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NON-ANTIBIOTIC SUBSTANCES IN THE TREATMENT AND PREVENTION OF RECURRENT URINARY TRACT INFECTIONS

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ABSTRACT

Urinary tract infections (UTI) create a serious health problem worldwide, affecting people of all ages. It represents one of the most common reasons for the use of antibiotics in outpatient care, leading to a reduction in their effectiveness through ever-increasing bacterial resistance to them. Thus, there is an urgent need to develop new and effective therapies. The purpose of this paper is to present alternative therapies that can help prevent and treat recurrent UTIs, such as cranberry preparations, D-mannose, robotics and topical estrogen. After analyzing the available studies, it was shown that each of these substances can have a beneficial effect on reducing recurrent UTIs, although their effectiveness varies. Substances with high therapeutic potential appear to be D-mannose and probiotics. Their action is based on supporting the natural human microflora and blocking bacterial adhesion to the epithelium of the urinary tract. A preventive strategy in the context of UTI in postmenopausal women seems to be vaginal estrogen. However, further robustly designed clinical trials need to be conducted to truly confirm that these therapies are effective and safe in terms of long-term efficacy.

KEYWORDS

Recurrent Urinary Tract Infections, rUTI, Non-Antibiotic Prophylaxis, D-Mannose, Cranberry Extract, Probiotics, Vaginal Estrogen, UTI Prevention, Alternative UTI Treatment

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Introduction

Recurrent urinary tract infection is a disease that significantly impairs patients' quality of life [1,2, 9]. Individuals report that the disease negatively affects their self-esteem, limits their ability to effectively work and has an impact on social contacts, as well as intimate relationships [2]. It is common in the bladder, with pyelonephritis occurring in only 1% [5]. For anatomical reasons, UTI is at least 4 times more common in women than in men [3]. The much shorter urethra in women compared to men as well as the close proximity of the perineum and rectum to the periurethral area predisposes women to this condition [3]. The recurrence rate of urinary tract infections is very high. It is estimated that about 25% of women who have had their first UTI will suffer from recurrent UTIs [2].

Recurrent urinary tract infection is defined as the occurrence of at least two episodes of disease within six months or three episodes within a year [1, 6, 7, 16].

The bacterium that is most often responsible for the onset of this disease is Escherichia Coli, but various pathogens like Klebsiella, Enterococcus, Pseudomonas, Staphylococcus, additionally, yeast (most commonly Candida), can also cause UTI [1, 3, 4, 7]. These organisms enter the bladder by an ascending route through urethra, then attack the bladder mucosal wall causing an inflammatory reaction [3]. Some of them possess adhesions with which they attach to the urothelial mucosal surface [3]. Additionally, UPEC (uropathogenic Escherichia Coli) has been shown to colonize the vaginal epithelium and gastrointestinal tract, where it can act as a reservoir of infection [2].

Risk factors and differential diagnosis

There are a number of factors that predispose both men and women to the disease. These include anatomical defects of the urinary tract leading to urinary stasis, stones in the urinary tract, intercourse, menopause, diabetes, mellitus, atrophic vaginitis, spermicide use, bladder urethral reflux, neurogenic bladder, incomplete bladder emptying, pelvic organ prolapsed in women, and the presence of a urinary catheter [1, 3, 6]. A complex interplay between mental health and UTIs has been found, with recent research finding depression to be a significant risk factor for the disease [10]. Additionally, improper hygiene habits in a women

such as frequent bathing instead of showering, wiping the vaginal area from back to front, and not using a gentle liquid soap when washing the intimate area increases the incidence of the disease [1].

A particular condition in which the frequency of detected UTIs is significantly higher is during pregnancy. A number of both anatomical (an enlarging uterus putting pressure on the uterus) and physiological changes (including an increase in the level of progesterone, which has a relaxing effect on smooth muscles) occurring in women during pregnancy adversely affect the bladder leading to urinary stasis and making it easier for bacteria through the ascending route to enter the bladder and further, potentially the kidneys [8]. In men with this type of complaint, the presence of possible prostatic hypertrophy should be checked [2]. In the differential diagnosis with recurrent episodes of infection, we must also consider pelvic inflammatory disease, urethritis and painful bladder syndrome [1].

Symptoms

We can distinguish a number of UTI symptoms that can cause significant emotional stress and discomfort. These primarily include pain during urination, urinary urgency, frequent urination, suprapubic pain, bladder spasm and difficulty initiating micturition [1,3]. In contrast, symptoms such as fever, vomiting, back pain and chills are typical of pyelonephritis, although they can overlap creating difficulties in differentiating UTIs and other serious conditions [3].

UTI treatment methods

There are many complications of untreated or improperly treated urinary tract infections infections including Chronic prostatitis, prostatic abscess, renal abscess, renal failure, persistent lower urinary tract symptoms and Pyelonephritis, which is why proper treatment of this condition is vital [3]. Treatment of recurrent UTI is much more difficult than acute UTI, which can be effectively treated on an outpatient basis [1]. Conversely, even treatment of acute infection with antibiotics does not prevent recurrence [11]. The current treatment regimen is based on the use of antibiotics [4]. Unfortunately, there is a continuous increase in the resistance of uropathogens to commonly used antibiotics, moreover, the antibiotics used prophylactically are no longer fully effective[11]. Due to the annual prescription exceeds the rate of development of new antibiotics, so it is imperative to look for alternative and new options for treating patients, without antibiotics [4,11]

Non-antibiotic methods of UTI treatment and prevention

Patients are advised to increase personal hygiene, take extra precaution after sexual contact such as urinating immediately after intercourse, wiping from front to back after using the toilet, avoiding postponing micturition and defecation [5]. An important element in the prevention of recurrent infection is drinking an adequate amount of fluids. Patients should be advised to increase their fluid intake to at least 2 liters per day, as this has been shown in studies to be effective [1,5].

Uropathogenic bacteria have evolved a number of adaptations such as attachment to urinary tract epithelium, invasion, colonization and intracellular replication [11]. Taking this into account, the researchers offer us potential alternative approaches that we will be able to use in combination therapies, that is, targeting multiple mechanisms of UPEC. Focusing on the anti adhesive effect of bacteria, we can mention cranberry and D-mannose, in immunomodulatory therapy – vaccines and topical prophylaxis with estrogen therapy and probiotics[11].

Cranberry

Cranberry (Vaccinium macrocarpon) is native to North America and is a small, evergreen shrub that bears red berries rich in a variety of bioactive compounds [12]. The most common use of cranberry products is related to the treatment and prevention of urinary tract inflammation due to the presence of proanthocyanidins, a group, od polyphenolic compounds known for their ability to prevent urinary tract infections [12,14]. A-type proanthocyanidins have anti-adhesive properties, interfering with the ability of Escherichia Coli to adhere to epithelial cells lining the urinary tract [1, 12]. Cranberry fruits are also rich in flavonols such as quercetin and myricetin, which have antioxidant properties. By scavenging reactive oxygen species and signaling pathways involved in inflammation, they regulate the inflammatory response, thereby exacerbating bladder inflammation symptoms and potentially aiding recovery[12]. Phenolic acids such as hydroxycinnamic acid and benzoic acid known for their anti-inflammatory and antimicrobial effects [12]. These compounds kill bacteria and inhibit their growth by, among other things, inhibiting the activity of bacterial enzymes [12] It has also been proven, that phenolic metabolites not only affect the urothelial

epithelium, but also the intestinal epithelium by improving their integrity [14]. In addition, cranberry juice is highly acidic, so it acidifies the urine creating an unfavorable environment for bacterial growth [14].

Cranberries come in many forms for consumption, including fresh berries, juices, smoothies and tablets. Unfortunately, the concentration of proanthocyanidins varies depending on the form taken [14].

Side effects of cranberry include gastrointestinal problems such as constipation, heartburn, diarrhea, migraines and vaginal dryness [18].

In summary, the components of cranberry contribute to the treatment of UTIs in various ways. The previously described anti-inflammatory and antioxidant properties act synergistically to complement and potentiate their effects [12,13].

D-mannose

D- mannose is a natural sugar that has protective properties in the context of urinary tract health. It shows promise in the treatment and prevention of urinary tract inflammation, especially in cases of recurrent infections.

It is a monosaccharide synthesized in the body from glucose to synthesize glycoproteins, and its physiological blood concentration ranges from 50 to 100 100 μM [15, 17]. It is sold worldwide as a dietary supplement to support Lower urinary tract health. It occurs naturally In a variety of plants including cranberries, peaches, apples, oranges, coffee beans and fenugreek seed occurring there in trace amounts [17].

D-mannose is available in various forms, such as a powder, capsules and tablets. Approximately 90% of ingested D-mannose is rapidly absorbed in the upper part of the human intestine, but it is not metabolized by the body which means it is not stored in the liver [15,19]. The low renal threshold for this sugar means that its excess is secreted in an untransformed form into the urine about 60 minutes after ingestion, where it realizes its potential to reduce bacterial pathogenicity [17,19].

It is particularly effective against Escherichia Coli bacteria, which is one of the main causes of urinary tract infections. They have many virulence factors such as envelopes, adhesions, toxins or lipopolysaccharides, but the main mechanism that causes UTI is its adherence to mannosylated protein components called uroplakins on the bladder epithelium [17]. UPECs have P-type and type 1 pilus, which are adhesion molecules [18]. Type 1 piluses additionally terminate in a FilmH molecule that binds strongly to the N-mannosylated glycan of the uroplakin protein UP1a located on the apical surface of the transitional epithelium in the bladder [18]. D-mannose has been shown to bind to FilmH molecules, thereby preventing bacteria from adhering to the transitional epithelium. Thus, it is safe to say that D-mannose has, so to speak, a barrier function of the transitional epithelium. Bacteria in the bladder bind free D-mannose thereby being “blocked” and eliminated by the urinary tract [19]. The previously mentioned type 1 pilus is also found in other Enterobacteriaceae bacteria such as K. pneumoniae, so in vitro D-mannose has shown the potential to inhibit adherence of a clinical isolate of K. pneumoniae [17].

This product is relatively expensive, and while a dose of 500mg twice a day is commonly suggested, the optimal dosage is still undetermined [1]. However, it has been shown, based on an animal study, that even at very low concentrations of about 20 μg/ml, D-mannose can effectively block bacterial adherence to the urinary tract [17]. Since D-mannose does not have bactericidal or bacteriostatic activity, it can successfully be used adjunctively with antibiotic therapy without interfering with the antibiotic [19].

D-mannose is relatively safe and well tolerated by the body, but like any supplement, it can cause side effects, which include diarrhea, nausea, headaches, and skin rashes, among others [15,17]. It should also be taken into account that in diabetic patients, taking this supplement can upset the blood glucose balance [17].

The use of D-mannose in clinical practice requires further research, especially in terms of the long-term and efficacy of its use.

Probiotics

The human microbiota is diverse and plays a key role in maintaining health. In healthy individuals, the commensal microbiome present in the gut can protect against the colonization of pathogenic Enterobacterales, which have their reservoir in the gut, by selectively eliminating these bacteria or regulating the host immune response [20]. However, the use of frequent antibiotics therapy leads to its disruption, causing greater susceptibility to UTIs. Studies have shown that the intestinal microbiome in people with UTIs differs from that of healthy individuals, confirming the role of dysbiosis of the intestinal microbiome in the pathogenesis of UTIs [21,24]. Bacteria that are significantly less abundant in sick individuals are Parasuterella, Akkermansia and Bilophila [20].

It was once thought that the urinary tract, particularly the bladder, was sterile, but thanks to the development of next-generation sequencing, which enabled the unbiased detection of resident microbial DNA, it has been proven that it contains a diverse microbiota, the composition and function of which may be crucial to human health [22]. The microbiome in the urinary tract has a larger niche biomass than, for example, the gut microbiome. Additionally, its impact on the pathobiology of urinary tract infections is not fully understood [22]. The types of bacteria that have been successfully identified in the urine of healthy individuals include Lactobacillus, Corynebacterium, Prevotella, Staphylococcus and Streptococcus [22]. It has been suggested that the bacteria that physiologically reside in the urinary tract provide a line of defense against uropathogens [22]. In women, the urinary tract microbiota is composed of the same Lactobacillus species found in the vagina [17]. It has been shown in studies that they produce lactic acid and produce H2O2 causing a decrease in vaginal pH which results in inhibiting the growth of pathogenic bacteria such as E.Coli, and may ultimately reduce the risk of urinary tract colonization by such organism [17,22]. The diversity of species according the age of women has also been demonstrated, with premenopause being dominated by Lactobacillus or Gardnerella, while after menopause the microbiota changes to a more diversified one with a definite predominance of E.coli [17]. Evidence also shows that vaginal lactic acid bacilli provide some level of protection against genitourinary diseases such as bacterial vaginosis, sexually transmitted infections and urinary tract infections[22].

Antibiotic therapy causes depletion of the microbiome also in the vagina resulting in loss of properties of Lactobacillus spp making the vaginal route a potential reservoir for uropathogenic bacteria ascending from the gastrointestinal tract [17]. Clinical studies have shown that the use of probiotics can reduce the risk of recurrent UTIs by, among other things, preventing the formation of uropathogen biofilms, increasing protective microbial colonization, and thereby competing for nutrients [23]. However, most studies have shown that only certain Lactobacillus strains caused a decrease in the frequency of UTIs, these are L. rhamnosus GR-1, L. reuteri B-54, L. reuteri RC-14, L. casei shirota and L.crispatus CTV-05 and these are the ones recommended for use in the prevention of UTIs [23]. Although there are promising results from clinical trials, further well-designed studies are needed to unequivocally determine the efficacy and optimal regimens for probiotic use in the prevention of UTIs.

Topical estrogen therapy

Menopause is a significant risk factor for recurrent urinary tract infections in women. Decreased estrogen levels after menopause lead to changes in the genitourinary tract, including atrophy of the vaginal and bladder mucosa favoring the occurrence of recurrent urinary tract infections in perimenopausal and postmenopausal women [26, 27]. Additionally, it has been proven that Lactobacillus strains often disappear in the absence of estrogen leading to increased vaginal pH [5,25]. Thus, treatment aimed at restoring a vaginal flora similar to that of the premenopausal state and accompanying an acidifying vaginal pH that reduces the replication of uropathogens will be warranted [23].

Vaginal estrogen is recommended for postmenopausal women with recurrent UTI, especially in cases of urogenital atrophy, not only for the prevention of bladder inflammation, but also for reducing the sensation of urinary urgency, relieving vaginal dryness and pruritus, and dyspareunia [27].

We can distinguish between many forms of topical estrogen, such as estradiol in the form of a vaginal tablet, vaginal cream, gel pad or vaginal ring, which differ in terms of systemic absorption [27]. It is low for vaginal tablets and vaginal tablets and vaginal creams with doses of 0,5 mg of estradiol [27]. Additionally, estrogen in such low doses has not been proven to increase the risk of thromboembolic disease, cardiovascular disease, or breast and endometrial cancer [27]. It is well tolerated, with reported side effects including vaginal irritation, burning and itching [28].

Meta-analyses have shown that treatment with topical estrogen is an effective method of preventing recurrent urinary tract infection [5, 23, 28]. For example, a retrospective analysis of 5,600 women with hypoestrogenism who used vaginal estrogen showed a 51,9% reduction in the incidence of rUTIs one year after starting therapy [29].

Conclusions

The text provides an overview of various substances that support the prevention and treatment of recurrent urinary tract infections. Taking them is aimed at reducing the use of antibiotics and reducing the risk of recurrence. Unfortunately, the etiopathogenesis of rUTIs is multifactorial, consisting of impaired immune function recolonization from bacterial reservoirs within the intestines and vagina, and disruption of the integrity of the urothelial epithelium, among other factors. Therefore, given the multiplicity and complexity of these mechanisms, multilevel treatment, targeting not only antibiotic therapy, but also immunomodulatory therapy and support of the body's protective barriers, is very important. If we consider the anti-adhesion mechanism of bacteria, we can mention cranberry and D-mannose, while to stimulate the body's immune activity – estrogen therapy and probiotics. The review analyzes the effectiveness of the mentioned non-antibiotic substances. There is a constant need to develop new therapies and treatment strategies, as there is still a lack of effective non-antibiotic alternatives to help patients.

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REFERENCES

1. Aggarwal N, Leslie SW. Recurrent Urinary Tract Infections. 2025 Jan 20. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. PMID: 32491411.
2. Cornelius SA, Basu U, Zimmern PE, De Nisco NJ. Overcoming challenges in the management of recurrent urinary tract infections. Expert Rev Anti Infect Ther. 2024 Dec;22(12):1157-1169. doi: 10.1080/14787210.2024.2412628. Epub 2024 Oct 10. PMID: 39387179; PMCID: PMC11634670..
3. Bono MJ, Leslie SW. Uncomplicated Urinary Tract Infections. 2025 Feb 21. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. PMID: 29261874.
4. Timm MR, Russell SK, Hultgren SJ. Urinary tract infections: pathogenesis, host susceptibility and emerging therapeutics. Nat Rev Microbiol. 2025 Feb;23(2):72-86. doi: 10.1038/s41579-024-01092-4. Epub 2024 Sep 9. PMID: 39251839.
5. Schmiemann G, Kranz J, Mandraka F, Schubert S, Wagenlehner F, Gágyor I. The Diagnosis, Treatment, and Prevention of Recurrent Urinary Tract Infection. Dtsch Arztebl Int. 2024 May 31;121(11):373-382. doi: 10.3238/arztebl.m2024.0068. PMID: 38686602; PMCID: PMC11539874.
6. Patel D. Intravesical Therapies for Recurrent Urinary Tract Infections: A Systematic Review. Cureus. 2024 Oct 23;16(10):e72175. doi: 10.7759/cureus.72175. PMID: 39507191; PMCID: PMC11540250.
7. Wawrysiuk S, Naber K, Rechberger T, Miotla P. 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 Oct;300(4):821-828. doi: 10.1007/s00404-019-05256-z. Epub 2019 Jul 26. PMID: 31350663; PMCID: PMC6759629.

8. Habak PJ, Carlson K, Griggs, Jr RP. Urinary Tract Infection in Pregnancy. 2024 Apr 20. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. PMID: 30725732.
9. Pat JJ, Steffens MG, Witte LPW, Marcelissen TAT, Blanker MH. Comparison of the diagnostic yield of routine versus indicated flowmetry, ultrasound and cystoscopy in women with recurrent urinary tract infections. Int Urogynecol J. 2022 Aug;33(8):2283-2289. doi: 10.1007/s00192-021-04871-2. Epub 2021 Jun 14. PMID: 34125244; PMCID: PMC9343267.
10. Shi L, Ren J, Jin K, Li J. Depression and risk of infectious diseases: A mendelian randomization study. Transl Psychiatry. 2024 Jun 8;14(1):245. doi: 10.1038/s41398-024-02950-8. PMID: 38851830; PMCID: PMC11162453
11. McLellan LK, Hunstad DA. Urinary Tract Infection: Pathogenesis and Outlook. Trends Mol Med. 2016 Nov;22(11):946-957. doi: 10.1016/j.molmed.2016.09.003. Epub 2016 Sep 28. PMID: 27692880; PMCID: PMC5159206.
12. Jangid H, Shidiki A, Kumar G. Cranberry-derived bioactives for the prevention and treatment of urinary tract infections: antimicrobial mechanisms and global research trends in nutraceutical applications. Front Nutr. 2025 Feb 26;12:1502720. doi: 10.3389/fnut.2025.1502720. PMID: 40078413; PMCID: PMC11896822.
13. González de Llano D, Roldán M, Taladrid D, Relaño de la Guía E, Moreno-Arribas MV, Bartolomé B. Cranberry Polyphenols and Prevention against Urinary Tract Infections: New Findings Related to the Integrity and Functionality of Intestinal and Urinary Barriers. J Agric Food Chem. 2024 May 8;72(18):10328-10338. doi: 10.1021/acs.jafc.3c07169. Epub 2024 Apr 23. PMID: 38651941; PMCID: PMC11082924.
14. Ioannou P, Baliou S. The Molecular Mechanisms and Therapeutic Potential of Cranberry, D-Mannose, and Flavonoids against Infectious Diseases: The Example of Urinary Tract Infections. Antibiotics (Basel). 2024 Jun 26;13(7):593. doi: 10.3390/antibiotics13070593. PMID: 39061275; PMCID: PMC11273536.
15. Kyriakides R, Jones P, Somani BK. Role of D-Mannose in the Prevention of Recurrent Urinary Tract Infections: Evidence from a Systematic Review of the Literature. Eur Urol Focus. 2021 Sep;7(5):1166-1169. doi: 10.1016/j.euf.2020.09.004. Epub 2020 Sep 22. PMID: 32972899.
16. Hayward G, Mort S, Hay AD, Moore M, Thomas NPB, Cook J, Robinson J, Williams N, Maeder N, Edeson R, Franssen M, Grabey J, Glogowska M, Yang Y, Allen J, Butler CC. d-Mannose for Prevention of Recurrent Urinary Tract Infection Among Women: A Randomized Clinical Trial. JAMA Intern Med. 2024 Jun 1;184(6):619-628. doi: 10.1001/jamainternmed.2024.0264. PMID: 38587819; PMCID: PMC11002776.
17. Ala-Jaakkola R, Laitila A, Ouwehand AC, Lehtoranta L. Role of D-mannose in urinary tract infections - a narrative review. Nutr J. 2022 Mar 22;21(1):18. doi: 10.1186/s12937-022-00769-x. PMID: 35313893; PMCID: PMC8939087.
18. 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 Dec 5;11(12):1471. doi: 10.3390/pathogens11121471. PMID: 36558804; PMCID: PMC9788503.
19. Parazzini F, Ricci E, Fedele F, Chiaffarino F, Esposito G, Cipriani S. Systematic review of the effect of D-mannose with or without other drugs in the treatment of symptoms of urinary tract infections/cystitis (Review). Biomed Rep. 2022 Jun 15;17(2):69. doi: 10.3892/br.2022.1552. PMID: 35815191; PMCID: PMC9260159.
20. Choi J, Thänert R, Reske KA, Nickel KB, Olsen MA, Hink T, Thänert A, Wallace MA, Wang B, Cass C, Barlet MH, Struttmann EL, Iqbal ZH, Sax SR, Fraser VJ, Baker AW, Foy KR, Williams B, Xu B, Capocci-Tolomeo P, Lautenbach E, Burnham CD, Dubberke ER, Dantas G, Kwon JH; CDC Prevention Epicenters Program. Gut microbiome correlates of recurrent urinary tract infection: a longitudinal, multi-center study. EClinicalMedicine. 2024 Apr 26;71:102490. doi: 10.1016/j.eclinm.2024.102490. PMID: 38813445; PMCID: PMC11133793.
21. Nelwan EJ, Herdiman A, Kalaij AGI, Lauditta RK, Yusuf SM, Suarthana E. Role of probiotic as adjuvant in treating various infections: a systematic review and meta-analysis. BMC Infect Dis. 2024 May 21;24(1):505. doi: 10.1186/s12879-024-09259-3. PMID: 38773400; PMCID: PMC11106949.
22. Neugent ML, Hulyalkar NV, Nguyen VH, Zimmern PE, De Nisco NJ. Advances in Understanding the Human Urinary Microbiome and Its Potential Role in Urinary Tract Infection. mBio. 2020 Apr 28;11(2):e00218-20. doi: 10.1128/mBio.00218-20. PMID: 32345639; PMCID: PMC7188990..
23. Chen YC, Lee WC, Chuang YC. Emerging Non-Antibiotic Options Targeting Uropathogenic Mechanisms for Recurrent Uncomplicated Urinary Tract Infection. Int J Mol Sci. 2023 Apr 11;24(8):7055. doi: 10.3390/ijms24087055. PMID: 37108218; PMCID: PMC10138837.
24. Young MG, Straub TJ, Worby CJ, Metsky HC, Gnirke A, Bronson RA, van Dijk LR, Desjardins CA, Matranga C, Qu J, Villicana JB, Azimzadeh P, Kau A, Dodson KW, Schreiber HL 4th, Manson AL, Hultgren SJ, Earl AM. Distinct Escherichia coli transcriptional profiles in the guts of recurrent UTI sufferers revealed by pangenome hybrid selection. Nat Commun. 2024 Nov 2;15(1):9466. doi: 10.1038/s41467-024-53829-7. PMID: 39487120; PMCID: PMC11530686.
25. Vaughan MH, Mao J, Karstens LA, Ma L, Amundsen CL, Schmader KE, Siddiqui NY. The Urinary Microbiome in Postmenopausal Women with Recurrent Urinary Tract Infections. J Urol. 2021 Nov;206(5):1222-1231. doi: 10.1097/JU.0000000000001940. Epub 2021 Jun 28. PMID: 34181466; PMCID: PMC8497440.

26. Jung C, Brubaker L. The etiology and management of recurrent urinary tract infections in postmenopausal women. Climacteric. 2019 Jun;22(3):242-249. doi: 10.1080/13697137.2018.1551871. Epub 2019 Jan 9. PMID: 30624087; PMCID: PMC6629580.
27. Davis SR, Pinkerton J, Santoro N, Simoncini T. Menopause-Biology, consequences, supportive care, and therapeutic options. Cell. 2023 Sep 14;186(19):4038-4058. doi: 10.1016/j.cell.2023.08.016. Epub 2023 Sep 6. PMID: 37678251.
28. Anglim B, Phillips C, Shynlova O, Alarab M. The effect of local estrogen therapy on the urinary microbiome composition of postmenopausal women with and without recurrent urinary tract infections. Int Urogynecol J. 2022 Aug;33(8):2107-2117. doi: 10.1007/s00192-021-04832-9. Epub 2021 May 18. PMID: 34003309.
29. Tan-Kim J, Shah NM, Do D, Menefee SA. Efficacy of vaginal estrogen for recurrent urinary tract infection prevention in hypoestrogenic women. Am J Obstet Gynecol. 2023 Aug;229(2):143.e1-143.e9. doi: 10.1016/j.ajog.2023.05.002. Epub 2023 May 11. PMID: 37178856.