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SYSTEMATIC REVIEW

Cranberry extract for urinary tract infection treatment in pregnancy: A systematic review

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ABSTRACT

Objective: Urinary tract infections (UTIs) represent the second most common infectious disease worldwide, affecting nearly 150 million people annually. Owing to anatomical and physiological alterations, UTIs are especially frequent during pregnancy, manifesting with symptoms including dysuria, cloudy urine, increased urinary frequency, and occasionally hematuria. Recurrent UTIs are defined as two or more episodes within six months or three episodes within a year. Cranberries are widely recognized for their potential in preventing UTIs during pregnancy. Their protective action involves blocking the adhesion of uropathogenic bacteria to the urinary tract epithelium, a process mediated by phenolic compounds and A-type proanthocyanidins (PACs).

Materials and Methods: In this systematic review, the authors searched PubMed, ScienceDirect, ResearchGate, and Google Scholar for eligible articles published from 2013 to 2024. The search strategy employed Medical Subject Headings (MeSH) and keywords pertaining to Cranberry Extract/Juice and UTI Assessment Methods in Pregnancy. Search expressions were adapted to the specific requirements of each database to optimize retrieval precision. All identified studies were assessed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Results: Of the 30 studies included, a daily administration of 500 mg cranberry extract over six months exhibited notable effectiveness as an alternative therapeutic approach for UTIs in pregnancy.

Conclusion: Cranberry (*Vaccinium macrocarpon*) extract prevents UTIs by impeding bacterial adherence and exerting antibacterial properties. This review supports cranberry as a promising and safe alternative for UTI prevention and management in pregnancy, appropriate for routine daily use.

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Highlights:

- 1. Cranberry represents a promising and effective alternative for both the treatment and prevention of urinary tract infections during pregnancy.
- 2. Cranberry acts by inhibiting bacterial adhesion to the urinary tract epithelium and exerting direct antibacterial activity.



INTRODUCTION

Due to their pelvic anatomy, women are more susceptible to urinary tract infections (UTIs) than men, as bacteria readily ascend from the urethra into the bladder and may extend to the kidneys. The warm, moist vulvar environment near the rectum further increases contamination risk. UTIs are the second most common infection worldwide, often presenting as a significant complication in pregnancy, frequently progressing to recurrent urinary tract infections (RUTIs).²⁻⁴ Their increased incidence in pregnancy results from anatomical and physiological changes, including ureteral dilation and reduced bladder tone.⁵ Symptoms include dysuria, cloudy urine, urinary frequency, and occasionally hematuria. Recurrent UTI is defined as two or more episodes within six months or three episodes in one year. Uncomplicated UTIs, especially prevalent in women, have a 20-30% recurrence rate, creating a persistent health burden.⁷

Uncomplicated UTI symptoms, typically managed in primary care, are usually treated with antibiotics. Their high occurrence during pregnancy has increased antibiotic use, raising concerns about antimicrobial resistance (AMR). AMR is a major global health threat, responsible for 2.8 million infections and more than 35,000 deaths annually in the United States in 2019. Consequently, alternative approaches, including herbal therapies, are being explored for UTI prevention and as novel treatments for RUTIs to reduce antibiotic reliance.

Cranberry (Vaccinium macrocarpon) is a widely applied medicinal plant, recognized for its role in preventing UTIs during pregnancy. ^{10,11} The mechanism underlying cranberry's preventive action has not been fully defined. Evidence shows that phenolic compounds and A-type proanthocyanidins (PACs) inhibit adhesion of uropathogenic bacteria to the urinary tract epithelium. ^{10,12,13} These agents limit bacterial binding to bladder cells but do not dislodge attached bacteria. ¹⁴ Cranberry also exhibits antibiofilm, antiproliferative, immunomodulatory, and anti-inflammatory effects, strengthening its principal antiadhesive action. ¹⁵⁻¹⁷ By lowering antibiotic exposure, cranberry extract reduces the risk of resistant pathogens, offering important clinical benefits. ¹⁸

Recent metabolomics analyses reveal that cranberry juice alters the urinary metabolome, increasing excretion of exogenous and endogenous metabolites. As cranberries are not metabolized, they are eliminated in urine, likely contributing to their antiadhesive effect. 18 This study investigated cranberry extract's efficacy in preventing and treating UTIs in pregnancy, determines its optimal dosage, and examines its potential to mitigate AMR-related complications in practice.

MATERIALS AND METHODS

Literature searching

This review involved a comprehensive and systematic search of the literature performed in PubMed, ScienceDirect, ResearchGate, and Google Scholar to identify publications directly relevant to the research question. The search strategy integrated both MeSH terms and carefully selected keywords, focusing on Cranberry Extract/Juice and Methods of Measurement and Analysis for UTIs during pregnancy. Search expressions were specifically customized to the requirements of each database to optimize precision and completeness of retrieval. Articles published between 2013 and 2024 were collected, screened, and assessed in detail. This systematic review was conducted in full compliance with PRISMA guidelines and prospectively registered in PROSPERO (CRD42024620931).

Eligibility criteria

The data used in this review were classified according to explicit inclusion and exclusion criteria. Eligible studies encompassed experimental research, cohort investigations, longitudinal studies, case reports, social or pilot studies, and observational designs that were published within the last decade and written in English. The study population consisted of healthy pregnant women, irrespective of race, with or without Urinary Tract Infections (UTIs), with particular emphasis on those presenting recurrent UTI symptoms. These groups were selected as the central focus of this review. Inclusion further required that studies employ uniform measurement units, or where variations occurred, that they were appropriately standardized through validated calculations to ensure accuracy and comparability. Exclusion criteria incorporated all review articles, editorials, letters to editors, and conference abstracts. Studies were also excluded if titles or abstracts were judged irrelevant, if complete full texts could not be accessed, if reporting of measurement units was insufficient, or if datasets were incomplete.

Study selection and screening

Screening was carried out independently by a team of reviewers. Titles, abstracts, and keywords were systematically evaluated in several steps. PRISMA guidelines and the Mixed Methods Appraisal Tool (MMAT) were utilized to assess both methodological quality and reporting clarity of studies included in this systematic review. The MMAT applies five criteria to each methodological category, with responses rated as Y (YES = 1), N (NO = 0), or C (Cannot tell = 0). Final



quality scores were derived from the total number of affirmative responses obtained (see <u>Table 1</u>).

Data extraction

Urinary Tract Infections (UTIs) are identified based on characteristic clinical manifestations of genitourinary tract infection and microbiological confirmation by the presence of one or more microorganisms in urine exceeding a recognized diagnostic threshold (102 to 103 colony-forming units/mL).19,20 Recurrent Urinary Tract Infections (RUTIs) are defined as three positive urine cultures in a 12-month interval or two infections within a six-month period.21 Cranberry Extract, derived from the fruits and leaves of Vaccinium macrocarpon, is a traditional herbal preparation widely used in UTI prophylaxis. Numerous clinical and preclinical studies, including those supported by the National Center for Complementary and Alternative Medicine, have examined its potential protective role in urinary tract health.22 Eligible studies comprised experimental, cohort, review, and observational designs directly addressing this systematic review. The target population included women of reproductive age (20-50 years) and older. In addition to the six domains outlined, detailed information was extracted regarding study duration, geographic setting, characteristics of intervention and control groups, outcome measurement tools (e.g., standardized questionnaires), and principal findings—such as the effectiveness of interventions on clinical and psychological outcomes, adherence to therapy, and any reported adverse events.

RESULTS AND DISCUSSION

Overview of literature searching

The PRISMA flow diagram illustrating the study selection process is presented in Figure 1. A total of 743 studies were initially retrieved from PubMed, ResearchGate, ScienceDirect, and Google Scholar. After removal of 805 duplicate entries, 358 records remained for title and abstract screening. In accordance with the predefined eligibility criteria, 253 articles were excluded. Subsequently, 105 full-text articles were reviewed, of which 59 were excluded due to irrelevant outcomes, the use of active control groups, or publication in languages other than English or Indonesian. Ultimately, 30 studies fulfilled all inclusion criteria and were incorporated into the qualitative synthesis.

Table 1. RCT (Randomized Controlled Trial; Y=YES, N=NO, C=Cannot Tell)

Design	Methodological quality criteria / study ID	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Quantitative RCT	Is randomization appropriately performed?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	Are the group comparable at baseline?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	Are there complete outcome data?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	Are outcome assessors blinded to the intervention provided?	C	C	C	C	Y	Y	C	C	C	C	C	Y	Y	Y	Y
	Did the participants adhere to the assigned intervention?	C	Y	C	C	C	C	C	Y	Y	Y	Y	Y	Y	Y	Y
	Is randomization appropriately performed?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	Are the group comparable at baseline?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	Are there complete outcome data?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	Are outcome assessors blinded to the intervention provided?	C	C	C	C	Y	C	C	C	Y	C	C	Y	Y	Y	Y
	Did the participants adhere to the assigned intervention?	C	Y	Y	Y	C	C	Y	Y	Y	Y	Y	Y	Y	Y	Y



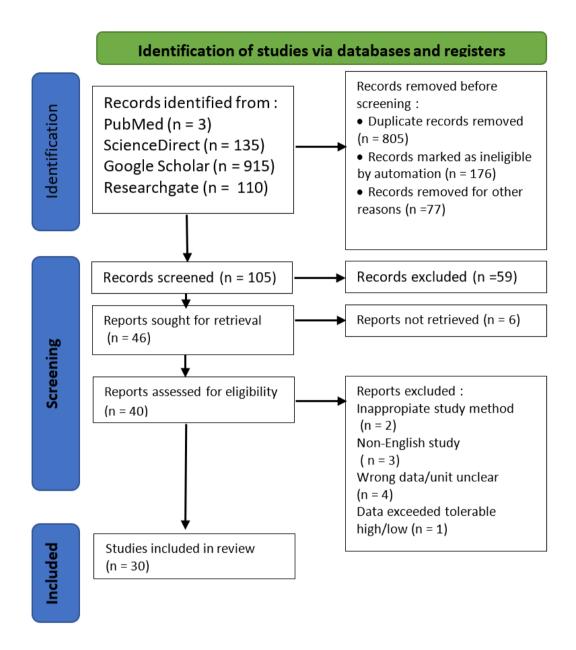


Figure 1. PRISMA Flowchart of The Literature Selection

Study characteristics

The characteristics of the 30 studies included in this qualitative analysis are summarized in Table 2. Altogether, 30 studies involving participants assessed for the use of Cranberry Extract in the treatment of Urinary Tract Infections (UTIs) during pregnancy were reviewed. The majority of investigations were

conducted in the United States (10), followed by the United Kingdom (3), Spain (2), China (2), the Netherlands (2), Germany (2), and one study each from Canada, Switzerland, Norway, Italy, Mexico, Australia, Iraq, Poland, and Finland. Collectively, these 30 studies provided analytical evaluation of the preventive application of Cranberry (*Vaccinium macrocarpon*) extract in the management of UTIs during pregnancy.



Table 2. Characteristics of included study

Countries	Authors	Years	Study designs
Spain	Llano, Dolores Gonzales et al	2020	Observational Study
Canada	Babar, Asma et al	2018	Double Blind Randomized Controlled Study
USA	Zhuxuan, Fu et al	2017	Cohort Study
UK	Gbinigie, Oghenekome et al	2019	Randomized Clinical Study
USA	Hudson, Rachel E et al	2021	Cohort Study
USA	Bolgarina, Zoryana et al	2023	Clinical Trial and Observational Study
Switzerland	Gbinigie, Oghenekome et al	2020	Cohort Study
USA	Wing, Deborah A et al	2014	Clinical Trial and Observational Study
China	Wang, Chih-Hung et al	2013	Randomized Control Study
Norway	Heitmann, Kristine et al	2013	Cohort Study
Germany	Jeitler, Michael et al	2022	Prospective, Uncontrolled Exploratory Study
Italy	Ledda, A et al	2017	Clinical Study
Germany	Vostalova, Jitka et al	2015	Randomized Double Blind and Placebo Controlled Study
USA	Wing, Deborah A et al	2013	Pilot Study
USA	Stapleton, Ann E. et al	2013	Randomized Controlled Study
Netherland	Beerepoot, Marielle A.J et al	2013	Randomized Double-Blind Non-Inferiority Study
Spain	Perez-Lopez, Faustino R et al	2013	Observational Study
USA	Koradia, Parshottam et al	2019	Controlled Pilot Study
Mexico	Monroy-Torres, Rebeca et al	2018	Observational Actual Evidence Study
Australia	Konesan, Jenane et al	2022	Cohort Study
UK	Maki, Kevin C et al	2016	Double-blind Randomized Placebo-controlled Study
USA	Liska, DeAnn J et al	2016	Cohort Study
Iraq	Al Gaoale, Zubaidah Ibrahim	2022	Observational Study
-	Younus et al		
Poland	Wawrysiuk, Sara et al	2019	Cohort Study
UK	Griffiths, Peter	2013	Observational Social Study
USA	Efros, Mitchell et al	2013	Clinical Study
Netherland	van Wietmarschen, Herman et al	2022	Observational Study
USA	Gupta, K et al	2013	Clinical Study
Finland	Kontiokari, Tero et al	2013	Randomized Study
China	Xia, Jia-yue et al	2021	Sequential Analysis Study

Table 3 contains detailed descriptions of the 30 primary articles selected for the systematic review on Cranberry Extract in Urinary Tract Infections (UTIs) during pregnancy, comprising a total sample size of 3,657 women in healthy reproductive age, pregnant, or breastfeeding.

UTIs represent the second most common infectious condition globally, affecting approximately 150 million individuals. This infection is highly prevalent during pregnancy, with frequent recurrence attributed to anatomical and physiological changes associated with gestation.^{2,23} The prevalence of UTIs is higher in women due to shorter urethral anatomy, which facilitates bacterial colonization and ascending infection to the bladder and kidneys.¹ During pregnancy, UTIs are often associated with complications affecting both the mother and fetus. Studies have reported a higher

incidence of preterm birth among women experiencing recurrent UTIs.³ Recurrent UTIs (r-UTIs) are defined as two episodes within six months or three within twelve months.²⁴ This condition often necessitates extended or higher-dose antibiotic therapy. Some women may present with asymptomatic UTIs, posing challenges for timely diagnosis and effective treatment. Standard treatment for UTIs primarily involves antimicrobial or antibiotic therapy. However, growing concerns have emerged due to increasing antibiotic resistance associated with recurrent infections. 8.9 This situation has led to a growing interest in alternative therapies, such as herbal medicine, for their protective effects. Beyond resistance, additional concerns regarding antibiotic use in pregnancy include risks of miscarriage and increased incidence of sick leave, as also reported in the literature. 13



Table 3. PICO table summary of primary articles sources with sample size (n = 3657 women)

Author (Year)	Country Sample		P	I	С	0	
Llano, Dolores Gonzales et al (2020)	Spain	170 women	<u> </u>		Placebo	Protective effect of cranberry extract for UTIs	
Babar, Asma et al (2018)	Canada	148 women; ages \geq 18 years old, with \geq 2 symptoms of UTIs in 6 months or \geq 3 symptoms of UTIs in 12 months	Divided into 2 groups (74 women for each group)	2x18,5 mg PACs per day for 6 months	2x1 mg PACs per day for 6 months	New standardized of High Doses of cranberry extract for Prevention of r-UTI	
Zhuxuan, Fu et al (2017)	USA	154 women; ages ≥ 18 years old with history of UTI in pregnancy	Divided into 2 groups (77 women for each group)	Cranberry juice and extract	Placebo	Effect of cranberry for UTIs in women	
Gbinigie, Oghenekome et al (2019)	UK	45 women; ages ≥ 18 years old consulting in primary care for pregnancy and problems of acute UTIs; get antibiotic for prescription	20 women with problem of UTIs who got the early prescription of first line antibiotics; 25 women with UTIs who got delayed or never get antibiotics	Cranberry extract combines with primary line antibiotics	Antibiotics	Effect of cranberry for acute UTIs and how much it can reduce antibiotics use for treatment of UTIs	
Hudson, Rachel E et al (2021)	USA	100 women with symptoms of UTIs in pregnancy	25 women as control group get conventional treatment for UTIs; 75 women in intervention group divided into 2 groups; 35 women with standard dosage of cranberry and 40 women with high dosage of cranberry extract	Standard dosage of cranberry extract and high dosage of cranberry extract	Conventional Treatment for UTIs	Examine the complementary and dosage of cranberry for better treatment	
Bolgarina, Zoryana et al (2023)	USA	200 women; with symptoms of UTIs or RUTIs in pregnancy	Divided into 2 groups	Cranberry supplement	Placebo	Evaluate the effectiveness of cranberry supplement for UTIs in pregnancy women	
Gbinigie, Oghenekome et al (2020)	Switzerland	140 women; ages ≥18 years old, outpatient in primary care with symptoms of UTIs	Divided into 2 groups	Cranberry extracts	Placebo	Efficacy of cranberry extract for acute UTIs in pregnancy	
Wing, Deborah A et al (2014)	USA	49 pregnant women with gestational ages between 12 to 16 weeks	Divided into 2 groups	Cranberry capsules	Placebo	Preventive effect of cranberry for UTIs in pregnancy	
Wang, Chih-Hung et al (2013)	China	414 women; ages ≥18 years old with UTIs symptoms in pregnancy	Divided into 2 groups (consist of 207 each group), then divided into 2 smaller groups each; 1 group for r-UTIs during pregnancy and 1 group without r-UTIs symptoms	Cranberry juice and extract for 3 until 6 months prior to the symptoms	Placebo	Analyze the effect of cranberry extract for treatment in UTIs of pregnant women	
Heitmann, Kristine et al (2013)	Norway	300 women; gestational age between 12 to 16 weeks	Divided into 2 groups base on primiparous and nulliparous	Cranberry extract	Placebo	Pregnancy UTIs symptoms and condition after consume cranberry extract	
Jeitler, Michael et al (2022)	Germany	23 women; ages ≥18 years old reported with chronic recurrent UTIs problem in pregnancy	Divided into 2 groups	Cranberry supplement within 6 months consumption	Cranberry supplement for 1 – 3 months consumption	UTIs outcome with different duration of cranberry supplement consumption	
Ledda, A et al (2017)	Italy 36 women; ages ≥18 years old suffering with r-UTI in pregnancy women as control (get the standard management for UTIs) and 19 women as intervention who obtained oral cranberry supplementation		Oral cranberry supplementation contain of 120 mg cranberry extract, standardized to 36 mg proanthocyanidins for 60 days	Standard management and medication	Effectiveness of prevention of UTIs in pregnancy		



Vostalova, Jitka et al (2015)	, Jitka et al Germany 182 women; history of pregnancywith 2 or more UTIs episodes in the last year Divided into 2 groups; 89 received the cranberry extract and 93 as control received the placebo		Daily 500 mg cranberry extract for 6 months	Placebo	Efficacy of high dosage of proanthocyanidins as the key of successful treatment and prevention of UTIs in pregnancy	
Wing, Deborah A et al (2013)	USA	28 pregnant women and 15 non- pregnant women in reproductive age	Both category divided into 2 and randomly made into 2 large groups, consisted of 24 intervention groups (14 pregnant women and 10 non-pregnant) and the rest as the control group	Low calorie cranberry juice (consist of 100% cranberry) 240 ml two times daily	Placebo	Antimicrobial effect of cranberry juice cocktail daily
Stapleton, Ann E. et al (2013)	USA	176 women; ages between 18 to 45 years old which history of clinical diagnosed UTIs in pregnancy	Divided into 2 groups of 120 women in intervention group and 56 women in control group. The intervention group divided into 2 groups obtaining different intervention	Group 1A: received 4 oz of cranberry juice Group 2A: received 8 oz of cranberry juice	Placebo	The preventive effect of cranberry juice for recurrent UTIs and Urinary Eschericia colli Infection in women
Beerepoot, Marielle A.J et al (2013)	Netherland	221 women; ages between 18 to 45 with history of UTIs symptoms in pregnancy or breastfeeding (at least 3 symptomatic UTIs) that have been receiving antibiotics treatment	istory of UTIs symptoms in intervention groups and 1 placebo ancy or breastfeeding (at least 3 omatic UTIs) that have been		Placebo	Analyze the preventive effect between antibiotics and cranberry for UTIs problem in women
Perez-Lopez, Faustino R et al (2013)	Spain	20 women; ages ≥18 years old with history of UTIs in pregnancy	Divided into 2 groups	Cranberry extract	Placebo	The effect of cranberry for prevent the case of recurrent UTIs
Koradia, Parshottam et al (2019)	USA	115 women; which 90 enrolled and 81 subjects completed the study; ages 18 to 55 years old which have history of UTIs in pregnancy	Divided into 2 groups for 26 weeks treatment	180 days (full treatment) of cranberry capsule	90 days cranberry capsule	Evaluate the duration of probiotic and cranberry capsule for recurrent UTIs in women
Monroy-Torres, Rebeca et al (2018)	Mexico	150 pregnant women (early pregnancy or first semester) with the history of UTIs, but not in active UTIs problem	Divided into 2 groups, each consisted of 75 women	Cranberry juice daily for 6 months	Placebo	The efficacy of cranberry juice for prevention of r-UTIs in pregnant women
Konesan, Jenane et al (2022)	Australia	172 women; ages between middle 20 to 50s years old with history of UTIs in pregnancy	Divided into 2 groupss	Cranberry extract	Placebo	The effect of cranberry for UTIs in women
Maki, Kevin C et al (2016)	UK	373 women; ages 20 – 70 years old with history of UTIs in pregnancy and BMI < 40, that have been treated in health care professional	Divided into 2 groups; 185 women in intervention group and 188 women in control group	240 mL of cranberry beverages/day	240 ml placebo beverages/day	Evaluate the effect of cranberry beverages for UTIs problem
Liska, DeAnn J et al (2016)	USA	90 women; ages 18 – 45 years old with history of recurrent UTIs in pregnancy and breastfeeding	Divided into 2 groups; 50 women in intervention group and 40 women in control group	Cranberry extract	Placebo	The effect in cranberry extract consumption for UTIs problem
Al Gaoale, Zubaidah Ibrahim Younus et al (2022)	Iraq	24 pregnant women with uncomplicated UTIs problem	Divided into 2 groups	Cranberry (combination) supplement	Placebo	Therapeutic effect of cranberry for anti-relapse uncomplicated UTIs in women
Wawrysiuk, Sara et al (2019)	ara et al Poland 30 women; ages ≥18 years old with history of UTIs in pregnancy or r-UTI		Cranberry extract	Placebo	Evaluate the preventive and treatment effect of cranberry in UTIs	



Griffiths, Peter (2013)	UK	20 women; ages ≥18 years old outpatient in primary health care with history of UTIs in pregnancy	Divided into 2 groups	Cranberry juice for 7 days	Cranberry juice for ≥14 days (standardized)	Role of cranberry for treatment and prevention of UTIs
Efros, Mitchell et al (2013)	USA	28 women; ages ≥18 years old with history of UTIs in pregnancy and breastfeeding in minimum 6 months	Divided into 5 groups	Oral cranberry extract at : Group (1) 15 mL, (2) 30 mL, (3) 45 mL, (4) 60 mL and (5) 75 mL for 12 weeks	· -	The recommend dose of cranberry extract to get the preventive effect of recurrent UTIs problem
van Wietmarschen, Herman et al (2022)	Netherland	40 women; ages ≥18 years old with history of UTIs in pregnancy	Divided into 2 groups	Cranberry extract	Placebo	The preventive effect of cranberry extract for recurrent UTIs
Gupta, K et al (2013)	USA	20 women; ages ≥18 years old with history of specific UTIs in pregnancy (<i>E. coli</i>) infection	Divided into 2 groups	Cranberry supplement (consist of 9 mg proanthocyanidin per gm)	Placebo	The effect of cranberry extract in inhibit adherence of P-Fimbriated <i>Eschericia coli</i> in UTIs problem
Kontiokari, Tero et al (2013)	Finland	150 women; have the history of pregnancy UTIs caused by <i>Eschericia coli</i> bacteria in Oulu University Hospital	Divided into 3 groups, consisted 2 intervention groups and 1 control group	Group 1A: 50 women received 50 mL of cranberry juice concentrate a day for 6 months Group 2A: 50 women received 100 mL <i>Lactobacillus</i> GG drink 5 days a week for one year	Placebo	Evaluate better option for prevention of recurrent UTIs caused by <i>E.coli</i>
Xia, Jia-yue et al (2021)	China	24 women; reproductive age, with history of UTIs in pregnancy that have been treated by antibiotics	Divided into 2 groups	Cranberry extract	Primary Line of Antibiotics	Evaluate the effect of cranberry as the adjuvant therapy of UTIs problem in women



Herbal therapies for UTI prevention include cranberry (Vaccinium macrocarpon). Cranberry contains polyphenols, flavonoids, and phenolic acids, which have been demonstrated to contribute to UTI prevention. 5,6 Early investigations proposed that cranberry acted by increasing urinary acidity, whereas more recent studies suggest its mechanism primarily involves inhibiting bacterial adhesion to the urinary tract epithelium. 25,26 Consumption of cranberry has been associated with a reduced incidence of UTIs among women. 5 While multiple studies support its efficacy in both symptom alleviation and UTI prevention, some have produced inconsistent findings. Results from in vivo and in vitro experiments strongly endorse cranberry as a preventive intervention for UTIs.⁵ In this review, such claims are corroborated by more than 20 included studies. Evidence indicates that cranberry extract, administered either as juice or in capsule formulation, may be utilized as an adjunct to antibiotic therapy or as a standalone treatment.²⁷⁻²⁹ Both approaches demonstrate beneficial outcomes in reducing recurrent UTIs.⁹ Nevertheless, challenges persist, including insufficient knowledge regarding product formulation, lack of standardization, uncertainty about optimal dosing regimens, and ongoing concerns about toxicity and adverse effects. 6,10

One study evaluated in this review demonstrated that daily supplementation of 500 mg cranberry containing 2.8 mg of proanthocyanidins (PACs) over six months reduced UTI recurrence. 18 Another investigation revealed that cranberry exhibited antibacterial activity against Escherichia coli, with decreased colony counts observed following single or double doses of cranberry intake. 19 Although issues of tolerability remain, several trials have reported statistically significant reductions in recurrent UTIs in women consuming cranberry. 30-32 Furthermore, evidence suggests that daily cranberry use for 6 to 12 months is safe in pregnant women and children. 33,34 Additional investigations confirm the high efficacy of cranberry for UTI prevention during pregnancy, particularly given its practicality for daily consumption. 35,36

Despite these positive findings, two studies included in the review reported no significant differences in the protective effects of cranberry. Additionally, extended study durations led to high rates of loss to follow-up, thereby limiting the robustness of available evidence. 4-7 The incidence of symptomatic UTIs across cranberry, antibiotic, and placebo groups demonstrated minimal variation. 3-8 The limitations of this review include the lack of well-designed trials published beyond 2018, insufficient data to establish definitive clinical guidelines, and continued absence of standardized formulations as of 2022. Nonetheless, the evidence presented highlights the potential of cranberry as a viable alternative treatment and preventive approach for

UTIs in pregnancy, thereby underscoring the therapeutic role of herbal medicine in infectious disease management.

Strength and limitation

An important strength of this review is the consistent finding that cranberry represents a promising and effective alternative for both the prevention and treatment of UTIs during pregnancy. The primary limitation, however, is the restricted number of high-quality trials and the limited availability of comprehensive sources suitable for inclusion.

CONCLUSION

This systematic review highlights that UTIs remain a common and clinically significant health concern among women, particularly in pregnancy. At present, this infection may be managed and prevented using alternative interventions in addition to conventional approaches. Cranberry (Vaccinium macrocarpon) extract has been frequently employed for its prophylactic potential against UTIs. Based on the studies included in this review, daily intake of 500 mg cranberry extract for six months provides an effective option for UTI prevention in pregnancy, with no adverse effects reported. The mechanism of action is thought to involve inhibition of bacterial adherence to the uroepithelial surface, in addition to demonstrating antibacterial properties. Collectively, these findings reinforce the conclusion that cranberry is a promising and effective alternative therapeutic strategy for both treatment and prevention of UTIs in pregnancy, appropriate for routine use.

DISCLOSURES

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Conflict of interest

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Author contribution

All of the authors prepared, collected, analyzed, wrote, and approved this work.

REFERENCES

 Hoffman BL, Schorge JO, Bradshaw KD, et al. William Gynecology. 3rd Edition. McGraw Hill Education, 2016.



- Getaneh T, Negesse A, Dessie G, et al. Prevalence of urinary tract infection and its associated factors among pregnant women in Ethiopia: A systematic review and meta-analysis. Biomed Res Int. 2021;2021:6551526. doi: 10.1155/2021/6551526. PMID: 34901276; PMCID: PMC8654570.
- Balachandran L, Jacob L, Al Awadhi R, et al. Urinary tract infection in pregnancy and its effects on maternal and perinatal outcome: A retrospective study. Cureus. 2022;14(1):e21500. doi: 10.7759/ cureus.21500. PMID: 35223276; PMCID: PMC88 60729.
- Schneeberger C, Geerlings SE, Middleton P, et al. Interventions for preventing recurrent urinary tract infection during pregnancy. Cochrane Database Syst Rev. 2012;11:CD009279. doi: 10.1002/146518 58.CD009279.pub2. Update in: Cochrane Database Syst Rev. 2015;(7):CD009279. doi: 10.1002/1465 1858.CD009279.pub3. PMID: 23152271.
- González de Llano D, Moreno-Arribas MV, Bartolomé B. Cranberry polyphenols and prevention against urinary tract infections: Relevant considerations. Molecules. 2020;25(15):3523. doi: 10.3390/molecules25153523. PMID: 32752183; PMCID: PMC7436188.
- 6. Babar A, Moore L, Leblanc V, 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. doi: 10.1186/s12894-021-00811-w. PMID: 33757474; PMCID: PMC7986024.
- Fu Z, Liska D, Talan D, et al. Cranberry reduces the risk of urinary tract infection recurrence in otherwise healthy women: A systematic review and meta-analysis. J Nutr. 2017;147(12):2282-88. doi: 10.3945/jn.117.254961. Epub 2017 Oct 18. PMID: 29046404.
- Gbinigie O, Allen J, Boylan et al. Does cranberry extract reduce antibiotic use for symptoms of acute uncomplicated urinary tract infections (CUTI)? Protocol for a feasibility study. Trials. 2019;20(1): 767. doi: 10.1186/s13063-019-3860-z. PMID: 3187 0413; PMCID: PMC6929469.
- Hudson RE, Job KM, Sayre CL, et al. Examination of complementary medicine for treating urinary tract infections among pregnant women and children. Front Pharmacol. 2022;13:883216. doi: 10.3389/fphar.2022.883216. PMID: 35571128; PMCID: PMC9094615.
- 10. Bolgarina Z, Gonzalez-Gonzalez LF, Rodroiguez GV, et al. Cranberry supplements for urinary tract infection prophylaxis in pregnant women: A systematic review of clinical trials and observational studies on efficacy, acceptability, outcomes measurement methods, and studies' feasibility.

- Cureus. 2023;15(10):e46738. doi: 10.7759/cureus. 46738. Erratum in: Cureus. 2023;15(10):c140. doi: 10.7759/cureus.c140. PMID: 38022216; PMCID: PMC10631496.
- Gbinigie OA, Spencer EA, Heneghan CJ, et al. Cranberry extract for symptoms of acute, uncomplicated urinary tract infection: a systematic review. Antibiotics (Basel). 2020;10(1):12. doi: 10.3390/antibiotics10010012. PMID: 33375566; PMCID: PMC7824375.
- 12. Wing DA, Rumney PJ, Hindra S, et al. Pilot study to evaluate compliance and tolerability of cranberry capsules in pregnancy for the prevention of asymptomatic bacteriuria. J Altern Complement Med. 2015;21(11):700-6. doi: 10.1089/acm.2014.0272. Epub 2015 Aug 21. PMID: 26535612; PMCID: PMC4642828.
- Wang CH, Fang CC, Chen NC, et al. Cranberry-containing products for prevention of urinary tract infections in susceptible populations: a systematic review and meta-analysis of randomized controlled trials. Arch Intern Med. 2012;172(13):988-96. doi: 10.1001/archinternmed.2012.3004. PMID: 22777 630.
- Heitmann K, Nordeng H, Holst L. Pregnancy outcome after use of cranberry in pregnancy the Norwegian Mother and Child Cohort Study. BMC Complement Altern Med. 2013;13:345. doi: 10.1186/1472-6882-13-345. PMID: 24314317; PMCID: PMC3924191.
- Stapleton AE, Dziura J, Hooton TM, et al. Recurrent urinary tract infection and urinary Escherichia coli in women ingesting cranberry juice daily: A randomized controlled trial. Mayo Clin Proc. 2012;87(2):143-50. doi: 10.1016/j. mayocp.2011.10.006. PMID: 22305026; PMCID: PMC349 7550.
- Liska DJ, Kern HJ, Maki KC. Cranberries and urinary tract infections: How can the same evidence lead to conflicting advice? Adv Nutr. 2016;7(3): 498-506. doi: 10.3945/an.115.011197. PMID: 271 84277; PMCID: PMC4863270.
- Konesan J, Liu L, Mansfield KJ. The clinical trial outcomes of cranberry, D-mannose and NSAIDs in the prevention or management of uncomplicated urinary tract infections in women: A systematic review. Pathogens. 2022;11(12):1471. doi: 10.3390/pathogens11121471. PMID: 36558804; PMCID: PMC9788503.
- Jeitler M, Michalsen A, Schwiertz A, 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. doi: 10.1089/jicm.2021.0300. Epub 2022 Mar 14. PMID: 35285701; PMCID: PMC9127832.



- 19. Guay DR. Cranberry and urinary tract infections. Drugs. 2009;69(7):775-807. doi: 10.2165/0000 3495-200969070-00002. PMID: 19441868.
- 20. Ledda A, Belcaro G, Dugall M, et al. Highly standardized cranberry extract supplementation (Anthocran®) as prophylaxis in young healthy subjects with recurrent urinary tract infections. Eur Rev Med Pharmacol Sci. 2017;21(2):389-93. PMID: 28165546.
- 21. Vostalova J, Vidlar A, Simanek V, et al. Are high proanthocyanidins key to cranberry efficacy in the prevention of recurrent urinary tract infection? Phytother Res. 2015;29(10):1559-67. doi: 10.1002/ptr.5427. Epub 2015 Aug 13. PMID: 26268913.
- 22. Wing DA, Shell A, Lee YL, et al. Antimicrobial activity of urine after ingestion of differing daily doses of cranberry juice cocktail in pregnancy: A pilot study. Open Complement. Med. J. 2001;2: 15–9. doi: 10.2174/1876391X01002010015.
- Salari N, Khoshbakht Y, Hemmati M, et al. Global prevalence of urinary tract infection in pregnant mothers: a systematic review and meta-analysis. Public Health. 2023;224:58-65. doi: 10.1016/j. puhe.2023.08.016. Epub 2023 Sep 19. PMID: 37734277.
- 24. Koradia P, Kapadia S, Trivedi Y, et al. Probiotic and cranberry supplementation for preventing recurrent uncomplicated urinary tract infections in premenopausal women: a controlled pilot study. Expert Rev Anti Infect Ther. 2019;17(9):733-40. doi: 10.1080/14787210.2019.1664287. Epub 2019 Sep 13. Erratum in: Expert Rev Anti Infect Ther. 2019;17(11):939. doi: 10.1080/14787210.2019.167 3041. PMID: 31516055.
- 25. van Wietmarschen H, van Steenbergen N, van der Werf E, et al. Effectiveness of herbal medicines to prevent and control symptoms of urinary tract infections and to reduce antibiotic use: A literature review. Integr Med Res. 2022;11(4):100892. doi: 10.1016/j.imr.2022.100892. Epub 2022 Oct 9. PMID: 36345487; PMCID: PMC9636546.
- Gupta K, Chou MY, Howell A, et al. Cranberry products inhibit adherence of p-fimbriated *Escherichia coli* to primary cultured bladder and vaginal epithelial cells. J Urol. 2007;177(6):2357-60. doi: 10.1016/j.juro.2007.01.114. PMID: 17509 358; PMCID: PMC3684265.
- Xia JY, Yang C, Xu DF, et al. 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. doi: 10.1371/journal.pone.0256992. PMID: 34473789; PMCID: PMC8412316.

- 28. Kontiokari T, Sundqvist K, Nuutinen M, et al. Randomised trial of cranberry-lingonberry juice and *Lactobacillus GG* drink for the prevention of urinary tract infections in women. BMJ. 2001;322 (7302):1571. doi: 10.1136/bmj.322.7302. 1571. PMID: 11431298; PMCID: PMC33514.
- 29. Maki KC, Kaspar KL, Khoo C, et al. Consumption of a cranberry juice beverage lowered the number of clinical urinary tract infection episodes in women with a recent history of urinary tract infection. Am J Clin Nutr. 2016;103(6):1434-42. doi: 10.3945/ajcn.116.130542. Erratum in: Am J Clin Nutr. 2017;106(2):708. doi: 10.3945/ajcn.117. 161851. PMID: 27251185.
- Gurley BJ. Cranberries as antibiotics?: Comment on "Cranberries vs antibiotics to prevent urinary tract infections: a randomized double-blind noninferiority trial in premenopausal women". Arch Intern Med. 2011;171(14):1279-80. doi: 10.1001/ archinternmed.2011.332. PMID: 21788543.
- 31. Pérez-López FR, Haya J, Chedraui P. *Vaccinium macrocarpon*: an interesting option for women with recurrent urinary tract infections and other health benefits. J Obstet Gynaecol Res. 2009;35(4):630-9. doi: 10.1111/j.1447-0756.2009.01026.x. PMID: 19751320.
- 32. Monroy-Torres R, Medina-Jiménez AK. Cranberry juice and other functional foods in urinary tract infections in women: a review of actual evidence and main challenges. Bentham Science. 2019;29: 183–211. doi: 10.2174/9781681086378119050007.
- 33. Younus Al Gaoale ZI, Sheekhoo Al Azzawi KG, Dhannooon Al-Sabaawi MB. Urinary tract infections in pregnant women. New opportunities anti-relapse therapy. Medico-Legal Updat. 2022; 22(3). doi: 10.37506/mlu.v22i3.3307.
- 34. Wawrysiuk S, Naber K, Rechberger T, et al. Prevention and treatment of uncomplicated lower urinary tract infections in the era of increasing antimicrobial resistance-non-antibiotic approaches: a systemic review. Arch Gynecol Obstet. 2019;300 (4):821-8. doi: 10.1007/s00404-019-05256-z. Epub 2019 Jul 26. PMID: 31350663; PMCID: PMC675
- 35. Griffiths P. The role of cranberry juice in the treatment of urinary tract infections. Br J Community Nurs. 2003;8(12):557-61. doi: 10. 12968/bjcn.2003.8.12.11853. PMID: 14688663.
- 36. Efros M, Bromberg W, Cossu L, et al. Novel concentrated cranberry liquid blend, UTI-STAT with Proantinox, might help prevent recurrent urinary tract infections in women. Urology. 2010; 76(4):841-5. doi: 10.1016/j.urology.2010.01.068. PMID: 20399486.

