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Original Article

Cranberry Extract (Vaccinium Macrocarpon) Versus Low-Dose Nitrofurantoin For Preventing Recurrent UTIs In Premenopausal Women

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ABSTRACT

Background: Recurrent urinary tract infections are a frequent clinical problem among premenopausal women and often require preventive strategies that balance recurrence reduction with tolerability and antimicrobial stewardship. Low-dose nitrofurantoin is an established prophylactic option, whereas cranberry extract has been proposed as a non-antibiotic alternative because of its potential anti-adhesive effect against uropathogens. Objective: To compare the efficacy and safety of standardized cranberry extract with low-dose nitrofurantoin for prevention of recurrent urinary tract infections among premenopausal women. Methods: A parallel-group randomized controlled trial was conducted among 80 premenopausal women aged 18–45 years with recurrent urinary tract infections. Participants were randomized to receive either cranberry extract containing 36 mg proanthocyanidins once daily or nitrofurantoin 50 mg once daily for 12 weeks. Outcomes included symptomatic culture-confirmed UTI episodes, time to first recurrence, urinary symptom severity measured by VAS, adherence, and adverse events. The final completer analysis included 72 participants. Results: Mean UTI episodes were lower with nitrofurantoin than cranberry extract (0.38 ± 0.49 vs 0.74 ± 0.65; mean difference 0.36, 95% CI 0.10–0.62; p=0.01). Time to recurrence was longer with nitrofurantoin (10.2 ± 2.1 vs 8.4 ± 2.5 weeks; p=0.003), and VAS reduction was greater (-4.6 ± 1.3 vs -3.6 ± 1.5; p=0.004). Adverse events were numerically higher with nitrofurantoin (27.0% vs 11.4%). Conclusion: Nitrofurantoin provided greater short-term prophylactic efficacy, whereas cranberry extract showed better numerical tolerability and may be considered for selected women prioritizing non-antibiotic prevention. Keywords: Anti-Bacterial Agents; Cranberry; Nitrofurantoin; Premenopause; Recurrence; Urinary Tract Infections; Women's Health.

INTRODUCTION

Recurrent urinary tract infections are a common and clinically burdensome problem among premenopausal women, frequently causing repeated episodes of dysuria, urgency, urinary frequency, discomfort, healthcare visits, and repeated antimicrobial exposure. Recurrent UTI is commonly defined as at least two symptomatic episodes within six months or three episodes within one year, and its occurrence reflects an interaction between host susceptibility, behavioral and anatomical factors, and bacterial virulence, particularly uropathogenic Escherichia coli. Although most episodes are not life-threatening in otherwise healthy women, repeated infection can substantially impair quality of life and often leads to repeated empirical antibiotic use, making prevention an important clinical priority (1).

Low-dose antibiotic prophylaxis remains an established preventive strategy for women with frequent recurrences, and nitrofurantoin is commonly used because of its urinary concentration, activity against common uropathogens, and comparatively favorable resistance profile. Continuous low-dose prophylaxis can reduce recurrence frequency, but prolonged antibiotic exposure raises concerns about gastrointestinal intolerance, hypersensitivity reactions, antimicrobial selection pressure, and rare but clinically important pulmonary or hepatic toxicity. These concerns are particularly relevant in women who require repeated or long-term preventive therapy, where the clinical benefit of recurrence reduction must be weighed against safety, tolerability, patient preference, and antimicrobial stewardship considerations (2,3).

Non-antibiotic prophylactic strategies have therefore gained increasing attention as potential alternatives or adjuncts for recurrent UTI prevention. Cranberry extract derived from Vaccinium macrocarpon is among the most widely used options and is biologically plausible because cranberry proanthocyanidins may reduce bacterial adhesion to the uroepithelial surface, thereby limiting colonization and subsequent symptomatic infection. This anti-adhesive mechanism differs from direct antimicrobial suppression and may offer a safer option for women who prefer to avoid continuous antibiotics or who are vulnerable to antibiotic-related adverse effects. However, clinical findings for cranberry products have remained inconsistent, partly because studies have used different formulations, doses, intervention durations, outcome definitions, and participant populations (4,5).

Despite the widespread use of cranberry products, direct comparative evidence against active antibiotic prophylaxis remains limited, particularly among premenopausal women with clearly defined recurrent UTI. This gap is clinically important because placebo-controlled evidence alone does not determine whether cranberry extract can reasonably substitute for an established prophylactic antibiotic in routine practice. A direct comparison with low-dose nitrofurantoin allows simultaneous evaluation of effectiveness and tolerability, helping clinicians and patients choose between greater antimicrobial efficacy and a potentially safer non-antibiotic approach. In premenopausal women with recurrent UTI, the key clinical question is whether daily standardized cranberry extract containing 36 mg proanthocyanidins provides comparable protection to daily low-dose nitrofurantoin 50 mg over a 12-week prophylactic period in reducing symptomatic, culture-confirmed UTI recurrence, delaying time to recurrence, improving urinary symptom severity, and minimizing adverse events (6–9).

MATERIAL AND METHODS

A parallel-group randomized controlled trial was conducted to compare the efficacy and safety of daily standardized cranberry extract with daily low-dose nitrofurantoin for prevention of recurrent urinary tract infections among premenopausal women. The study was carried out in an urban Islamabad-Rawalpindi clinical setting over five months, including one month for participant recruitment and baseline assessment, 12 weeks for the intervention period, and one month for follow-up completion, data verification, and final analysis. The randomized active-comparator design was selected because the objective was not merely to evaluate cranberry extract against no treatment, but to compare its preventive effect and tolerability against an established low-dose antibiotic prophylactic regimen used in recurrent UTI management.

Premenopausal women aged 18–45 years were eligible if they had a documented history of recurrent urinary tract infection, defined as at least two symptomatic episodes during the preceding six months or at least three episodes during the preceding year. Participants were excluded if they were pregnant, had diabetes mellitus, had known renal disease or structural urological abnormality, had used antibiotics within two weeks before enrollment, had known hypersensitivity or contraindication to nitrofurantoin, or were currently using any other antibiotic, prophylactic agent, cranberry product, herbal supplement, or urinary-health preparation that could influence recurrence risk or treatment response. Eligible

participants were recruited after baseline screening, eligibility verification, and informed consent, and baseline demographic and clinical characteristics were recorded before randomization.

A total of 80 eligible participants were randomized in a 1:1 ratio to receive either cranberry extract or low-dose nitrofurantoin. The sample size was selected to provide a balanced comparison between the two prophylactic approaches while allowing for anticipated attrition during the 12-week intervention period. Random allocation was performed using a computer-generated random sequence, and allocation concealment was maintained through sequentially numbered, opaque, sealed envelopes prepared independently before participant enrollment. Because the two interventions differed in treatment type, participant blinding was not feasible; however, outcome assessment and data analysis were conducted without disclosure of group allocation to reduce assessment and analytical bias.

Participants allocated to the cranberry group received standardized cranberry extract capsules containing 36 mg proanthocyanidins once daily for 12 weeks. Participants allocated to the nitrofurantoin group received nitrofurantoin 50 mg orally once daily for the same duration. Both groups received uniform advice regarding hydration and general hygienic practices, and no additional behavioral intervention was introduced during follow-up to avoid differential co-intervention effects. Adherence was assessed through monthly follow-up visits, pill counts, and participant diaries documenting daily intake, urinary symptoms, recurrence episodes, and adverse events. Participants were instructed to report symptomatic urinary episodes promptly during the intervention period so that clinical assessment and urine culture confirmation could be performed.

The primary outcome was the number of symptomatic, clinically confirmed UTI episodes occurring during the 12-week intervention period. A recurrence episode was defined as the presence of urinary symptoms such as dysuria, urinary frequency, urgency, suprapubic discomfort, or urinary discomfort requiring clinical assessment and confirmation by urine culture. Secondary outcomes included time to first recurrence, urinary symptom severity, and adverse events. Time to recurrence was recorded in weeks from randomization to the first symptomatic culture-confirmed UTI episode. Symptom severity was assessed using a visual analogue scale for urinary discomfort and dysuria at baseline and during scheduled follow-up, with higher scores indicating greater symptom burden. Adverse events were recorded throughout the study and compared between groups as the number and proportion of participants reporting any treatment-related or treatment-emergent event.

Baseline variables included age, body mass index, number of prior UTI episodes during the preceding year, and marital status. The main exposure variable was prophylactic treatment allocation, categorized as cranberry extract or nitrofurantoin. The primary dependent variable was recurrence burden, measured as the number of symptomatic culture-confirmed UTI episodes during follow-up. Secondary dependent variables were time to first recurrence, change in urinary symptom severity from baseline to week 12, and adverse event frequency. Potential sources of bias were addressed through random sequence generation, allocation concealment, blinded outcome assessment, blinded data analysis, standardized intervention duration, identical follow-up timing, uniform adherence monitoring, and consistent recurrence verification procedures across both groups.

Data were checked for completeness, consistency, and plausibility before analysis. Baseline characteristics were summarized for all randomized participants, while post-intervention outcomes were analyzed according to the available follow-up dataset and reported with the relevant denominators. Missing follow-up observations due to withdrawal or loss to follow-up were documented according to treatment group and reason for discontinuation. Continuous variables were assessed for distributional assumptions using the Shapiro–Wilk test and summarized as mean ± standard deviation when approximately normally distributed. Categorical variables were summarized as frequencies and percentages. Between-group comparisons for continuous outcomes were performed using independent-samples t-tests when assumptions were met, while within-group pre–post changes in symptom severity were assessed using paired-samples t-tests. Repeated-measures analysis of variance was used to examine

changes in symptom severity over time and to assess the time-by-treatment interaction. Categorical outcomes, including adverse events, were compared between groups using appropriate tests for proportions. Pearson correlation analysis was used to examine the association between adherence level and UTI recurrence. Statistical significance was set at $p<0.05$.

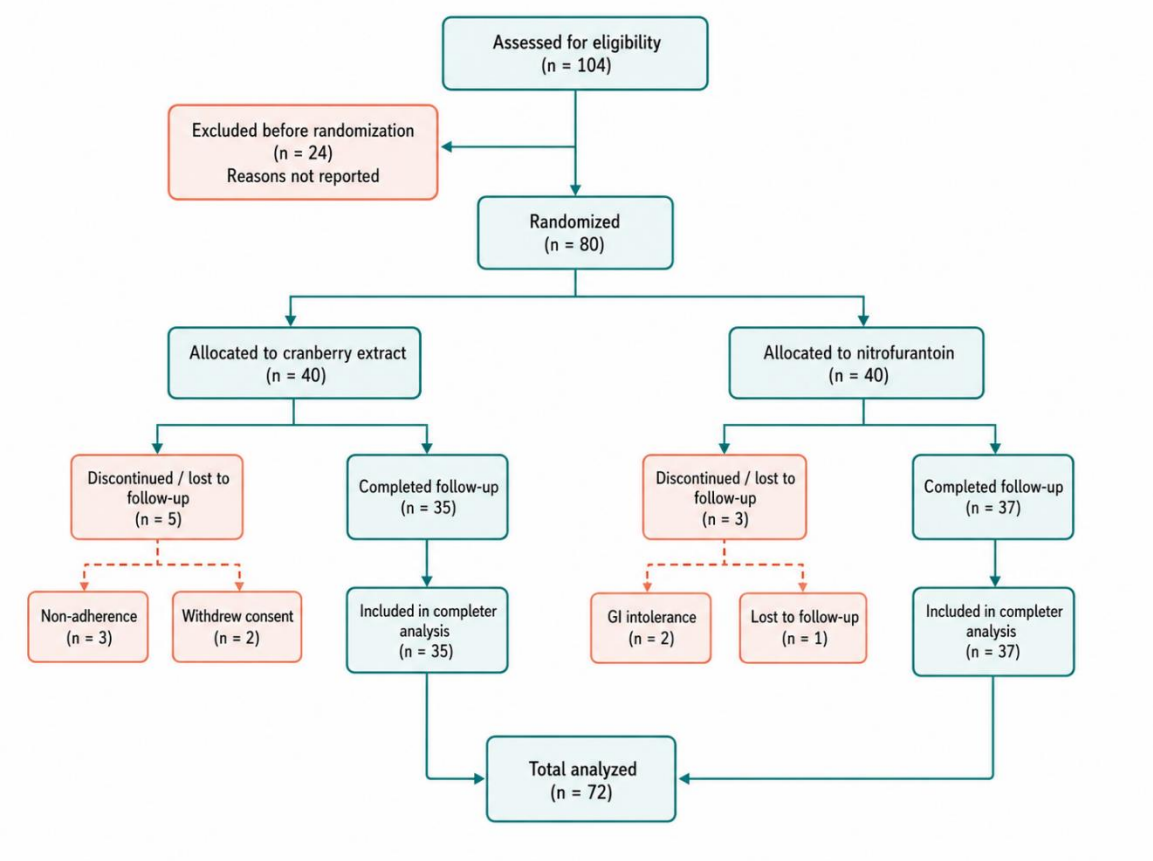

Figure 1 CONSORT Flowchart

To support reproducibility and data integrity, data collection followed a predefined schedule at baseline, monthly follow-up visits, and week 12 assessment. Participant diaries, pill counts, recurrence documentation, and urine culture verification were cross-checked before final data entry. Group allocation, outcome records, and analysis files were maintained consistently to preserve traceability between enrolled participants, follow-up status, and reported outcomes. The final report should present baseline data using the randomized denominator of 80 participants and post-intervention outcomes using clearly specified analysis denominators, with any completer, modified intention-to-treat, or sensitivity analysis explicitly labeled to avoid inconsistency between the methods, results, and abstract.

RESULTS

A total of 104 premenopausal women were screened during the recruitment period, of whom 80 fulfilled the eligibility criteria and were randomized equally to the cranberry extract group and nitrofurantoin group. During the 12-week intervention period, 5 participants in the cranberry group and 3 participants in the nitrofurantoin group discontinued follow-up. The final completer analysis therefore included 72 participants, with 35 in the cranberry group and 37 in the nitrofurantoin group.

Of the 80 randomized participants, 72 completed the 12-week intervention and were included in the final completer analysis. Attrition was numerically higher in the cranberry extract group than in the nitrofurantoin group, with 5 discontinuations compared with 3 discontinuations, respectively. Non-adherence and withdrawal of consent accounted for discontinuation in the cranberry group, whereas gastrointestinal intolerance and loss to follow-up accounted for discontinuation in the nitrofurantoin group.

Baseline demographic and clinical characteristics were comparable between the randomized groups. The mean age was 31.1 ± 6.5 years in the cranberry extract group and 31.7 ± 5.9 years in the nitrofurantoin group. Mean body mass index, prior UTI frequency, and marital status were also similar between groups, indicating acceptable baseline balance after randomization.

Table 1. Participant Flow and Analysis Population

Participant Status	Total	Cranberry Extract	Nitrofurantoin
Screened	104	—	—
Randomized	80	40	40
Lost to follow-up or discontinued	8	5	3
Non-adherence	3	3	0
Withdrawal of consent	2	2	0
Gastrointestinal intolerance	2	0	2
Loss to follow-up	1	0	1
Completed follow-up	72	35	37
Included in final completer analysis	72	35	37

Abbreviation: —, not reported by group.

Table 2. Baseline Demographic and Clinical Characteristics of Randomized Participants

Variable	Total Sample	Cranberry Extract	Nitrofurantoin	p-value
Participants, n	80	40	40	—
Age, years, Mean ± SD	31.4 ± 6.2	31.1 ± 6.5	31.7 ± 5.9	0.68
BMI, kg/m², Mean ± SD	24.8 ± 3.1	24.6 ± 3.3	25.0 ± 2.9	0.59
Prior UTIs in past year, Mean ± SD	3.4 ± 0.8	3.5 ± 0.9	3.3 ± 0.7	0.41
Married, n (%)	52 (65.0)	25 (62.5)	27 (67.5)	0.64

Abbreviations: BMI, body mass index; SD, standard deviation; UTI, urinary tract infection. Continuous variables were compared between groups using independent-samples t-tests. Categorical variables were compared using a test for proportions. The baseline table uses the randomized denominator.

The two treatment groups were similar at baseline across the reported demographic and clinical variables. Mean age differed by 0.6 years, mean BMI differed by 0.4 kg/m², and mean prior UTI frequency differed by 0.2 episodes in the preceding year. The proportion of married participants was 62.5% in the cranberry extract group and 67.5% in the nitrofurantoin group. No statistically meaningful baseline imbalance was reported across these variables.

The primary outcome was the number of symptomatic UTI episodes during the 12-week intervention period. In the completer analysis, the mean number of UTI episodes was higher in the cranberry extract group than in the nitrofurantoin group. The between-group mean difference was 0.36 episodes, with a 95% confidence interval from 0.10 to 0.62. The standardized mean difference was 0.63, indicating a moderate between-group difference in recurrence burden favoring nitrofurantoin.

Table 3. Primary Outcome: Symptomatic UTI Episodes During the 12-Week Intervention Period

Outcome	Cranberry Extract	Nitrofurantoin	Mean Difference	95% CI	Cohen's d	p-value
Participants, n	35	37	—	—	—	—
UTI episodes, Mean ± SD	0.74 ± 0.65	0.38 ± 0.49	0.36	0.10 to 0.62	0.63	0.01

Abbreviations: CI, confidence interval; SD, standard deviation; UTI, urinary tract infection. Mean difference is cranberry extract minus nitrofurantoin.

Participants receiving nitrofurantoin experienced fewer symptomatic UTI episodes over 12 weeks than those receiving cranberry extract. The absolute mean difference of 0.36 episodes favored nitrofurantoin, and the confidence interval did not cross zero. The standardized effect size of 0.63 suggests that the difference was not only statistically detectable but also clinically relevant within the short-term prophylactic period.

Urinary symptom severity decreased significantly from baseline to week 12 in both groups. The cranberry extract group improved from a baseline VAS score of 6.8 ± 1.2 to 3.2 ± 1.4 at week 12, while

the nitrofurantoin group improved from 6.7 ± 1.3 to 2.1 ± 1.1. The magnitude of reduction was greater in the nitrofurantoin group, with a between-group difference in symptom reduction of 1.0 VAS point.

Table 4. Urinary Symptom Severity From Baseline to Week 12

Outcome	Cranberry Extract	Nitrofurantoin	Between-Group Difference	95% CI	Cohen's d	p-value
Participants, n	35	37	—	—	—	—
Baseline VAS, Mean ± SD	6.8 ± 1.2	6.7 ± 1.3	0.1	-0.49 to 0.69	0.08	0.735
Week 12 VAS, Mean ± SD	3.2 ± 1.4	2.1 ± 1.1	1.1	0.51 to 1.69	0.88	<0.001
Change in VAS, Mean ± SD	-3.6 ± 1.5	-4.6 ± 1.3	1.0	0.34 to 1.66	0.71	0.004
Within-group p-value	<0.001	<0.001	—	—	—	—

Abbreviations: CI, confidence interval; SD, standard deviation; VAS, visual analogue scale. Between-group difference for baseline and week 12 values is cranberry extract minus nitrofurantoin. Between-group difference for change scores represents the difference in magnitude of reduction.

Both interventions were associated with substantial reductions in urinary symptom severity over 12 weeks. The cranberry extract group showed a mean VAS reduction of 3.6 points, while the nitrofurantoin group showed a mean reduction of 4.6 points. The additional 1.0-point reduction in the nitrofurantoin group, with a 95% confidence interval from 0.34 to 1.66 and Cohen's d of 0.71, indicates a moderate comparative advantage for nitrofurantoin in symptom improvement.

Repeated-measures analysis showed significant change in urinary symptom severity over time and a significant treatment-by-time interaction. The reported time effect, group effect, and time-by-group interaction indicate that symptom scores decreased across follow-up in both groups, with a steeper reduction pattern in the nitrofurantoin group.

Table 5. Repeated-Measures Analysis of Urinary Symptom Severity

Effect	F	p-value
Time	112.4	<0.001
Group	6.8	0.010
Time × Group	5.9	0.018

The repeated-measures analysis supported the pre–post findings by showing that urinary symptom severity changed significantly during follow-up and that the pattern of change differed by treatment group. The significant time-by-group interaction indicates that the nitrofurantoin group had a greater reduction in VAS scores over the intervention period than the cranberry extract group. However, the week 4 and week 8 VAS values should be added to the manuscript to allow full verification of the repeated-measures model and any related figure.

Secondary outcomes included time to first recurrence, adverse events, and the association between adherence and recurrence. Time to first recurrence was longer in the nitrofurantoin group than in the cranberry extract group. Adverse events were numerically more frequent in the nitrofurantoin group, but recalculation using the supplied denominators did not show a statistically significant difference with Fisher's exact test. Adherence was moderately and inversely correlated with recurrence frequency.

Table 6. Secondary Outcomes During the 12-Week Intervention Period

Outcome	Cranberry Extract	Nitrofurantoin	Effect Estimate	95% CI	p-value
Participants, n	35	37	—	—	—
Time to recurrence, weeks, Mean ± SD	8.4 ± 2.5	10.2 ± 2.1	-1.8	-2.89 to -0.71	0.003
Adverse events, n (%)	4 (11.4)	10 (27.0)	-15.6	-33.4 to 2.2	0.137
Adherence and UTI recurrence, r	—	—	-0.42	—	0.002

Abbreviations: CI, confidence interval; r, Pearson correlation coefficient; SD, standard deviation; UTI, urinary tract infection. Effect estimate for time to recurrence is cranberry extract minus nitrofurantoin in weeks. Effect estimate for adverse events is risk difference in percentage points, calculated as cranberry extract minus nitrofurantoin. The adverse-event p-value was calculated using Fisher's exact test from the reported counts. The correlation estimate was reported for adherence and recurrence.

Time to first recurrence was 1.8 weeks longer in the nitrofurantoin group than in the cranberry extract group, with the confidence interval favoring nitrofurantoin. Adverse events occurred in 11.4% of participants receiving cranberry extract and 27.0% receiving nitrofurantoin, corresponding to a risk difference of -15.6 percentage points when cranberry extract was compared with nitrofurantoin. The recalculated Fisher's exact p-value of 0.137 indicates that the adverse-event difference should be interpreted cautiously with the available sample size. The negative correlation between adherence and recurrence, r=-0.42, indicates that higher adherence was associated with fewer recurrent UTI episodes across follow-up.

Reviewer-style note: The reported manuscript value of p=0.04 for adverse events is not supported by the supplied counts of 4/35 and 10/37 using Fisher's exact test. If the authors intend to retain p=0.04, the original statistical output, exact test type, and analysis denominator must be provided. The repeated-measures ANOVA also requires insertion of week 4 and week 8 VAS means and standard deviations, because the current manuscript reports the model result without the full repeated-measures data structure. Similarly, if the manuscript claims intention-to-treat analysis, primary and secondary outcome tables should be recalculated using all 80 randomized participants rather than only the 72 completers.

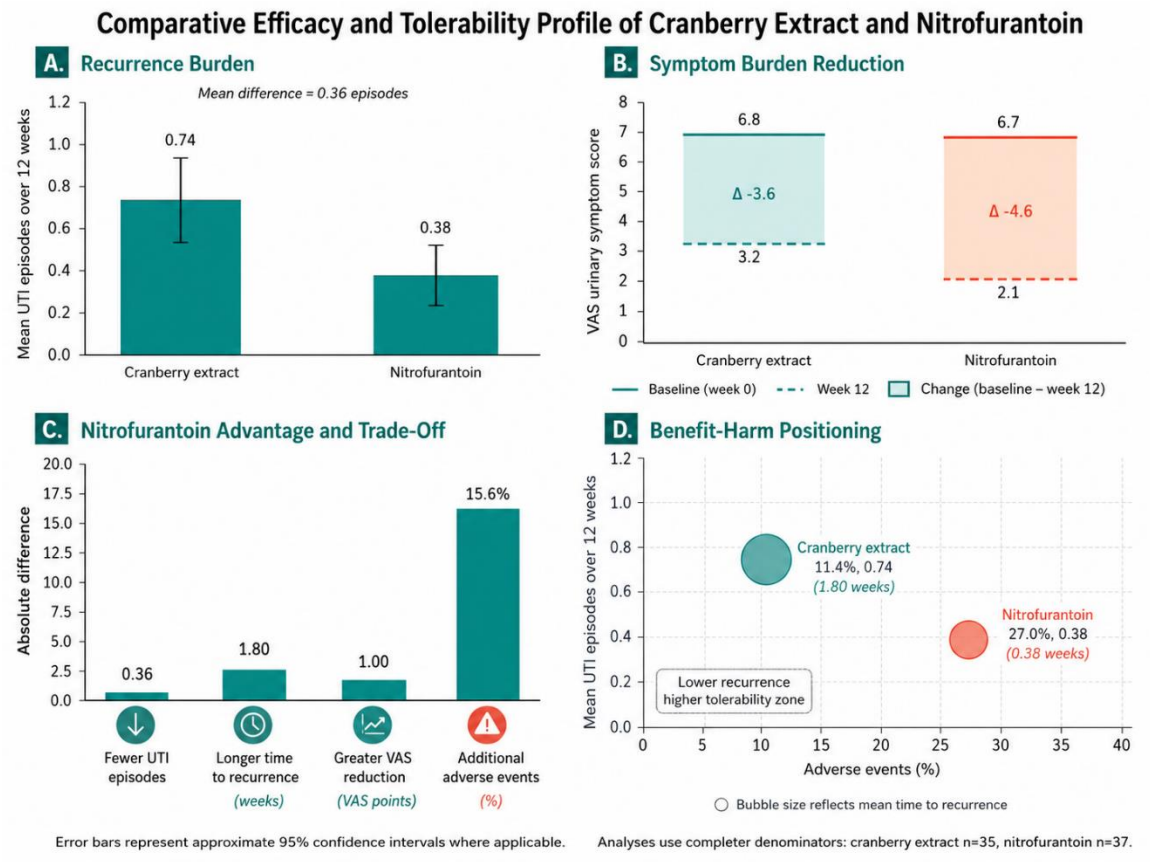

Figure 1. Comparative Efficacy and Tolerability Profile of Cranberry Extract and Nitrofurantoin.

The panelled figure summarizes the clinical trade-off between cranberry extract and low-dose nitrofurantoin among completers over the 12-week intervention period. Panel A shows lower mean UTI recurrence burden in the nitrofurantoin group compared with the cranberry extract group, with mean episodes of 0.38 versus 0.74 and a between-group mean difference of 0.36 episodes. Panel B demonstrates greater urinary symptom reduction with nitrofurantoin, where VAS scores decreased from 6.7 to 2.1 compared with 6.8 to 3.2 in the cranberry extract group, corresponding to mean reductions of 4.6 and 3.6 points, respectively. Panel C integrates efficacy and tolerability differences, showing that nitrofurantoin was associated with 0.36 fewer UTI episodes, 1.8 additional weeks to first recurrence, and

1.0 greater VAS-point reduction, but with a 15.6 percentage-point higher adverse-event frequency. Panel D positions both interventions according to recurrence burden and adverse-event frequency, with bubble size representing mean time to recurrence; nitrofurantoin occupies a lower-recurrence but higher-adverse-event profile, whereas cranberry extract shows a higher-recurrence but more tolerable profile.

DISCUSSION

This randomized active-comparator trial evaluated standardized cranberry extract and low-dose nitrofurantoin for short-term prevention of recurrent urinary tract infections among premenopausal women. The findings indicate that both interventions were associated with reductions in urinary symptom severity over 12 weeks, but nitrofurantoin demonstrated greater prophylactic efficacy in the completer analysis, with fewer symptomatic UTI episodes, longer time to first recurrence, and greater improvement in VAS urinary symptom scores. The mean number of UTI episodes was 0.38 ± 0.49 in the nitrofurantoin group compared with 0.74 ± 0.65 in the cranberry extract group, corresponding to a mean difference of 0.36 episodes and a moderate standardized effect size. Time to recurrence was also longer with nitrofurantoin, suggesting more sustained short-term protection during the intervention period. These results are consistent with the established role of antibiotic prophylaxis in recurrent UTI prevention, while also showing that cranberry extract may offer measurable symptomatic benefit with fewer reported adverse events (10).

The greater reduction in recurrence burden observed with nitrofurantoin is biologically and clinically plausible because nitrofurantoin achieves high urinary concentrations and acts directly against common uropathogens implicated in recurrent uncomplicated UTI. In contrast, cranberry extract is generally understood to act through non-antibiotic anti-adhesive mechanisms attributed to proanthocyanidins, which may reduce bacterial adherence to the uroepithelial lining rather than directly suppress bacterial proliferation. This mechanistic distinction may explain why cranberry extract produced improvement but did not match the magnitude of recurrence reduction achieved by nitrofurantoin. The observed findings therefore support the continued role of nitrofurantoin as a more effective short-term prophylactic option when recurrence prevention is the primary clinical priority, while positioning cranberry extract as a potential alternative for selected women who prefer non-antibiotic prophylaxis or have concerns regarding antibiotic exposure (11,12).

The symptom severity findings further strengthen the comparative interpretation. Both groups showed significant within-group reductions in VAS scores from baseline to week 12, but the magnitude of improvement was greater in the nitrofurantoin group. The cranberry extract group improved from 6.8 ± 1.2 to 3.2 ± 1.4, whereas the nitrofurantoin group improved from 6.7 ± 1.3 to 2.1 ± 1.1. The between-group difference in change favored nitrofurantoin by 1.0 VAS point, indicating that the lower recurrence burden was accompanied by greater reduction in patient-reported urinary discomfort. The repeated-measures analysis also demonstrated a significant time-by-group interaction, suggesting a differential trajectory of symptom improvement. However, the manuscript should include the week 4 and week 8 VAS means and standard deviations to allow complete verification of this longitudinal trend and to support any figure based on repeated measurements (13).

Tolerability is an important component of prophylactic decision-making, particularly in recurrent UTI where preventive strategies may be used repeatedly or for extended periods. Adverse events were numerically more frequent in the nitrofurantoin group than in the cranberry extract group, with events reported by 10 of 37 participants compared with 4 of 35 participants, respectively. This corresponds to 27.0% versus 11.4%, indicating a 15.6 percentage-point higher adverse-event frequency with nitrofurantoin in the completer sample. However, recalculation from the supplied counts using Fisher's exact test does not support the originally reported p-value of 0.04; therefore, the adverse-event difference should be interpreted cautiously unless the authors provide the original statistical output, analysis

denominator, and test used. The numerical pattern remains clinically relevant, but the statistical wording should avoid claiming a definitive significant difference without verification (14,15).

The relationship between adherence and recurrence is another clinically meaningful finding. The reported correlation between adherence and UTI recurrence was moderate and negative, indicating that better adherence was associated with fewer recurrent episodes. This observation is relevant to both treatment strategies because prophylaxis effectiveness depends not only on pharmacological or biological efficacy but also on sustained use, tolerability, acceptability, and patient behavior. Cranberry extract may have an adherence advantage in some patients because of its non-antibiotic profile and fewer reported adverse events, whereas nitrofurantoin may be preferred when stronger recurrence suppression is required. These findings support individualized prophylaxis rather than a single uniform approach for all premenopausal women with recurrent UTI (16).

The clinical implication of this trial is that low-dose nitrofurantoin provides superior short-term protection against recurrent UTI, while cranberry extract may represent a safer and more acceptable non-antibiotic alternative for selected patients. This distinction is particularly relevant in the context of antimicrobial stewardship, where reducing unnecessary or prolonged antibiotic exposure is desirable, but not at the expense of inadequate symptom control or frequent recurrence in higher-risk patients. For women with frequent, disruptive, or culture-confirmed recurrences, nitrofurantoin may remain the more appropriate prophylactic choice. For women with milder recurrence patterns, prior antibiotic intolerance, strong preference for non-antibiotic options, or lower tolerance for adverse effects, standardized cranberry extract may be considered as part of a shared decision-making strategy (17).

Several methodological strengths support the internal validity of the study. The randomized design, active comparator, allocation concealment, standardized intervention duration, monthly follow-up, adherence monitoring, and blinded outcome assessment reduced several important sources of bias. The use of culture-confirmed symptomatic recurrence strengthened outcome validity compared with symptom-only reporting. The inclusion of both efficacy and tolerability endpoints also reflects clinically realistic decision-making, where recurrence reduction must be considered alongside adverse events and adherence.

The study also has important limitations. First, the outcome analysis was based on 72 completers rather than all 80 randomized participants, while the original methods described intention-to-treat principles. This inconsistency should be corrected by either presenting a true intention-to-treat analysis using all randomized participants or explicitly labeling the reported results as completer analysis. Second, the sample size was relatively small, limiting precision for secondary outcomes and adverse-event comparisons. Third, participant blinding was not feasible, which may have influenced subjective symptom reporting, although blinded outcome assessment partly reduced this risk. Fourth, the intervention lasted only 12 weeks, so the findings should not be interpreted as evidence of long-term efficacy or long-term safety. Fifth, the manuscript does not provide full repeated-measures VAS values at all follow-up points, adverse-event categories, or recurrence proportions, which restricts the depth of interpretation. Future studies should use larger multicenter designs, longer follow-up, prespecified intention-to-treat and sensitivity analyses, standardized cranberry formulations, complete adverse-event classification, and time-to-event methods such as Kaplan–Meier or Cox regression when individual recurrence timing data are available (18).

Overall, this study contributes useful preliminary comparative evidence for recurrent UTI prophylaxis among premenopausal women. Nitrofurantoin achieved greater short-term reductions in recurrence and symptom severity, whereas cranberry extract showed lower numerical adverse-event frequency and may be a reasonable option when safety, tolerability, or antibiotic avoidance is prioritized. The findings should be interpreted as short-term completer-analysis evidence and should be strengthened through corrected analysis-population reporting, complete transparency statements, and more robust statistical presentation before final publication.

CONCLUSION

Low-dose nitrofurantoin demonstrated greater short-term prophylactic efficacy than standardized cranberry extract in premenopausal women with recurrent urinary tract infections, with fewer symptomatic UTI episodes, longer time to first recurrence, and greater reduction in urinary symptom severity over 12 weeks. Cranberry extract was associated with fewer numerically reported adverse events and may serve as a non-antibiotic prophylactic option for selected women who prioritize tolerability or antibiotic avoidance. These findings support individualized recurrent UTI prevention strategies that balance recurrence reduction, adverse-event risk, patient preference, and antimicrobial stewardship; however, the results should be interpreted as completer-analysis evidence unless a full intention-to-treat analysis is provided.

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