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The Study of Cranberry Products Use among Elderly Women with Urinary Tract Infection

A Scoping Review

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Abstract

Introduction: Urinary tract infections (UTIs) rank among the most prevalent bacterial infections among elderly women, the present treatment of urinary tract infection is mainly antibiotics, while it can cause serious antibiotics resistance, thus, it's important to find another alternative therapy. The aim of this scoping review was to synthesis the evidence to explore what is the outcome of cranberry used for urinary tract infection among elderly women?

Results: The current evidence indicated that cranberry products decreased the incidence of the UTI number and symptom, and it can be also possible to reduce the antibiotics use with low side effect among elderly women, furthermore, it can improve the well-being of patients with UTI. However, some of the results should be interpreted with caution because of the limited number of studies and low compliance of some of the selected studies.

Conclusion: Cranberry has positive outcome used for the UTI prevention and treatment, in terms of the benefits for the reduction of the incidence of UTI number and symptom, low side effects and improve in the of well-being of patients with UTI.

Language: English
Key Words: Cranberry, Urinary tract infection, Elderly women

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1 Introduction

Urinary tract infection (UTI) ranks among the most prevalent bacterial infections in older individuals. Women are more likely to have UTI than men due to women's shorter urethra. Women above 50 years old are more likely to have recurrent UTI and the infection risk increase with age (Czajkowski et al., 2021).

Due to the report from the Finnish Institute of Health and Welfare, there were approximately 100,000 cases of healthcare-associated infections happened in Finland each year, however, with one half of these cases occurring within long-term care facilities as well as another half in hospitals. Among these infections, urinary tract infection has became one of the most common infections (THL, 2023).

The present treatment of urinary tract infection is mainly antibiotics (AUA Guidelines on Recurrent UTI, 2022). However, antibiotic resistance which refers to the survivability of pathogens against the exposure and administration of antibiotics that could kill them or restrain their proliferation has become a global challenge for human health, as it is associate with high rates of mortality and morbidity (Muteeb et al., 2023). And some assessments had found that more than 90% of UTIs exhibited bacteria that was drug resistant, with most resistant to two or more antibiotics (Moro et al., 2024).

In a study analyzed over 25 million emergency department visits where a urinary tract infection (UTI) was diagnosed, only 32% of cases had urinary symptoms. And the percentage dropped to 24% among older individuals aged 65 to 84 years. This indicated a significant portion of UTI cases may present without identified symptoms. The unnecessary use of antibiotics for asymptomatic bacteriuria (ASB) can lead to antibiotic resistance and increase the risk of recurrent UTIs and progression to pyelonephritis. Continued use of antibiotics in recurrent urinary tract infection (rUTI) patients are associated with many adverse events, which may include allergic reactions, organ toxicities, future infection with resistant organisms. Thus, substantial effort should be made to avoid unnecessary

treatment unless there is a high suspicion of an acute cystitis episode (AUA Guidelines on Recurrent UTI, 2022).

According to a systematic review, there was a study which guided physicians in advising cranberry consumption to lower the incidence of urinary tract infections, especially in those prone to recurrent UTI (Luís, Domingues& Pereira, 2017). Moreover, a study by Bartlett et al. suggested that cranberry (Vaccinium macrocarpon) may benefit for the prevention of UTI among elderly care residents (Bartlett& De Bellis, 2022).

In order to improve the management of the urinary tract infection which can also improve the quality of the elderly care, it's important for nurse to know some alternative method instead of only antibiotics to the management of UTI.

Therefore, the purpose of this research is to explore more knowledge about the outcome of cranberry used for UTI among elderly women.

2 Background

This chapter describes background information of urinary tract infection and brief introduction about cranberry and its mechanism of action used for the urinary tract infection treatment. Firstly, definition, symptoms, risk factors, diagnosis and treatment of UTI are discussed; then followed by the information of cranberry and its mechanism of action.

2.1 What is UTI?

The human urinary tract system consists of upper urinary tract (kidneys and ureters) and lower urinary tract (bladder and urethra) (Mangera et al., 2013). UTIs are common infections with the bacteria usually infected the urinary tract from the skin or rectum, enter the urethra. The infections can affect several parts of the urinary tract, but the most common type is bladder infection which known as cystitis (CDC, 2021).

Based on European Association of Urology Guidelines on Urological Infection, Classification systems of UTI were different, most frequently used were those developed by the Centers for Disease Control and Prevention (CDC), Infectious Diseases Society of America (IDSA), European Society of Clinical Microbiology and Infectious Diseases (ESCMID), as well as the U.S. Food and Drug Administration (FDA) (EAU guidelines, 2024). UTIs usually have been divided into uncomplicated and complicated UTIs, and urosepsis, which based on clinical symptoms, laboratory data, and microbiological findings. However, most UTIs are uncomplicated (Smelov et al., 2016). For the purposes of this study, the following classification of UTIs was adopted from the EAU Urological Infections Guidelines (Figure 1 and Figure 2, EAU guidelines, 2024), and what researcher explored for this review were mainly focus on uncomplicated UTI.

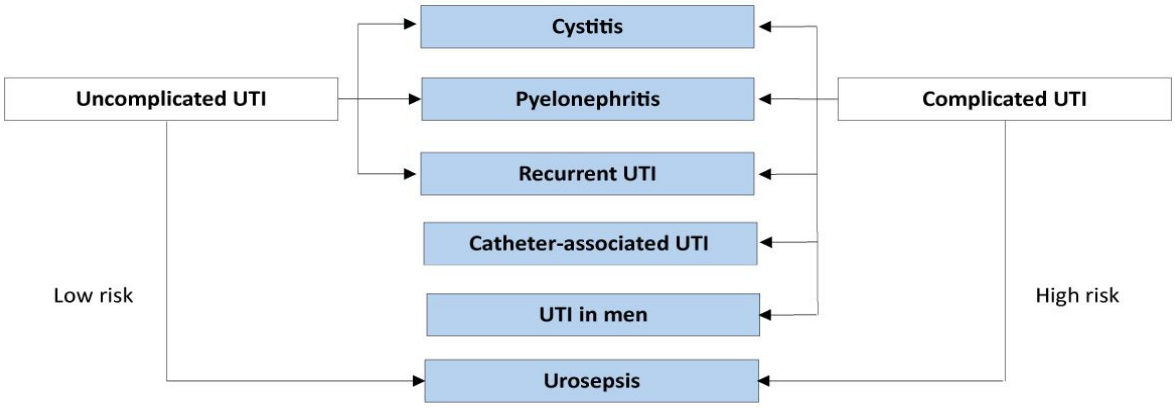


Figure 1: Concept of uncomplicated and complicated UTI (EAU guidelines, 2024): https://uroweb.org/guidelines/urological-infections/chapter/the-guideline

Classification of UTI	
Uncomplicated UTIs	Acute, sporadic or recurrent lower (uncomplicated cystitis) and/or upper (uncomplicated pyelonephritis) UTI, limited to non-pregnant women with no known relevant anatomical and functional abnormalities within the urinary tract or comorbidities.
Complicated UTIs	All UTIs which are not defined as uncomplicated. Meaning in a narrower sense UTIs in a patient with an increased chance of a complicated course: i.e. all men, pregnant women, patients with relevant anatomical or functional abnormalities of the urinary tract, indwelling urinary catheters, renal diseases, and/or with other concomitant immunocompromising diseases for

	example, diabetes.
Recurrent UTIs	Recurrences of uncomplicated and/or complicated UTIs, with a frequency of at least three UTIs/year or two UTIs in the last six months.
Catheter-associated UTIs	Catheter-associated urinary tract infection (CA-UTI) refers to UTIs occurring in a person whose urinary tract is currently catheterised or has had a catheter in place within the past 48 hours.
Urosepsis	Urosepsis is defined as life threatening organ dysfunction caused by a dysregulated host response to infection originating from the urinary tract and/or male genital organs .

Figure 2: Classification of UTI (EAU guidelines, 2024):

https://uroweb.org/guidelines/urological-infections/chapter/the-guideline

2.2 Symptom

Urinary tract infections may have symptoms (symptomatic) or without any symptoms (asymptomatic) which caused by the growth and proliferation of microbes. The typical symptoms of UTIs include frequent urination and strong urge to urinate, burning sensation when urinate, lower abdomen pain even when pass with littel urine, urine blood and the urine more smell than usual (Kaur & Kaur, 2021). Asymptomatic bacteriuria (ABU) is the presence of $>10^5$ bacteria/mL in two consecutive clean-catch urine cultures without signs or symptoms of UTI (Glover & Sheerin, 2023).

In older adults, the symptoms of UTI may be less clear. Older women frequently have nonspecific symptoms that may be identified as a UTI (AUA guidelines, 2022). And it may have different symptoms such as changes in mental status, unexplained lethargy, or disorganized speech, rather than the typical urinary symptoms seen in younger adults (Bono et al., 2023). Other indicators include abnormal urinalysis findings, dysuria, nocturia, incontinence, and a general sense of malaise (Mody & Juthani-Mehta. 2014).

2.3 Risk factors

Females are more prone to get UTI than males because the females' urethra is shorter which is about 2.5-5cm compare with 18-20.5cm for male. This makes it easier for bacteria to enter the urinary tract (Lippincott et al.,2006, p.935).

Other factors that can increase the risk of UTIs included antibiotics use and increasing bacterial resistance (Bono et al., 2023), genetic variants (Isali et al. ,2023), a previous UTI, sexual activity, changes in the bacteria that live inside the vagina, or vaginal flora, pregnancy, structural problems in the urinary tract, poor hygiene (AUA guidelines, 2022).

However, elderly residing in long-term care facilities are more likely to acquire infection because of exposing them to healthcare-associated pathogens. And the risk of developing UTI will be increased with age-associated changes in adaptive and immunity, especially for those elderly with significant functional and cognitive impairments (Rowe& Juthani-Mehta, 2014).

2.4 Diagnoses

Escherichia coli (E. coli) had been reported to be the most common cause of uncomplicated UTIs. *Staphylococcus saprophyticus*, *Gram-positive* bacterium, ranks as the second most common cause of such infections. Additionally, *Klebsiella pneumoniae* and *Proteus mirabilis* are less frequent causes for UTIs. (Güven, et al. 2023).

The typical diagnosis of cystitis requires the presence of acute-onset symptoms combine the identification of a uropathogen in urine, primarily *Escherichia coli* (*E. coli*) (75-95%). The acute-onset symptoms include dysuria and variable presence of urinate frequency, urgency, suprapubic pain and hematuria (AUA guidelines, 2022). According to European Association of Urology Guidelines on Urological Infection, the diagnosis of uncomplicated cystitis can based on a medical history of lower urinary tract symptoms and the absence of vaginal discharge, but it's unnecessary with genitourinary symptoms among elderly women (EAU guidelines, 2024).

UTI is difficult to differentiate from asymptomatic bacterial (ABU) in institutionalized older adults and the prevelance of ABU are more common in frail elderly women. In addition, it is also challenging to assess symptoms of UTI for those with mental impairment or chronic symptoms, with those are unable to identify or describe the presence of symptoms (Biggel et al., 2019).

Urine dipsticks should not be performed in older women as they are unreliable. Guidance states that clinicians should be better send a urine specimen for culture and sensitivity before starting antibiotics. This is because the higher rates of resistance between older women (Nazarko, 2013).

Be attention that if the diagnosis of UTI is mainly based on the urinanalysis or culture without clinical signs or symptoms, it is most commonly not a UTI (Bono, Leslie & Reygaert, 2023). Misdiagnosis is common, with urine culture showed that only 24–66% of women in the UK who received antibiotic treatment had a confirmed UTI. If misdiagnosis increase, there will be more women receive unnecessary antibiotic therapy (Nazarko, 2023).

2.5 Treatment

Clinicians treating symptomatic UTIs in women are advised to use first-line antibiotics based on local antibiograms, including nitrofurantoin, TMP-SMX, or Fosfomycin, first-generation cephalosporins. Pivmecillinam is also considered first-line therapy outside US (Bono et al., 2023). The antibiotic treatment of the UTI should consistently target the bacteria present in the patient's urine which require the selection of the medicine should be consider on the potential infections, microorganisms, and their antimicrobial susceptibility characteristics. (Marsh, Mundy, et al, 2019). According to the 2010 Infectious Diseases Society of America (IDSA) updated guideline, the preferred medications for treating uncomplicated urinary tract infections include nitrofurantoin (100 mg twice daily for five days), TMP-SMX (160/800 mg twice daily for three days), or a single 3 g dose of Fosfomycin. While a study from Jazan Region, Saudi Arabia which assess the effectiveness and resistance rates of both Nitrofurantoin, TMP-SMX and fluoroquinolone (ciprofloxacin) to treat the uncomplicated urinary tract infection

found that Nitrofurantoin was the most effective antimicrobial agent against *E. coli* (sensitivity rate of 91.7%), followed by fluoroquinolone (75%), TMPSMX (70%), and cefaclor (62.5%) (Darraj, 2023).

Antibiotic prophylaxis is a brief course of antibiotics administered before or at the start of an intervention and used to minimize the infectious complications resulting from diagnostic and therapeutic interventions (Bootsma et al., 2008). However, it can be prescribed after discussing risks and benefits with women previously diagnosed with UTIs to reduce the risk of future infections (AUA guideline, 2022).

In some mild cases of UTIs, there are also some alternative treatment to help recovery, such as adequate hydration which can dilutes the urine and speeds up its way through the system, preventing the bacteria enter into the urinary organs. Taking probiotics is another benefit way to help to keep urinary tract away from pathogenic bacteria (Rajanbir & Rajinder, 2021).

Cranberry prophylaxis is an option for women with recurrent UTIs (AUA guideline, 2022). However, cranberry is a fruit widely recommended for the prophylaxis of UTIs in traditional medicine, and now has developed into a new alternative to antibiotics against UTIs and has become a new research subject in this area (Güven, et al. 2023).

2.6 Cranberry products

Cranberry (*Vaccinium macrocarpon Ait*.) is a fruit belonging to the Ericaceae family, native to North America, with mostly found in Canada and Chile. It is rich in vitamins and polyphenols such as flavonoids, anthocyanins, proanthocyanidins, and phenolic acids (Coutinho-Wolino et al., 2024), which have high antioxidant properties and are known to positively affect health (Güven, et al. 2023). Proanthocyanidin (PAC) with type A bindings or metabolites is considered the active ingredient in cranberries, which may help maintain urinary tract health (Howell et al., 2005). Numerous studies have shown the beneficial biological

effects of cranberry against urinary tract infections over the years (Coutinho-Wolino et al., 2024).

Cranberry products include juice, syrup, capsules and tablets (Jepson et al., 2012). In the treatment of urinary tract infections (UTIs), cranberries have been utilized in different doses, ranging from up to 300 ml in juice form to up to 10,000 mg in capsule form. While cranberry products are considered dietary supplements rather than medications, there have been associations reported between prophylactic cranberry products and urinary tract health (Bryce & Bryce, 2023).

2.7 Mechanism of action

The antibacterial properties of cranberries on the urinary system were first documented in 1923 by Blatherwick and Long. This effect was initially attributed to increased urinary acidification. (Temiz & Cavdar, 2018). Cranberries contain proanthocyanidins (PACs), which are stable phenolic compounds with anti-adhesion activity against *Escherichia coli* (Caljouw et al. 2014). PACs inhibit the adherence of p-fimbriated *Escherichia coli* to urothelial cells receptors, acting as antiadhesive agents. It binds tightly to fimbriae adhesins and lipopolysaccharides on the surface of bacterial cells, which leads to a reduction in fimbriae length, this weakens the adhesion between the bacteria and urothelial cells more vulnerable (Tsiakoulias et al., 2024).

3 Aim and Research Question

The aim of this research is to help the nurse to gain better knowledge of the alternative method for the management of urinary tract infection, especially amongst elderly women, and synthesize the evidence for the use of cranberry for urinary tract infection among elderly women. This will help the nurse improve better nursing care and find another alternative treatment which may decrease the antibiotics resistance.

Thus, the research question for this study is:

1: What is the outcome of cranberry use for urinary tract infection among elderly women?

4 Theoretical Framework

The Nola Pender Health Promotion Model Theory is the theoretical framework for this study. This model has been used by nurses to understand healthy behaviors and to develop health promotion actions that bring significant benefits to people's quality of life. And this is based on a holistic nursing perspective, social psychology, and learning theory. The health promotion module below (see Figure 3) identifies cognitive and perceptual factors as major determinants of health - promoting behavior, and it seeks to explain how individual characteristics and experiences, as well as behavior-specific cognition and affect influence the behavioral outcome (Alligood, 2018， p325-328).

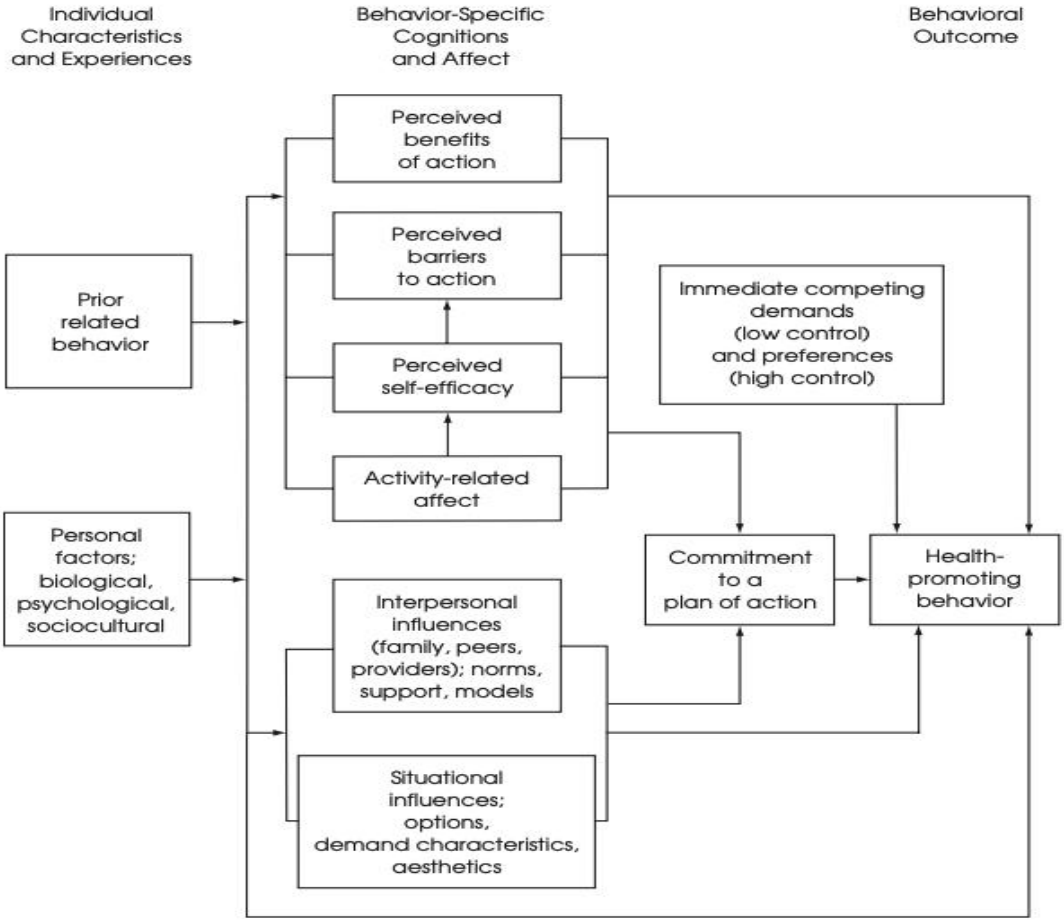


Figure 3: Revised health promotion model retrieved from Alligood, 2018, p328

Health-promoting behavior identified as positive actions which aims to achieve positive health outcomes, such as optimal well-being, personal fulfillment, and a productive life. While, in terms of the outcome of health-promoting behavior, it is directly based on commitment to a plan of action, which is affected by behavior-specific cognitions, However, due to one of Pender's assumption, health professional constitute a part of the interpersonal environment which acts as an important role of the behavior-specific cognitions, it exerts influence on persons throughout their life spans, furthermore, another crucial role belong to behavior-specific cognitions is perceived benefits of action, which is defined as an anticipated positive outcomes that will result from health behavior (Alligood, 2018, p327-329).

5 Research Methodology

The methodology chosen for this research paper is a scoping review synthesize research literature in an inductive approach. The review follows the five stages defined by Arksey and O'Malley : (1) Identifying the research questions, (2) Identifying the relevant studies, (3) Selecting the studies, (4) Charting the data, (5) Collating, summarizing and reporting the results (Arksey & Malley, 2005).

5.1 Scoping review

A scoping review is one of the methods for synthesizing evidence, which aims to provide a comprehensive overview of a potentially extensive and varied body of literature associated with a broad thematic domain. And it is particularly useful to identify research gaps in a specific field. Differ from systematic review which typically characterized by a focus on high-quality published studies, thereby excluding a range of study designs and diverse research methodologies, the use of a scoping review lies in providing crucial insights into the breadth, diversity, and fundamental characteristics of research activities, which can help researchers in developing a detailed methodology tailored to their specific study needs (Department of Anatomy, School of Medical Sciences, Universiti Sains Malaysia, Kelantan, MALAYSIA & Hadie, 2024)

Align with this study, based on several recent consensus and guidelines on UTI management, the effectiveness of cranberry supplementation as an adjuvant therapy has not yet reached a definitive conclusion on preventing and treating UTIs, with the quality of evidence was low (Xia et al. 2021). Thus, it's better to conduct a scoping review in this study.

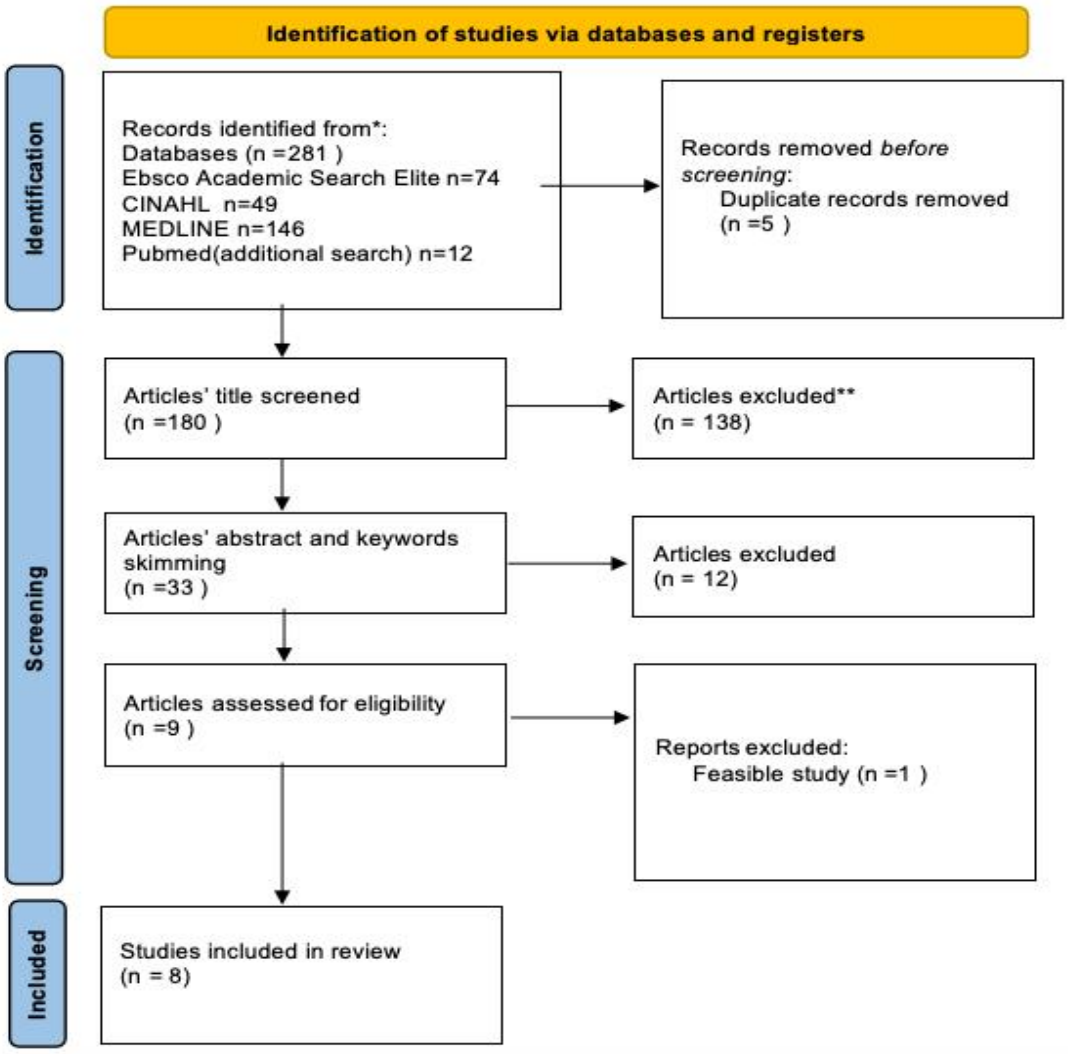
5.2 Data collection

To this research paper, literature search is mainly carried out in EBSCO combine Academic Search Elite, CINAHL Complete, and MEDLINE database. Furthermore, PUBMED is also included. Searching keywords include cranberry or cranberry extract or cranberry supplement AND urinary tract infection or uncomplicated

urinary tract infection or recurrent urinary tract infection. Searching criteria full-text and peer-reviewed are also employed. The inclusion and exclusion criteria of the selection of research data are summarized in the PRISMA chart below. Moreover, the reviewers manually examined the reference lists of the eligible articles to search potentially relevant studies.

The studies were collected if they met the following inclusion criteria: (1) Literature published between 2014 to 2024; (2) Study design was made of randomized controlled trial (RCTs) or clinical trial; (3) The population included participants with urinary tract infection, elderly women or women; (4) For the intervention used, we only include trials which compared cranberry-containing products to a placebo or non-placebo control group; (5) Outcomes were related to the treatment or prevention of UTI. The following exclusion criteria were used: (1) The trials whose intervention contained cranberry in combination with another bioactive compound; (2) Studies conducted in vitro; (3) The participants only included men or children.

Data extracted from the included studies, using a standardized data-charting form for comparison. To make comparisons between study characteristics, studies with similar population were grouped together. Groupings included 2 categories, with one of them conducted only on elderly group, and the other was conducted on adult population. The form included the following information: study and author, design and duration, population, intervention & PAC content, comparison, main outcomes which related to the search aim and the method by which UTI was diagnosed. (see Appendix 1)



PRISMA flowchart showing the search and screening process

5.3 Data analysis

An inductive approach was used to thematically organize and summarize the results from the included studies to answer the research question (Arksey & Malley, 2005). The extracted results from each selected study were read several times to identify similarities, and differences in the outcomes of using cranberry for the urinary tract infection. The identified forming trends were organized in five thematic groupings for the result report, followed by a discussion upon the final groupings of the results.

5.4 Ethical consideration

This study will totally follow the guidelines provided by The Finnish Advisory Board on Research Integrity (TENK): the principles of Reliability, Honesty, Respect and Accountability. It is ensured that the method of data collection, research and evaluation conforms to scientific criteria and is ethically responsible, and devoid of any form of Fabrication, Falsification, plagiarism and Misappropriation; the results will be published in an open and responsible manner. (The Finnish Advisory Board on Research Integrity, TENK, 2023).

6 Result

The outcomes of this research paper were drawn from data synthesis of 8 articles. Details of these articles can be found in Appendix 1. Results have been summarized below which include study characteristics and the outcomes of cranberry used for UTI among elderly women with 5 themes.

6.1 Study characteristics

Seven randomized controlled trials (RCTs) and one observation clinical trial study met the inclusion criteria for data synthesis (see Appendix 1). Briefly, 3 trials (Macías-Núñez et al., 2021; Caljouw et al., 2014; Juthani-Mehta et al., 2016) were conduted in elderly institution, 3 trials (Güven et al., 2023; Maki et al., 2016; Tsiakoulias et al., 2024) were conduted from clinic, while 1 trial (Babar et al., 2021) was from free-living, another 1 trial (Singh et al., 2016) was unclear. 6 trials aim to assess the efficity of cranberry used for the prevention of recurrent urinary tract infection, 1 trial aim to test the effect of cranberry capsules on presence of bacteriuria plus pyuria, 1 trial determined whether cranberry capsules prevent clinical defined UTI. Six trials administered cranberry capsules, whereas 1 trial used tablets and 1 trial used beverage. Five trials used placebo as comparison, whereas 1 trial used antibiotics, 1 trial used low dose cranberry extract, 1 trial used cranberry product up to 1 month compare with up to 12 months. The

definitions of UTI were different, and the clinical symptoms to define UTI were required in most trials.

6.2 Outcomes

The results for the outcomes of cranberry used for UTI among elderly women is summarized in a diagram below (see diagram 1), which include 5 themes.

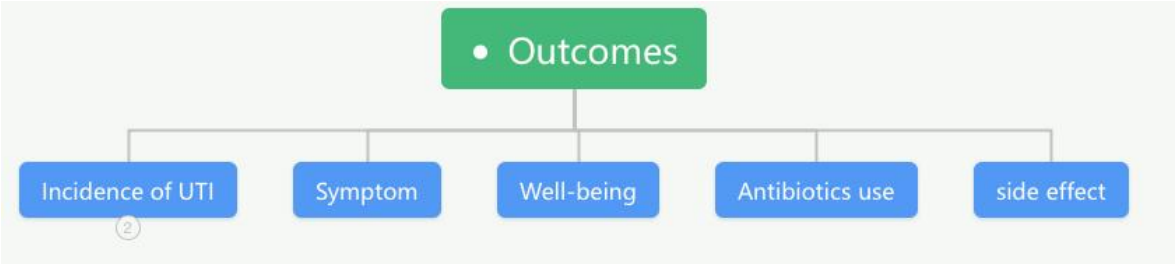


Diagram 1: summary of results

6.2.1 Incidence of urinary tract infection

There were 6 studies that contributed to the analysis (see Table 1 below), with 4 direct comparisons between cranberry capsule and placebo capsule, one direct comparison between cranberry beverage and placebo beverage, one direct comparison between high dose cranberry 2×18.5 mg daily and low dose cranberry 2×1 mg daily. Maki et al. provide evidence that the annualized UTI incidence density was significantly reduced in the cranberry beverage compared with in the placebo arm. The result of another trail conducted by Tsiakoulias et al also showed that the number of UTIs was significantly lower in the cranberry capsule group who took Cysticlean™ 240 mg capsule daily campared with the placebo group without cranberries. Caljouw et al. found that in his high-UTI-risk(risk factors included long-term catheterization, diabetes mellitus, ≥1 UTI in preceding year) group, twice-daily intake of cranberry capsules resulted in a 26% lower incidence of clinically defined UTI (based on the presence of a minimum of one of the following characteristics: specific and nonspecific micturition-related symptoms and signs, a positive test, antibiotic treatment for UTI, or UTI reported in the medical record) than placebo, but no difference was found in UTI incidence of strictly defined UTI (based on a scientific approach, including the presence of

micturition-related symptoms and signs confirmed with a positive dipslide or culture). In a study by Singh et al, the outcome concluded that cranberry capsule group who took 2×60mg daily decreased r-UTI by about 55 % at the end of the 12-week observation period compared with placebo arm. However, Babar et al. found that a non-significant 24% decrease in the number of symptomatic urinary tract infections was observed between high dose cranberry group who take 2×18.5 mg daily compared with low dose cranberry those took 2×1 mg daily arm, but a history of less than 5 UTIs per year, the daily consumption of 2×18.5 mg PACs resulted in a significant reduction in the rate of symptomatic UTI during the trial period compared to 2×1 mg PAC. whereas a trail by Juthani-Mehta et al. reported from result that there were no significant differences in number of symptomatic UTIs between cranberry groups and placebo arm among older women in nursing home.

Author	Treatment group	Comparator group	Population& Follow up	Outcome
Maki et al., 2016	Cranberry beverage 240ml/d	Placebo	Ruti women & 24 weeks	UTI indencity significantly reduced.
Tsiakoulias et al., 2023	Cranberry capsule 1×240mg daily	Placebo	Ruti women & 12 months	Number of UTI siginicantly lower
Caljouw et al., 2014	Cranberry capsule 2× 9 mg daily	Placebo	UTI women(703)& men(225) & 12 months	26% lower incidence of clinically defined UTI among high risk group
Singh et al., 2016	Cranberry capsule 2×60mg daily	Placebo	Ruti patients & 12 weeks	RUTI decreased by about 55 %
Babar et al., 2021	Cranberry capsule 2 × 18.5 mg daily	Cranberry capsule 2 × 1 mg daily	Ruti women & 24 weeks	A non-significant 24% decrease in the number of symptomatic urinary tract infections was observed between groups.
Juthani-Mehta et al., 2016	Cranberry capsule 2× 36mg daily	Placebo	Bacteriuria plus pyuria women & 12 months	No significant differences in number of symptomatic UTIs

Table 1: Incidence of urinary tract infection outcome

6.2.2 Antibiotics use

Three studies contributed to the analysis (see Table 2 below), with one direct comparison between cranberry tablet and antibiotics, one direct comparison between cranberry beverage and placebo, one direct comparison between cranberry capsule take one month and 12 months.

Güven et al. used cranberry extract, which is high in PAC content (36 PAC=514 mg cranberry). When a comparison was made between the leukocyte levels in the urinalysis before and after the treatment, the results were similar compared with the group using Fosfomycin. This suggested that UTIs can be treated without using antibiotics.

Maki et al. in their randomized, double-blind, placebo-controlled, multicenter study in women with a recent UTI history, the daily consumption of a cranberry beverage for 24 weeks, a course of antibiotic therapy for a clinical UTI was prevented for every 3.2 woman-years of the cranberry intervention. The result suggested that the consumption of cranberry is a useful strategy for reducing antibiotic use that is associated with the treatment of these events.

Macías-Núñez et al. conducted an observational clinical trial among 160 elderly ambulatory and nursing home patients suffering from recurrent Cystitis were treated with cranberry extract. Cranberry-based cystitis treatment was successful in a significantly high rate in both 2 groups which included 1 capsule of cranberry extract every 12 hours for one month and 1 capsule of cranberry extract every 12h for up to 12 months. The result showed that cranberry dosed extract (CYS) showed to be an effective alternative therapy to antibiotics to treat and prevent cystitis recurrences caused by *Escherichia coli*.

Author	**Treatment group**	**Comparator group**	**Population& Follow up**	**Outcome**

Güven et al., 2023	Cranberry tablet 36mg× 1/d	Two sachets of fosfomycin every 3 days(TID)	Single UTI women(117) and men(53) & 7 days	The results of leukocyte levels in the urinalysis before and after the treatment were similar between 2 groups
Maki et al., 2016	cranberry beverage 240ml/d	Placebo	Ruti women & 24 weeks	Antibiotic therapy for a clinical UTI was prevented for every 3.2 woman-years of the cranberr intervention.
Macías-Núñez et al., 2021	Cranberry capsule 2× 240mg/d for 12 months	Cranberry capsule 2× 240mg daily up to 1month	Ruti women(99)& men(61) & 1-12 months	Cranberry-based cystitis treatment was successful in a significantly high rate in both groups.

Table 2: Antibiotics use outcome

6.2.3 Symptom

Two studies reported urinary symptoms (see Table 3 below). Of these two studies, Maki et al. reported the incidence density of pyuria, The incidence density for symptomatic UTIs with pyuria was significantly reduced in the cranberry beverage arm compared with in the placebo arm. Whereas another study by Juthani-Mehta et al. found from their trial demonstrated no significant difference in presence of bacteriuria plus pyuria among women who received cranberry capsules vs placebo over 1 year.

Author	**Treatment group**	**Comparator group**	**Population& Follow up**	**Outcome**
Maki et al., 2016	Cranberry beverage 240ml/d	Placebo	Ruti women & 24 weeks	The incidence density for symptomatic UTIs with pyuria was significantly reduced.
Juthani-Mehta et al., 2016	Cranberry capsule 2×36mg daily	Placebo	Bacteriuria plus pruria women & 12 months	No significant difference in presence of bacteriuria plus pyuria among two groups

Table 3: Symptom

6.2.4 Side effects

There were six studies recorded the event of side effects (see Table 4 below), with 2 of them reported no adverse events during the study. Maki et al. reported one subject in the cranberry group had a serious adverse event (chest pain) but was classified as either unrelated or unlikely to be related to the treatment. Babar et al. found no serious adverse events occurred in either of the study groups. The only reported side effect, dyspepsia, led to a discontinuation of the intervention of one participant in each group. Juthani-Mehta et al. recorded the frequency of the 14 protocol-related and anticipated nonserious adverse events (ie, altered mental status, gastrointestinal disturbance, oral cavity disturbance, skin and soft tissue event, weight loss) was similar in both treatment groups. Singh et al. found no major side effects/adverse events/reactions (apart from one patient in each group with self-limiting constipation) in their study.

Author	Treatment group	Comparator group	Population & Follow up	Outcome
Macías-Núñez et al., 2021	Cranberry capsule 2× 240mg/d for 12 month	Cranberry capsule 2× 240mg/d up to 1 month	Ruti women(99)& men(61)& 1-12 months	No side effects reported
Tsiakoulias et al., 2023	Cranberry capsule 1×240mg/d	Placebo	Ruti women & 12 months	No adverse events reported
Maki et al., 2016	cranberry beverage 240ml/d	Placebo	Ruti women & 24 weeks	One serious adverse event (chest pain) in the cranberry group, but it was classified as either unrelated or unlikely to be related to the treatment.
Babar et al., 2021	Cranberry capsule 2 × 18.5 mg/d	Cranberry capsule 2 × 1 mg/d	Ruti women & 24 weeks	No major side effects reported.
Juthani-Mehta et al., 2016	cranberry capsule 2× 36mg/d	Placebo	Bacteriuria plus pruria women & 12 months	Frequency of the 14 protocol-related and anticipated nonserious adverse events (ie, altered mental status, gastrointestinal disturbance, oral cavity disturbance, skin and soft tissue event, weight loss) was similar in both

				treatment groups.
Singh et al., 2016	Cranberry capsule 2×60mg/d	Placebo	Ruti patients & 12 weeks	No adverse events reported

Table 4: Side effects

6.2.5 Well-being

Two study contributed to the analysis (see Table 5 below), with the study by record the rate of well-being of patients during the study, the result showed that the rate of well-being and the portion of patients that reported to be “very well” on days 3 and 7 in the cranberry group was significantly higher compared with the Fosfomycin group. Whilst another study by Tsiakoulias et al. reported that cranberry compare with placebo led to a significant prolongation of UTI-free survival and a significant UTIs reduction, which translated into an improvement in general Quality of Life in women with a history of rUTIs.

Author	**Treatment group**	**Comparator group**	**Population& Follow up**	**Outcome**
Güven et al., 2023	Cranberry tablet 36mg× 1/d	Two sachets of fosfomycin every 3 days(TID)	single UTI women(117) and men(53) & 7 days	Rate of well-being and the portion of patients that reported to be “very well” on days 3 and 7 in the cranberry group was significantly higher
Tsiakoulias et al., 2023	Cranberry capsule 1×240mg/d	Placebo	Ruti women & 12 months	Significant prolongation of UTI-free survival and improvement in general Quality of Life

Table 5: Well-being

7 Disccusion

This chapter discusses the result connection with previous research findings, followed by discusses the research methodology and the limitation for this study.

7.1 Result discussion

This systematic review explore the outcome of cranberry used in women who suffer from UTI based on existed evidence, identified evidence that cranberry results in a lowered rate of UTIs compared with placebo both in beverage and capsule formulation, while no significant different decrease in incidence of UTI between high dose compare with low dose cranberry capsule, however, There were no significant differences in number of symptomatic UTIs between cranberry groups and placebo arm among older women in nursing home. The use of cranberry extract also effected the prevalence of symptoms associated with UTIs, with one study showed reduced the pyuria symptom compare cranberry beverage with placebo, another resulted in no significant difference in presence of bacteriuria plus pyuria among women who received cranberry capsules vs placebo over 1 year. Due to 3 studies, cranberry also benefits the reduction of antibiotic use, and 6 studies did not report evidence of serious side effects directly associated with cranberry consumption. Combined of these, it provides significant clinical outcomes for the use of cranberry for the prevention and treatment of UTIs. However, the evidence of these results must be interpreted with caution as they come from a limited number of studies for the outcomes of interest in this review.

Our study exhibited some similarities with previous studies. A previous meta-analysis by Fu et al. suggested cranberry fruit powder containing 2.8mg of PACs/day for 6months was associated with a reduction in incidence of recurrent UTIs (Fu et al., 2017). A recent systematic review by Moro et al. showed that with moderate to low certainty, the evidence supports the use of cranberry juice for the prevention of UTIs. (Moro et al. 2024). We concluded that supplementing cranberry may be beneficial in preventing and treating UTIs in susceptible populations, particularly for women with recurrent UTIs.

However, even though cranberry products remain an appealing UTI prevention strategy, but evidence is still Contradictory (Wang et al., 2012; Juthani-Mehta et al. 2016). A systematic review by Gbinigie et al. identified that evidence of the effectiveness and safety of cranberry extract as a treatment for symptoms of acute, uncomplicated UTI is inconclusive (Gbinigie et al., 2020). In a Cochrane review in 2012, the authors performed a meta-analysis based on two studies evaluating cranberry used in elderly adults, cranberry did not significantly reduce UTI in this population (Jepson et al, 2012).

Compare with previous review, in current study found a positive effect of treatment and prevention with cranberry on UTI among elderly, this could be multifactorial owing to the heterogeneity of the older population as well as inconsistencies in the recommended dose of PAC in the current literature. Even though not all of the population in these selected studies are elderly, but 3 of the studies were only focus on elderly, with mostly are women (Macías-Núñez et al., 2021; Juthani-Mehta et al., 2016; Caljouw et al., 2014). However, one study by Juthani-Mehta et al. reported among older women residing in nursing homes, administration of cranberry capsules vs placebo resulted in no significant difference in presence of bacteriuria plus pyuria over 1 year. There are two possible explanations for the result, First, there appeared to be an initial effect on bacteriuria plus pyuria in the first 6 months, but these rates returned to baseline in the second 6 months of study due to the slightly lower adherence at the second phase. Secondly, it is possible because of worsening incontinence and changes to the vaginal microbiome with age, the effects of cranberry capsules were not sustained (Juthani-Mehta et al., 2016).

Consider the current literature supporting cranberry use in urinary tract infection is controversial. These could be due to the different populations studied (health background, age), the study settings (free-living, nursing home, clinic), subject compliance, furthermore, the cranberries used in the studies varied in composition, dosage, and formulation (capsule, juice, or tablet). In this regard, the efficacy of various cranberry products (cranberry beverage, cranberry capsule, cranberry tablet with different concentration of PAC) has been included in this review, however, these products have been largely variable in terms of company,

PAC content and administrated dosage, a study by Howell et al., reported that administration of 72mg PAC daily may offer benefit for protection against bacterial adhesion (Howell et al., 2010), while the PAC content used in this research are mostly lower than 72mg daily, making it difficult to assess their true potential bioefficacy.

Besides, half of the selected studies were lasted less than one year, thus, there is insufficient evidence to support the efficacy of cranberry products in clinical use. Future studies should be better performed for a longer period.

Based on the J. penders' health promotion model, it is important that nurses take on and implement the role of health promotion and disease prevention to help and educate patients so they will know what kind of behavior is healthy and effective in preventing urinary tract infection and promoting their own well-being. As nurse know more knowledge about urinary tract infection and use the evidence-based practice for the outcome of the use of cranberry with urinary tract infection, so they can give effective education regarding health-promoting behavior and thus individuals can do to prevent or treat urinary tract infections, also when the number of UTIs and recurrent UTIs decreased, they will really benefit greatly with the health promotion model.

7.2 Methodology discussion

Of the 8 studies included, there are totally 2205 participants included, with 1794 of them are females, and another 72 participants are not specified in gender. Three studies assessed only among elderly with total 1273 participants. Although another four studies not assessed only on elderly, but all of them at least aged 18 and older, which mean all of them are adults. The 8 selected studies are searched from year 2014-2024, with 4 of them are published recent 4 years, which meant it is an evidence-based review.

There are several limitations to our review. The methodology for this research is scoping review, thus, the risk of bias of the evidence was not performed. A meta-analysis was not performed as part of this scoping review. Results for all

extracted outcome measures were presented in a narrative assessment. There was heterogeneity in the outcomes reported by the studies, and in the amount of PAC in the interventions used, also the different definition of UTI, making it difficult to make direct comparisons between studies.

Furthermore, the initial purpose is to explore the cranberry use among elderly women, but since the study only focus on these population is limited, thereby another group included both elderly women and adult women were also concluded.

8 Conclusion

Cranberry has positive outcome used for the UTI prevention and treatment, in terms of the benefit for the reduction of the incidence of UTI number and symptom, and the improvement of well-being, and it can also possible suggested for the prevention of recurrent urinary tract infection and alternative treatment for the uncomplicated UTI instead of antibiotics. However, due to some limits of the included trials in this review, the conclusion therefore should be interpreted with caution.

However, during the search period, the RCT of cranberry use are mostly assessed in the prevention of recurrent urinary tract infection, but few studies have assessed the use of cranberry in treating UTIs, and since now, more focus on uncomplicated UTI, while the evidence on complicated UTI is still limited, further larger size, well-conducted randomized clinical trials are needed. These studies should use standardized interventions with a specified amount of PAC and also standardized definition of UTI, there would also be helpful if the outcomes reported were standardized, to allow direct comparisons to be made between studies. While, since now some benefit of cranberry used in UTI had been identified, but consider the cost and acceptance of this nonantibiotics therapy, more studies on the possibility for the implication for clinical are also needed.

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Appendix 1 : characteristics of selected studies

Study and author	Design and duration	Population	Intervention& PAC content	Comparison	Main outcome	UTI diagnosis
Elderly						
Cranberry dosed extract: an effective therapy for recurrent Escherichia coli cystitis in elderly patients. The GerHogar Cysticlean® study Macías-Núñez et al., 2021	Observational clinical trial 2-arm parallel; 15 months	160 nursing home patients & 61 men, 99 women & aged 71-104 years	Cysticlean® capsule 2×240mg daily for 12 month	Cysticlean® capsule 2×240mg daily up to 1months	Cystitis treatment	Cystitis was defined as a positive urinary-culture, plus 2 or more signs/symptoms such as: dysuria, polakiuria, leucocyturia, pyuria, haematuria,nycturia , urinary urgency (micturition emergency) dysuria and itching
Effectiveness of cranberry capsules to prevent urinary	Double-blind randomized placebo-	928 LTCF residents &	Cranberry capsule	Placebo	The incidence of clinically	Presence of a minimum of one of the following

tract infections in vulnerable older persons. A double-blind randomized placebo-controlled trial in long-term care facilities. Caljouw et al., 2014	controlled multicenter trial 2-arm parallel; 12 months	703 women 225 men & aged 65 and older	2×9 mg daily		defined UTI	characteristics: specific and nonspecific micturition-related symptoms and signs, a positive test (nitrite test, leukocyte esterase test, dipslide, or culture), antibiotic treatment for UTI, or UTI reported in the medical record
Effect of Cranberry Capsules on Bacteriuria Plus Pyuria Among Older Women in Nursing HomesA Randomized Clinical Trial Juthani-Mehta et al., 2016	Double-blind randomized, placebo-controlled trial 2-arm parallel; 12 months	185 nursing home paitients & women & aged 65 years or older	Cranberry capsule 2×36mg daily	Placebo	The presence of bacteriuria plus pyuriaj and symptomatic UTI	Presence of bacteriuria (ie, at least 10^5 colony-forming units [CFUs] per milliliter of 1 or 2 microorganisms in urine culture) plus pyuria (ie, any number of white blood cells on urinalysis)

Adult						
Antibiotic versus cranberry in the treatment of uncomplicated urinary infection: a randomized controlled trial Güven et al., 2023	Prospective, randomized study 2-arm parallel; 7 days	170 outpatient clinic patients & 117 women 53 men & aged 18 years or older	Ocean Cranberry tablet 36mg × 1/d	Two sachets of fosfomycin every 3 days(TID)	The leukocyte level and rate of well-being	Complaints of dysuria, frequent urination, and nausea, having no known chronic kidney disease, and having only elevated leukocyte levels in the urine test results without pathology in blood tests.
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 Maki et al., 2016	Randomized, placebo-controlled, double-blinded ,multicenter clinical trial 2-arm parallel. 24weeks	373 clinic patients & women & 20-70 years	Cranberry beverage 240ml/d	Placebo beverage	The annualized UTI incidence density and the incidence density for symptomatic UTIs with pyuria.	≥2 within a 6month or≥3 within a 12-month period

Randomized, placebo-controlled, double-blinded study of prophylactic cranberries use in women with recurrent uncomplicated cystitis. Tsiakoulias et al., 2024	Randomized, placebo-controlled, double-blinded clinical trial 2-arm parallel; 12 months	172 clinic patients & women & 19–82 years old	Cysticlean™ capsule 1×240mg daily	Placebo	The number of UTIs and quality of life (QoL)	≥2 within a 6-month period or≥3 within a 12-month period
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.	Randomized, placebo-controlled, double-blinded clinical trial 2-arm parallel; 24 week	145 free-living & women & aged 18 years and over	Uropheno™ capsule 2×18.5 mg daily	A control low dose cranberry 2×1 mg daily	The number of symptomatic UTI	≥2 in the past 6 months or≥3 in the past 12 months

Babar et al., 2021						
Effect of oral cranberry extract (standardized proanthocyanidin-A) in patients with recurrent UTI by pathogenic E. coli: a randomized placebo-controlled clinical research study Singh et al., 2016	Double-blind randomized placebo-controlled multicenter trial 2-arm parallel; 12 weeks	72 patients & gender no defined & 15–76 years old	Cranpac™ capsule 2×60mg daily	Placebo—lactobacillus capsule 1	The episodes of UTI	R-UTI (>2 episodes) who had culture-positive UTI and had taken multiple antimicrobial courses in the past 1-year