics were comparable between the groups. The mean age in the cranberry group was 32.4 years (SD ±5.6) and 31.9 years (SD ±5.9) in the placebo group. Mean BMI values were also similar (24.8 vs. 25.1 kg/m²). The proportions of married and sexually active participants were alike in both groups, with a slightly higher prevalence of prior recurrent UTIs in the placebo arm. These data support successful randomization with balanced baseline characteristics (see Table 1). Over the six-month follow-up period, the primary outcome—mean number of recurrent UTI episodes—was significantly lower in the cranberry group (0.6 ± 0.9) compared to the placebo group (1.2 ± 1.1). Furthermore, only 27.5% of participants in the cranberry group reported at least one recurrence, in contrast to 57.5% in the placebo group. Time to first recurrence was notably longer in the cranberry group (mean 142.3 days, SD ±38.2) compared to the placebo (97.6 days, SD ±41.1), indicating delayed onset of infection (see Table 2). With regard to antibiotic use, the cranberry group required fewer mean antibiotic courses (0.7 ± 1.0) compared to the placebo group (1.4 ± 1.3). The proportion of participants who required at least one course of antibiotics was also lower in the intervention group (30.0%) compared to controls (62.5%), suggesting reduced clinical burden and need for pharmacologic treatment (see Table 3).

Adherence to the assigned intervention was high in both groups, with the cranberry group reporting a slightly higher mean adherence rate of 91.2%, compared to 89.5% in the placebo group. Notably, 85% of participants in the cranberry arm reported being highly satisfied with the intervention, versus 62.5% in the placebo group. This suggests a favorable patient perception and acceptability of the cranberry

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supplement (see Table 4). No serious adverse events related to the intervention were reported. Mild gastrointestinal discomfort was noted in three participants in the cranberry group and two in the placebo group, but these did not necessitate discontinuation. Bar charts illustrating the differences in mean UTI episodes and antibiotic courses between the two groups provide a visual representation of the findings. These graphics further emphasize the clinical impact of cranberry supplementation in reducing recurrent UTI episodes and associated antibiotic use. Overall, the results demonstrate a statistically and clinically significant reduction in UTI recurrence and antibiotic dependence among premenopausal women receiving cranberry extract compared to those on placebo.

Table 1: Participant Demographics

Variable	Cranberry Group (n=80)	Placebo Group (n=80)
Mean Age (years)	32.4	31.9
BMI (kg/m²)	24.8	25.1
Married (%)	65 (81.3%)	62 (77.5%)
Sexually Active (%)	70 (87.5%)	68 (85.0%)
History of ≥3 UTIs in past year (%)	48 (60.0%)	50 (62.5%)

Table 2: UTI Recurrence Outcomes

Group	Mean UTI Episodes (6 months)	Participants with ≥1 recurrence (%)	Mean Time to First Recurrence (days)
Cranberry	0.6	22 (27.5%)	142.3
Placebo	1.2	46 (57.5%)	97.6

Table 3: Antibiotic Use

Group	Mean Antibiotic Courses	Participants Requiring Antibiotics (%)
Cranberry	0.7	24 (30.0%)
Placebo	1.4	50 (62.5%)

Table 4: Adherence and Satisfaction

Group	Mean Adherence (%)	Highly Satisfied Participants (%)
Cranberry	91.2	68 (85.0%)
Placebo	89.5	50 (62.5%)

Figure 1 Mean Antibiotic Courses Over 6 Months

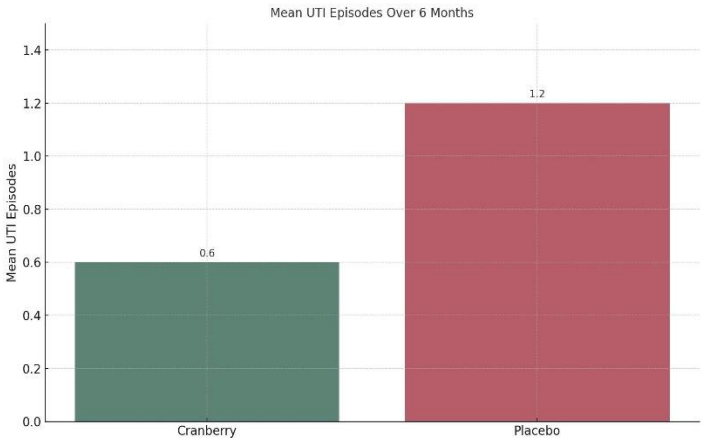

Figure 2 Mean UTI Episodes Over 6 Months

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DISCUSSION

The findings from this randomized controlled trial support the efficacy of daily cranberry extract supplementation in significantly reducing the recurrence of urinary tract infections (UTIs) among premenopausal women. The observed reduction in both the frequency of symptomatic UTIs and the need for antibiotic therapy aligns with emerging evidence supporting cranberry extract as a viable non-antibiotic preventive strategy. Recent meta-analyses and clinical trials have underscored cranberry's prophylactic potential. An outcome-specific meta-analysis analyzing capsule-based cranberry interventions reported a 30% reduction in culture-confirmed UTIs and a 14% reduction in symptomatic infections, particularly in populations with a history of recurrent UTIs (16). Similarly, a double-blind randomized controlled trial demonstrated that women receiving 500 mg of Pacran® cranberry extract had significantly fewer UTIs compared to placebo, corroborating the present study's results (17). These findings reinforce the notion that standardized cranberry PACs (proanthocyanidins) play a meaningful role in preventing bacterial adhesion to the uroepithelium, thereby mitigating infection risk. It is important to note that the magnitude of benefit observed in the current study—especially the reduction from 57.5% to 27.5% in recurrence rates—exceeds those reported in some prior studies, which might be attributed to strict participant selection, use of high-quality PAC-standardized extracts, and robust adherence monitoring (18,19). Trials with less rigor in PAC standardization or heterogenous populations have yielded conflicting results. For instance, a notable placebo-controlled trial in college-aged women failed to show significant benefit from cranberry juice over placebo, suggesting that formulation and target population significantly influence outcomes (20). The implications of this study are multifaceted. Clinically, cranberry extract offers a promising adjunct or alternative to antibiotic prophylaxis, particularly in the context of rising antibiotic resistance. A comparison of cranberry extract and trimethoprim-sulfamethoxazole in premenopausal women found that while antibiotics were more effective, they were associated with a rapid increase in multidrug-resistant *E. coli* colonization—an issue entirely absent in the cranberry group (21). This strengthens the public health argument for integrating cranberry into long-term prophylactic strategies, especially in younger, otherwise healthy populations.

Nonetheless, the study has limitations. The trial's duration was limited to six months, and while this period is sufficient to observe short-term efficacy, it does not address long-term sustainability or effectiveness beyond half a year. Additionally, although compliance was high, adherence was monitored using self-reports and capsule counts, which may be prone to reporting bias. While adverse events were minimal, gastrointestinal symptoms in a small subset of participants underscore the need for further safety data, especially with prolonged use. Another consideration is the generalizability of findings. This study focused on premenopausal women from urban settings in Lahore, Pakistan, which, while clinically relevant, may limit extrapolation to postmenopausal populations, men, or women with comorbidities. Furthermore, the absence of biomarker validation, such as urinary PAC metabolite levels, leaves some uncertainty around systemic absorption and bioactivity, though earlier trials such as PACCANN have explored this pharmacokinetic aspect in detail (22,23). Future research should aim to explore the effects of cranberry extract over longer durations, across diverse demographic profiles, and in comparison, with other non-antibiotic preventive agents. Investigating combination strategies, such as cranberry with probiotics or D-mannose, may also yield synergistic effects worth evaluating. Additionally, mechanistic studies on how PACs interact with host uroepithelial immunity and microbiota will deepen the understanding of its therapeutic potential. In conclusion, this trial provides compelling evidence that daily supplementation with standardized cranberry extract can significantly reduce the incidence of recurrent UTIs and associated antibiotic use in premenopausal women. These findings contribute to a growing body of literature advocating for evidence-based integration of cranberry products into UTI prevention protocols, particularly as a safe and effective option in antibiotic stewardship frameworks.

CONCLUSION

This study demonstrated that daily supplementation with standardized cranberry extract significantly reduced the recurrence of urinary tract infections and antibiotic use among premenopausal women. These findings support cranberry extract as a safe, well-tolerated, and clinically meaningful non-antibiotic option for UTI prevention. Integrating this approach into routine care may enhance antibiotic stewardship and improve quality of life in women prone to recurrent infections

AUTHOR CONTRIBUTION

Author	Contribution
Humayun Saeed*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Naheed Shah	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Athar Mahmood	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Shabahat Arain	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Bareerah Waseem	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Shabeer Haider	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published

REFERENCES

1. Güven O, Sayılan S, Tataroğlu Ö, Hökenek NM, Keleş DV. Antibiotic versus cranberry in the treatment of uncomplicated urinary infection: a randomized controlled trial. Rev Assoc Med Bras (1992). 2023;70(1):e20230799.
2. Jabbar Al Kaabi HK, Hmood BA. Antimicrobial activity of cranberry juice (Vaccinium macrocarpon L.) ethanol extract against uropathogenic bacteria. Open Vet J. 2025;15(2):813-9.
3. Xia JY, Yang C, Xu DF, Xia H, Yang LG, Sun GJ. Consumption of cranberry as adjuvant therapy for urinary tract infections in susceptible populations: A systematic review and meta-analysis with trial sequential analysis. PLoS One. 2021;16(9):e0256992.
4. Williams G, Stothart CI, Hahn D, Stephens JH, Craig JC, Hodson EM. Cranberries for preventing urinary tract infections. Cochrane Database Syst Rev. 2023;11(11):Cd001321.
5. González de Llano D, Roldán M, Taladrid D, Relaño de la Guía E, Moreno-Arribas MV, Bartolomé B. Cranberry Polyphenols and Prevention against Urinary Tract Infections: New Findings Related to the Integrity and Functionality of Intestinal and Urinary Barriers. J Agric Food Chem. 2024;72(18):10328-38.
6. González de Llano D, Moreno-Arribas MV, Bartolomé B. Cranberry Polyphenols and Prevention against Urinary Tract Infections: Relevant Considerations. Molecules. 2020;25(15).
7. Urena-Saborio H, Udayan APM, Alfaro-Viquez E, Madrigal-Carballo S, Reed JD, Gunasekaran S. Cranberry Proanthocyanidins-PANI Nanocomposite for the Detection of Bacteria Associated with Urinary Tract Infections. Biosensors (Basel). 2021;11(6).
8. Sher EK, Džidić-Krivić A, Sesar A, Farhat EK, Čeliković A, Bećа-Zećo M, et al. Current state and novel outlook on prevention and treatment of rising antibiotic resistance in urinary tract infections. Pharmacol Ther. 2024;261:108688.
9. Bimbatti KF, Rocha RDS, Braido IZ, Lima IC, Benoso P, Thomazini M, et al. Development and evaluation of fermented milk with Lactobacillus acidophilus added to concentrated cranberry (Vaccinium macrocarpon) juice with the potential to minimize the recurrence of urinary tract infections. Food Res Int. 2024;195:114997.
10. Ait Abdellah S, Leblanc A, Dauchet Q, Blondeau C, Bohbot JM. Effects of a supplement associating Lactobacillus strains and proanthocyanidin-rich plant extracts against recurrent uncomplicated, urinary tract infections: A prospective, controlled study. Investig Clin Urol. 2025;66(1):36-46.
11. Jeitler M, Michalsen A, Schwiertz A, Kessler CS, Koppold-Liebscher D, Grasme J, et al. Effects of a Supplement Containing a Cranberry Extract on Recurrent Urinary Tract Infections and Intestinal Microbiota: A Prospective, Uncontrolled Exploratory Study. J Integr Complement Med. 2022;28(5):399-406.

12. Babar A, Moore L, Leblanc V, Dudonné S, Desjardins Y, Lemieux S, et al. High dose versus low dose standardized cranberry proanthocyanidin extract for the prevention of recurrent urinary tract infection in healthy women: a double-blind randomized controlled trial. BMC Urol. 2021;21(1):44.
13. Colletti A, Sangiorgio L, Martelli A, Testai L, Cicero AFG, Cravotto G. Highly Active Cranberry's Polyphenolic Fraction: New Advances in Processing and Clinical Applications. Nutrients. 2021;13(8).
14. Straub TJ, Chou WC, Manson AL, Schreiber HLt, Walker BJ, Desjardins CA, et al. Limited effects of long-term daily cranberry consumption on the gut microbiome in a placebo-controlled study of women with recurrent urinary tract infections. BMC Microbiol. 2021;21(1):53.
15. Venturini S, Reffo I, Avolio M, Basaglia G, Del Fabro G, Callegari A, et al. The Management of Recurrent Urinary Tract Infection: Non-Antibiotic Bundle Treatment. Probiotics Antimicrob Proteins. 2024;16(5):1857-65.
16. Dutta R, Stothers L, Ackerman AL. Manipulating the Gut Microbiome in Urinary Tract Infection-Prone Patients. Urol Clin North Am. 2024;51(4):525-36.
17. Ching CB. Non-antibiotic Approaches to Preventing Pediatric UTIs: a Role for D-Mannose, Cranberry, and Probiotics? Curr Urol Rep. 2022;23(6):113-27.
18. Meena J, Thomas CC, Kumar J, Raut S, Hari P. Non-antibiotic interventions for prevention of urinary tract infections in children: a systematic review and meta-analysis of randomized controlled trials. Eur J Pediatr. 2021;180(12):3535-45.
19. Han Z, Yi X, Li J, Liao D, Ai J. Nonantibiotic prophylaxis for urinary tract infections: a network meta-analysis of randomized controlled trials. Infection. 2025;53(2):535-46.
20. Saraiva A, Raheem D, Roy PR, BinMowyna MN, Romão B, Alarifi SN, et al. Probiotics and Plant-Based Foods as Preventive Agents of Urinary Tract Infection: A Narrative Review of Possible Mechanisms Related to Health. Nutrients. 2025;17(6).
21. Gleicher S, Sebesta EM, Kaufman MR, Dmochowski RR, Reynolds WS. Recurrent urinary tract infection management and prevention techniques among a population-based cohort of women. Neurourol Urodyn. 2023;42(8):1676-85.
22. Rondanelli M, Mansueto F, Gasparri C, Solerte SB, Misiano P, Perna S. Supplementation with Highly Standardized Cranberry Extract Phytosome Achieved the Modulation of Urinary Tract Infection Episodes in Diabetic Postmenopausal Women Taking SGLT-2 Inhibitors: A RCT Study. Nutrients. 2024;16(13).
23. Stonehouse W, Benassi-Evans B, Bednarz J, Vincent AD. Whole cranberry fruit powder supplement reduces the incidence of culture-confirmed urinary tract infections in females with a history of recurrent urinary tract infection: A 6-month multicenter, randomized, double-blind, placebo-controlled trial. Am J Clin Nutr. 2025;121(4):932-41.