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## Herbal remedies for UTI Management: Medicinal plants in action

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### Abstract

Urinary tract infections (UTIs) are a prevalent health concern with significant impacts on individuals and healthcare systems. The increasing problem of antibiotic resistance has necessitated exploration of alternative and complementary approaches for UTI management. Medicinal plants, with their historical use in traditional medicine, have garnered attention as potential sources of natural remedies. Medicinal plants are easily available with minimal or no side effects and effective to combat pathogen resistance with high efficacy. Due to these factors, it has attracted the interest of researchers seeking to investigate herbal remedies for UTI. This research paper provides a comprehensive review of various medicinal plants from different literature sources that can be used for the management and cure of the UTI. It will be helpful to explore the medicinal value of the plants against UTIs and for the new drug discovery from them for the researchers and scientists around the world.

**Keywords:** Urinary tract infections, medicinal plants, uropathogens

### Introduction

Urinary tract infections (UTIs) can occur in the urethra (urethritis), bladder (cystitis), or kidneys (pyelonephritis). After respiratory tract infections, it is the second most common infection. There are 150-250 million people affected by this each year, resulting in significant morbidity and high healthcare costs<sup>[1, 2]</sup>. UTIs can affect men and women of any age, but women are more likely to contract them because of their anatomy. Since the urethra in women is shorter and closer to the anus than in men, they are significantly more vulnerable to uropathogen infections. Moreover, UTI incidence is affected by the health status of an individual. Patients suffering from chronic uncontrolled diabetes mellitus and immunocompromised individuals have considerably higher rates of UTIs as their immune systems are compromised. There are also environmental and lifestyle factors that contribute to the prevalence of UTIs<sup>[3]</sup>.

A 50-60% lifetime incidence occurs in females, 5-20% in males, and 5-8% in children, with a 25% recurrence rate. A UTI may be as simple as an inflammation of the bladder to as severe as uroseptic shock. Most common symptoms of UTI are increased and prolonged urogenital immediacy, painful burning sensations during urination, increased frequency of urination, and cloudy, foul-smelling urine. Typical UTI symptoms include lower back pain, pelvic pain, and back pain, particularly in women<sup>[4]</sup>. In order to determine whether a patient has an UTI, bacteria cultures are analyzed in the urine. The presence of more than 10<sup>3</sup> colony-forming units (CFU)/milliliter (mL) in a free collection of urine is generally considered a sign of symptomatic UTI<sup>[5]</sup>.

The possibility of recurrence of UTI is extremely high. More than 25% of women experience recurring infections caused by the same or a different bacteria. The risk of infection increases in postmenopausal women compared to premenopausal women. Inadequate care or behavioral disorders can lead to reinfection. The postmenopausal stage, poor hygiene, multiple relations, and the lack of immunity can all contribute to UTIs<sup>[6]</sup>.

### Classification of UTI

A urinary tract infection can be classified clinically as complicated (cUTI) or uncomplicated (uUTI). A complicated infection occurs when someone has an underlying condition or abnormality in any part of the genitourinary tract, making it more difficult and challenging to treat than an uncomplicated infection.

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Complicated UTIs are associated with underlying medical conditions, such as kidney infections (pyelonephritis), urinary tract obstructions, or catheter use. Uncomplicated urinary tract infections, on the other hand, are infections occurring in the absence of comorbidities or other anatomical abnormalities of the urinary tract or kidney and affect healthy individuals [7]. It can be divided into lower UTIs (cystitis) and upper UTIs (pyelonephritis) [8]. The incidence of complicated UTIs is substantially lower than that of uncomplicated UTIs [9]. Uncomplicated infections, however, usually respond well to antibiotic treatment with a short course. Children and males with urinary tract infections tend to be categorized as uncomplicated infections because they have a low probability of comorbidities [4].

### Causative agents

Bacteria are the primary causative agents of urinary tract infections (UTIs). Uropathogenic *Escherichia coli* (UPEC) is the most common causative agent for both uUTIs and cUTIs which alone contribute to 80% UTI cases, particularly uUTIs. However, other pathogenic microorganisms can also cause UTIs. Some of these include *Klebsiella pneumoniae*, *Proteus mirabilis*, *Enterococcus faecalis*, and *Staphylococcus* spp. In rare cases, fungi (e.g., *Candida* species) and certain viruses (e.g., adenovirus) can also be responsible for UTIs, especially in individuals with weakened immune systems. It's important to note that the choice of causative agent and the severity of the infection can vary depending on various factors, including the patient's health, immune status, and any underlying conditions [10].

Symptomatic UTIs are commonly treated with antibiotics, but overuse of antibiotics can alter the normal microbiota of the vagina and gastrointestinal tract and lead to the development of multidrug-resistant bacteria [11]. The increased use of antibiotics may weaken the immune system further and contribute to recurring UTIs. The increase in antimicrobial resistance made it necessary to search for alternatives to antibiotics for treating UTIs. Herbal remedies have promise as potential solutions in this regard. In view of this, this review aims to evaluate and investigate the potential therapeutic benefits of various medicinal plants and their natural compounds in treating and preventing UTIs.

### Medicinal plants in traditional medicine

Traditional and complementary medicine systems have used medicinal plants for centuries as a treatment for a variety of ailments, including urinary tract infections [12]. It has become increasingly popular as well as more reliable to use medicinal plants due to their fewer or no side effects, cost effectiveness, easy availability, lack of bacterial resistance, and tolerance for patients with urinary tract infections [12]. WHO reports that 80 percent of the world's population and more than 30 percent of pharmaceutical formulations are dependent on medicinal plants [13]. Despite the lack of research, the exact mechanism of herbal medicines for treating UTI has not been fully understood. However, phytochemical constituents have been reported to act as nutraceuticals, immunomodulators, to boost body oxidant status, to provide antioxidant compounds, to prevent microbes from adhering as well as to inhibit their proliferation or multiplication, and to act microbicidal. It is the presence of a variety of phytochemical constituents in medicinal plants that gives them these diverse properties, including alkaloids, anthraquinones, flavonoids, glycosides, phenols, saponins, steroids, terpenoids, tannins, terpenoids, triterpenoids, phytosterols, hydrocarbons, mono and

sesquiterpenes, phytosterols, and phlobatannins, among other secondary metabolites. For the treatment of UTI, flowers, leaves, bark, fruit, seeds, and even whole plants have been consumed these parts or their extracts can be consumed orally as a single preparation or might be mixed with a variety of other foods or drinks such as water, honey, milk, juices, and black pepper. It is also important to consider the age, gender, and current health status of a patient when prescribing herbal preparations [14]. Medicinal plants along with their common names and families and their main phytochemical constituents that are responsible for their therapeutic effects are described below. Other medicinal plants that have been used for the treatment of UTIs but are not yet adequately studied are listed in Table 1.

### Medicinal plants used for the management of UTIs

#### **Vaccinium macrocarpon**

**Family:** Ericaceae; **Common name:** Cranberry: Cranberries have indeed been used as a traditional remedy for urinary tract diseases for many years, and research has supported the notion that they may be beneficial in preventing and managing urinary tract infections (UTIs) [15]. The antimicrobial and potential therapeutic properties of cranberries are often attributed to various compounds found in them. Here are some of the key components and their potential roles.

**High Water Content:** The high-water content in cranberries can help with urinary tract health by promoting hydration and flushing out bacteria from the urinary system.

**Carbohydrates (Glucose and Fructose):** These sugars provide an energy source, which may be important for the immune system's function in combating infections.

**Phytoconstituents:** Cranberries contain various phytoconstituents, including anthocyanins, flavonoids, terpenoids, catechins, quercetin, myricetin, and phenolics. These compounds have antioxidant properties and may contribute to the overall health benefits of cranberries.

**Organic Acids:** Cranberries are rich in organic acids like citric acid, malic acid, quinic acid etc. These organic acids create an acidic environment in the urine, which can inhibit the growth of certain bacteria and help prevent UTIs. Ursolic acid inhibits *E. coli* biofilm formation, quinic acid is responsible for the excretion of hippuric acid and acidifies the urine and sialic acid has an anti-inflammatory and painkilling effect.

**Ascorbic Acid (Vitamin C):** Vitamin C, found in small amounts in cranberries, is known to have immune-boosting properties and may help with urinary tract health.

**Benzoic Acid:** Benzoic acid, found in cranberries, can contribute to the fruit's natural preservation and antimicrobial properties.

**Glucuronic Acids:** These compounds may have a role in the body's detoxification processes [16-18].

Fructose and A-type proanthocyanidins in cranberries inhibit the adhesion of *E. coli* to uroepithelial cells. Prolonged exposure to cranberry alters the morphology of *E. coli* preventing its adherence. This prevents bacterial colonization and reduces the risk of infection [19, 20]. A noteworthy result emerged from a clinical trial in which the administration of cranberry extract (at a dose of 500 mg/kg) over a six-month period reduced urinary tract infections (UTIs) to a similar level as trimethoprim (administered at 100 mg) [21]. Various cranberry varieties, including *V. Oxycoccus* (small/bog cranberry) and *V. Erythrocarpum* (southern mountain cranberry), have also been utilized for UTI treatment. These berries contain a multitude of biologically active compounds

believed to be responsible for their anti-uropathogenic properties [22].

### **Arctostaphylos uva-ursi (L.) Spreng**

**Family: Ericaceae, Common name: bearberry or upland cranberry:** Bearberry is rich in various chemical constituents, including glycosides like arbutin, methyl arbutin, and ericolin, as well as allantoin, flavonoids such as quercetin and myricacitrin, tannins, hydroquinone, ellagic acid, gallic acid, malic acid, and ursolic acid. In Germany, bearberry has received approval for the treatment of bladder infections and has demonstrated its effectiveness against *Escherichia coli* (*E. coli*) infections within the bladder [23]. This effectiveness is attributed to its antibacterial properties, especially against *E. coli*, its astringent attributes due to the presence of arbutin, and its diuretic qualities. Commercial products like Uvacin and Uva-E utilize extracts from bearberry leaves and have been reported to be successful in preventing recurrent urinary tract infections (rUTIs) [24].

A significant double-blind study involving 57 women assessed the herb's ability to prevent UTIs. Half of the participants were administered uva-ursi, while the other half received a placebo over the course of a year. The study's findings revealed that, at the end of the year, none of the women in the uva-ursi group had developed bladder infections, whereas five women in the placebo group had experienced such infections. These results underscore bearberry's potential as a natural remedy for UTIs, particularly in the context of preventing recurrent infections [25].

### **Cinnamom verum J Presl**

**Family: Lauraceae, Common name: Cinnamon:** It exhibits both antioxidant and antibacterial activities. It contains several bioactive phytochemical compounds, including trans-cinnamaldehyde, eugenol, trans-cinnamyl acetate, and proanthocyanidins, which have been employed in the treatment of UTIs. In particular, the ability of this to combat chronic recurrent UTIs is significant, especially in patients with urinary catheters. The long-term use of urinary catheters can lead to biofilm formation, particularly by multi-drug resistant *E. coli* strains, which can complicate treatment. Biofilms are structured communities of bacteria encased in a protective matrix, making them more resistant to antibiotics and the immune system. Amalaradjou *et al.* [26] demonstrated that trans-cinnamaldehyde (0%, 1%, 1.25%, or 1.5%) as an essential oil was effective in inhibiting biofilm formation by *E. coli* on urinary catheters. This inhibition occurred through the downregulation of major virulence genes associated with the bacterium's attachment and invasion of host tissues.

### **Juniperus communis**

**Family: Cupressaceae, Common name: Juniper:** It was reported that terpenoids in the leaf of the herbs are responsible for the antibacterial and diuretic activities of the herbs [27]. Juniper oil, as reported by Schilcher in 1995, has been found to be effective against urinary tract infections [28]. Both the leaves and berries of juniper plants exhibit antimicrobial activities against urinary tract infections. The primary antibacterial component in this herb is terpinen-4-ol, a volatile oil that plays a crucial role in the treatment of UTIs [29]. This plant also contains other active agents such as oxygenated sesquiterpene, monoterpene hydrocarbons,  $\beta$ -pinene, sabinene, limonene and myrcene [30].

### **Armoracia rusticana**

**Family: Brassicaceae, Common name: horseradish:** *A. rusticana* (synonyms: *Cochlearia armoracia*, *Radicula armoracia*) has shown promise in preventing recurrent urinary tract infections (UTIs) in pediatric patients [31]. The antibacterial properties of horseradish are attributed to its isothiocyanates, bioactive compounds found in the plant. Isothiocyanates are sulfur-containing compounds known for their antimicrobial properties. Specifically, in the context of UTIs, these compounds have been demonstrated to interfere with the pathogenic process by which uropathogenic *Escherichia coli* (*E. coli*) penetrates human cells, thereby helping to block the infection [32].

### **Agathosma betulina**

**Family: Rutaceae, Common names: Buchu, Boegoe, Bucco, Bookoo:** *Agathosma betulina*, is among the ancient herbal remedies used for treating uncomplicated urinary tract infections (UTIs) [33]. The leaves of this herb are rich in various compounds, including flavonoids (mainly diosmin), phenolic compounds, mucilage, resins, and essential oils such as limonene, isomenthone, diosphenol (also known as buchu camphor), and terpinen-4-ol [34]. Buchu leaf is recognized for its diuretic and urinary tract antiseptic properties, with the latter attributed to its essential oil content, particularly limonene and diosphenol. Research has demonstrated that the ethanolic leaf extract of *A. betulina* exhibits antibacterial activities against several bacteria, including *E. coli*, *K. pneumoniae*, *P. mirabilis*, *P. aeruginosa*, *S. aureus*, *Staphylococcus saprophyticus*, and *E. faecalis* [35].

### **Hydrastis canadensis**

**Family: Ranunculaceae, Common names - Goldenseal, yellow paint root, orange root, ground raspberry, eye root:** Goldenseal's rhizome, rootlets, and root hairs contain bioactive alkaloids and isoquinoline alkaloids. Berberine, an alkaloid, is the primary therapeutic compound in goldenseal when used to address urinary tract infections (UTIs). Berberine is particularly noteworthy for its ability to combat UTIs by disrupting the adhesion of *E. coli* to the bladder's epithelial cells [36]. Goldenseal can also be found in tincture or powdered forms. We can utilize either of these formats to prepare a tea, suitable for oral consumption or for storage and application as a topical antiseptic [23].

### **Equisetum arvense**

**Family: Equisetaceae Common names: Field Horsetail or Common Horsetail, or Bottle brush:** *Equisetum arvense* is one of the most ancient and renowned herbal remedies. It possesses diuretic and antibacterial properties. The plant contains a variety of active compounds, including minerals such as silicic acids, silicates, potassium, sulphur, manganese, and magnesium. It also features flavonoids like quercetin glycosides, phenolic acids, alkaloids (specifically equisetin), phytosterols (including cholesterol, isofucosterol, and campesterol), and tannins. Notably, the plant's antibacterial effects are primarily attributed to its phenolic compounds, particularly flavonoids [37, 38]. It has been demonstrated that the ethanol extract of this herb exhibits antibacterial properties against urinary tract pathogens, including *E. coli*, *K. pneumoniae*, *P. mirabilis*, *P. aeruginosa*, *S. aureus*, *S. saprophyticus*, and *E. faecalis* [37].

**Vaccinium myrtillus**

**Family: Ericaceae, Common name: Bilberry:** Bilberries have a long history of traditional use for the treatment and prevention of urinary tract infections (UTIs). Bilberry extracts contain anthocyanins and proanthocyanidins, similar to cranberry extracts. These compounds exhibit comparable anti-adhesive properties against uropathogenic bacteria, significantly reducing their ability to adhere to the bladder walls. While the exact mechanism of action for bilberries in UTI prevention and treatment remains uncertain, it was previously suggested that the presence of quinic acid in the berries led to the increased excretion of hippuric acid in the urine. This acidification of the urine was believed to contribute to the antibacterial effect [23, 39].

**Aronia melanocarpa (Michx.) Elliott**

**Family: Rosaceae, Common name: Black Chokeberry:** The fruit of *A. melanocarpa* is renowned for its high concentration of bioactive compounds, including vitamin C and polyphenolic compounds, notably anthocyanins, which exhibit potent antioxidant and antimicrobial properties. Extensive research in the past 15 years has delved into the

potential health benefits of these compounds [40]. Notably, black chokeberries contain four times the proanthocyanidin concentration found in cranberries and are rich in quinic acid. Both of these compounds play a role in combating and preventing urinary tract infections (UTIs) [41].

However, there is a lack of robust clinical data regarding the effectiveness of black chokeberry in UTI treatment. Only one clinical trial has been identified, which reported a reduction in UTI frequency after three months of administering black chokeberry juice to a specific population residing in nursing homes [42]. Black chokeberries contain specific bioactive substances such as polyphenols, anthocyanidins, epicatechin, and quinic acid, which have garnered interest for their potential to inhibit biofilm formation and provide antioxidant benefits. This anti-biofilm property is particularly relevant in the context of UTIs, as it may help prevent the attachment and growth of bacteria in the urinary tract. The bioactive substances present in black chokeberries may play a role in addressing recurrent UTIs (rUTIs). Additionally, *A. melanocarpa* fruits appear to offer superior health and wellness benefits, boasting higher antioxidant levels and fewer side effects when compared to cranberries.

**Table 1:** A list of medicinal plants used for UTI management and their active phytochemical constituents.

S. No.	Plant species	Family	Common Name	Phytochemicals	Mode of action
1	<i>Trachyspermum copticum</i>	Apiaceae	Ajwain	Terpinene, p-cymene, beta pinene, thymol, xylene, palmitic acid and oleic acid	Antibacterial
2	<i>Hybanthus enneaspermus</i>	Violaceae	Spade flower	Flavonoids, phenolic, terpenes, alkaloids, phenols, saponins, anthraquinones, glycosides and tannins	Antibacterial
3	<i>Phyllanthus amarus</i>	Phyllanthaceae	Jangli Amla	Tannins, flavonoids, triterpenoids, lignins, gallic acid, geraniin, corilagin, niranthin and phyllanthin.	Antibacterial and diuretic
4	<i>Moringa oleifera</i>	Moringaceae	Sohanjna	Thiocarbamate glycoside, acetylated carbamate, amino acids, tocopherol, moringine, spirochin and kaempferol	Antibacterial and anti-inflammatory
5	<i>Terminalia chebula</i>	Combretaceae	Hareer, har	Chebulin, tannic acid, gallic acid, beta sitosterol, fatty acids and betulonic acid.	Antibacterial
6	<i>Allium sativum</i>	Amaryllidaceae	Lehsan	Volatile oil, alliin, acrolein, phytycidin, diallyl-disulphide and diallyl-trisulfide	Antibacterial
7	<i>Ocimum sanctum</i>	Lamiaceae	Tulsi	Flavonoids, polyphenol, flavonols, flavones, carnosic acid, beta sitosterol, luteolin, myrtenal, apigenin, rosmarinic acid, eugenol, vicenin and orintin	Antibacterial and anti-inflammatory
8	<i>Zingiber officinale</i>	Zingiberaceae	Adrak, Sondh	Zingiberene, zingiberol, $\alpha$ -zingiberene, shogaols, gingerols and dihydroparadol.	Antibacterial and anti-inflammatory
9	<i>Boerhavia diffusa</i>	Nyctaginaceae	Bishkrapra	Arachidic acid, behenic acid, saturated fatty acids, vitamins C, lignin, phenolics, steroids, glycosides and boeravinone B	Antibacterial
10	<i>Apium graveolens</i>	Apiaceae	Celery seed	Succinic acid, beta sitosterol, falcariindiol, oplopandiol, lunularic acid, lunularin, 5,8-dimethoxy psoralen, trans-cinnamic acid, isofraxidin, trans-ferulic acid and eugenic acid	Diuretic
11	<i>Arctium lappa</i>	Asteraceae	Burdock	Arctigenin, arctiin, lignins, flavonoids, caffeoylquinic acid, cynarin, chlorogenic acid, caffeic acid, quercetin, quercitrin, luteolin and rhamnoside	Antibacterial and diuretic
12	<i>Urtica dioica</i>	Urticaceae	Nettle	Lignans Poly saccharides and lectins	Antibacterial and diuretic
13	<i>Plantago major L.</i>	Plantaginaceae	Plantain	Mucilage, organic acids, polysaccharides, and flavonoids	Diuretic
14	<i>Mentha piperita</i>	Lamiaceae	Peppermint	Menthone, menthol, limone, menthofuran and pulegone	Antibacterial
15	<i>Taraxacum officinale</i>	Asteraceae	Dandelion	Nitriles, norisoprenoids, methyl branched aliphatic acids, phenylacetic acid and dehydrovomifoliol	Antibacterial and diuretic
16	<i>Coleus aromaticus</i>	Lamiaceae	Pattharchur, Karpuravalli	Carvacrol, thymol, chlorogenic acid, rosmarinic acid, 1-octen-3-ol, terpine-4-ol, eugenol, trans-caryophyllene, caryophyllene oxide, and $\alpha$ -cadinol	Antibacterial
17	<i>Crataeva nurvala</i>	Capparidaceae	Varuna	Lupeol, lupeol acetate, $\alpha$ -spinasterol acetate, $\Psi$ -taraxasterol, 3-epi-lupeol, and $\beta$ -sitosterol	Antiinflammatory
18	<i>Hemidesmus indicus</i>	Asclepiadaceae	Indian Sarsaparilla	Hemidesmol, resins, glucoside, tannin, lupeol, $\alpha$ and $\beta$ -amyryns, $\beta$ sitosterol, hexa triconate acid, octacosonate	Antibacterial and diuretic
19	<i>Solanum xanthocarpum</i>	Solanaceae	Kantakari	Coumarin, $\beta$ -sitosterol, solasodine.	Antibacterial
20	<i>Tribulus terrestris</i>	Zygophyllaceae	Kharkhasak, Gokhru	Gitogenin, chlorogenin, tribuloside, kaempferol, rhamnose, saponins, stigmasterol, $\beta$ -sitosterol, neo-tigogenin, hecogenin, tribulosin, neo hecogenin glucoside and cinnamic amide	Antibacterial and diuretic



## Formulations

Ayurveda has formulated numerous herbal remedies to address urinary tract infections (UTIs) while ensuring their availability, ease of administration, palatability, and efficacy. Several Ayurvedic formulations for UTI treatment encompass Mutrakruhantak Ras, Trinetrakhya Ras, Varunadilauh, Eladi Churna, Tarkeshwar Ras, Trunpanchmula, Gokshurkath, Haritakyadiyog, Duralabhadikashaya, Varundya Lauh, and Chandrakala Ras<sup>[43]</sup>.

## Conclusion

In conclusion, the utilization of medicinal plants in the management of urinary tract infections (UTIs) presents a promising avenue for the development of effective and sustainable treatments. Throughout this paper, we have explored the diverse medicinal plants that have been used for centuries in various cultures to alleviate UTIs.

Medicinal plants such as cranberry, uva-ursi, and bearberry have shown their potential in preventing and managing UTIs. Their bioactive compounds, particularly proanthocyanidins in cranberries, exhibit the ability to inhibit the adhesion of uropathogenic bacteria to the urinary tract walls. This mechanism reduces the risk of infection and may provide a non-antibiotic alternative for UTI prophylaxis.

Furthermore, traditional knowledge and modern scientific research have converged to validate the efficacy of medicinal plants in UTI management. Their natural origin, coupled with reduced antibiotic resistance concerns and fewer side effects, make them an attractive option for individuals seeking alternative treatments. Combining these treatments with conventional medical approaches, where necessary, may offer the most comprehensive solution for UTI sufferers. In the context of a global rise in antibiotic resistance and the need for sustainable healthcare practices, medicinal plants present a compelling option for UTI management.

## Future prospects

As we continue to explore the potential of nature's pharmacy, it is clear that medicinal plants have a pivotal role to play in our ongoing battle against urinary tract infections. Future research and clinical studies will further refine our understanding of their applications, making them a vital component of holistic healthcare for UTIs and beyond. Additionally, further studies at molecular levels and tools to identify the mechanism of actions of phytoconstituents may be significantly helpful for novel drug designing for treatment of UTIs.

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