

## Natural Approach Used for urinary tract infections

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### Abstract:

Fifteen plants have been searched and mentioned in the article used for urinary tract infections (UTIs). These plants had been clinically proven with proposed mechanisms and traditionally they are in practice for the treatment of UTIs. The data was collected for google scholar with updated references. Among these plants, some are available commercially especially cranberry extracts for purpose as mentioned. These plants like *Vaccinium macrocarpon* [Cranberry], *Echinacea purpurea* [Cone flower], *Arctostaphylos uva-ursi* [Bearberry], *Hydrastis Canadensis* [Goldenseal], *Agathosmabetulina* [Buchu], *Equisetum arvense* [Horse tail], *Berberine*, *Vaccinium myrtillus* [Bilberry; Blueberry], *Trans-cinnamaldehyde*, *Zea mays* [maize], *P. granatum* [pomegranate], *Juniperus communis* [juniper], *Urtica dioica* [nettle], *Armoracia rusticana* (horseradish), *Solidago Canadensis* [Goldenrod] are effective like antibiotics and prevent or treat UTIs.

**Key words:** Urinary tract infection, Medicinal plants, Traditional uses

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## **1. Introduction:**

### **1.1. Epidemiology:**

Urinary tract infections (UTIs) are amongst the most well-known human infections around the globe. It is estimated that about 800 million people (equating to ~11% of the world's population) had developed at least one type of UTI at any stage of life [1, 2]. Such infections are quite rare in males except if associated with anatomic and functional abnormalities in the early years of life [3]. Infections are infrequent in females of age two to thirteen, but some young females experience repeated episodes of recurrent cystitis and pyelonephritis [3]. The incidence of Urinary tract infections noticeably increases among young females during adolescence, it is estimated that 7 million acute uncomplicated urinary tract infections occur every year in the US, on the ground of data collected from physicians [4].

### **1.2. Common definitions:**

Lower (limited to the bladder) and higher (pyelonephritis) urinary tract infections (UTIs) are separated into simple and difficult categories. In a simple situation a normal host with no structural or functional problem, who is not pregnant, or who has not been instrumented (for example, with a catheter), is considered to have a urinary tract infection (UTI). Complex urinary tract infections (UTIs) are all other UTIs. Uncomplicated urinary tract infections (UTIs) and catheter-associated UTIs are the main topics of this review. Urinary symptoms and urine cultures showing levels of a known uropathogen over a specific threshold (often defined as  $>1,000$  cfu/ml of urine) are used to diagnose urinary tract infections (UTIs) [5]. However, there are additional criteria that are employed that are 100 cfu/ml low and 100,000 cfu/ml high[6]. However, bacteriuria and urine symptoms frequently happen independently of one another: 20% of women who present with the 'classic' UTI symptoms have a negative urine culture [7]. Large amount of germs are frequently discovered in the urine of apparently healthy, asymptomatic people [8]. With increasing age and subsequent sexual activity, the incidence of asymptomatic bacteriuria rises. Except in women who are pregnant or having invasive genitourinary operations, asymptomatic bacteriuria should not be treated, despite the fact that it raises the risk of symptomatic urinary tract infections (UTIs) [9],

urinary tract infections (UTIs), which frequently follow in these individuals, are symptomatic. Additionally, treating asymptomatic bacteriuria may be harmful if it negatively affects a person's microbiome [10] and choosing for bacteria that are resistant to antibiotics (explained below). Urinary symptoms, especially increased frequency and urgency, are also rather prevalent and frequently develop without an infection [11]. In the absence of illness, asymptomatic microhematuria has been seen among apparently in healthy men and women, with no known cause or long-term effects [12–14].

### 1.3. Pathological causes of UTIS:

The main cause of UTIs (about 80%) is *E.coli*. However other bacteria causing an infection that are less frequent includes, *Klebsiella pneumoniae*, *Enterobacter*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Chlamydia trachomatis*, *Mycoplasma hominis*, *Serratia marcescens* and *Neisseria mucosa*. In addition to these many fungi (*Candida* and *Cryptococcus spp*) and parasites (*Trichomonas*, *Schistosoma*) also cause UTIs. Bladder infections can be caused by *Schistosoma haematobium*. [15-16]

### 1.4. Cause of using natural herbal remedies:

Due to resistance developed against many antibiotics apathetic system for the treatment of UTIs is now less frequently used. Many natural products are now the sight of interest in the treatment of UTIs. Herbs are generally a safe way to strengthen and tone the body's systems. Herbal remedies relieve UTIs by fighting the bacteria, decreasing the inflammation and accelerating healing. Some herbs also prevent recurrent infections. Commonly accepted and most used herbs like *Vaccinium macrocarpon* [Cranberry], *Hydrastis Canadensis* [Goldenseal], *Agathosma betulina* [Buchu], *Arctostaphylos uva-ursi* [Bearberry], *Echinaceae purpurea* [Cone flower] and *Equisetum arvense* [Horse tail] have been tested and proven clinically for the cure of UTIs and bladder infections [17]. Many patients with Spinal Cord Injury use herbal alternatives to antibiotics for the cure and prevention of UTIs. In 1991 a telephonic survey of the general population was conducted on national level and it was found that about 34% American population used any one herbal therapy for cure and prevention of medical conditions [18]. After 6 years, the usage of alternative therapies has markedly increased to about 42% [19]. The same finding were noted in disabled people survey

[20, 21]. Among different herbal remedies, three of the non-antibiotic therapies were cranberry, uva ursi, and echinacea [22, 23].

## 2. Non-Antibiotic or herbal remedies used for UTIs:

Early or ancient treatments for UTIs were based totally on natural herbs recorded in the Ebers papyrus [24]. 19th century gave a detailed view of UTIs with treatment that involves hospitalization, alteration of diet, bed rest, narcotics, enemas, douches, and surgery for kidney stones, abscesses, and about retention [25]. However, with time and modernization use of antibiotics and allopathic medicine came into great practice, which led to resistance developed against many antibiotics [26]. This raised interest in the use of alternative, herbal, non-antibiotic approaches for treatment preventing and controlling UTIs. Below is the are key medicinal plants used for the treatment of UTIs and other diseases.

### a. *Vaccinium macrocarpon* [Cranberry]:

**[Family:** Ericaceae]

**Part used:** Berries

**Chemical constituents:**

Flavan, arbutin, anthocyanins, benzoic acid.

Cranberries have a chemical constituent, arbutin that is reported to be having both antibiotic and diuretic-like properties. It is reported to produce hippuric acid in human urine which makes urine acidic, and inhibits its growth [27]. Still, it failed to decrease bacteriuria in a small number of fifteen kids having neurogenic bladders [28]. No antibacterial properties have been explained. It was believed to acidify urine but later on, this hypothesis was rejected [29]. Anti-adhesive properties of cranberry on certain uropathogens have been reported [30]. In a double-blind study, it was observed that those women who consume 300ml of cranberry juice have decreased the number of bacteria in their urine as compared to others [31]. Water and carbohydrates are more than 80 percent and 10 percent respectively in cranberry [32]. Terpenoids, citric acid, anthocyanins, ascorbic acid and little amount of benzoates and glucuronic acid are also present [33].

**Other uses:** Diabetes type II, Diarrhea, gout, gum disease, peptic ulcer [33].

**b. *Echinacea purpurea* [Cone flower]****[Family: Asteraceae]****Part used:** Root

*Echinacea purpurea* is also called as purple coneflower, which is an "immune booster". It is reported to increase the number of T cell and decrease any bacterial and viral infection [34].

**Chemical constituents:**

Echinacea have linoleic acid, mucopolycaccharides, copper, echinacoside, small quantity of iron isobutylmines, vitamin A, palmetic acids, same potassium essential oils, tocopherols, glycosides, ascorbic acid, inulin, phenolic, sulphur, sesquiterene [35].

**Other uses:** Flu, pain, inflammation and migraines [35].

**c. *Arctostaphylos uva-ursi* [Bearberry]****[Family: Ericaceae]****Part used:** Root and leaves

*Uva ursi* the **arcos** is used for bears so they are known as "bearberry" to honor the bears that found its bright pink and red color attractive. They are recommended frequently for the treatment of urinary tract infections [36-38].

**Chemical constituents:**

Arbutin is the primary compound, which is a hydroquinone derivative. It gets absorbed in stomach and alters to a substance having disinfectant, antimicrobial as well as astringent properties. Arbutin helps to heal infection, soothes irritation, and decreases inflammation in UTs [39].

Arbutin makes urine alkaline [40]. Taking *uva ursi* extract elevates *E.coli* cell surface lipophilicity making it difficult to stick to the cells. *Uva ursi* is reported to be a diuretic as well as effective against inflammations and both properties are quite helpful in UTIs [40].

**Other uses:** Astringent, diuretic and antiseptic [40].

**d. *Hydrastis Canadensis* [Golden seal, orange root, ground\_raspberry, eye root.]:**

**[Family:** Ranunculaceae]

**Part used:** Root extract

In urinary tract infections, berberine is believed to be the principal component as it prevents adhesion of *E.coli* to uroepithelial cells [42]. Goldenseal possesses a good antimicrobial, but its anti-inflammatory property is very less.

**Chemical constituents:**

Its main constituents are hydrastine, tetrahydro berberine like canadine as well as berberine. Roots contain flavonoids, saturated as well as unsaturated fatty acids but in greater percentages, chlorogenic acid, resins, volatile oils, meconin, and some amount of sugar [43,44].

**Other uses:** Cardiac diseases and cancer.

**e. *Agathosmabetulina* [Buchu]:**

**[Family:** Rutaceae]

**Part used:** leaves

Buchu has been used in urinary tract infections, catarrhal cystitis, and urethritis for a very long time [45]. In addition, buchu has mild diuretic properties antimicrobial as well [46].

**Chemical constituents:**

Buchu contains volatile oils (between 1% and 3.5%) (limonene , menthone, pulegone), flavonoids (rutin, diosmetin, diosmin, hesperidin, quercetin, and derivatives), B vitamins, tannins, resin, and mucilage. [1-3].

**Clinical Applications of Buchu:** Buchu has proven to be most useful for treating urinary tract infections. It is used in conditions like urinary discharges and unusually too much acidic urine,

and prostate-related incontinence. Buchu leaf is a diuretic and urinary tract antiseptic, the latter activity is considered to be due to its essential oil content [47,48]

**Other uses:** Healthy skin, remove toxins, used as a repellent [47].

**f. *Equisetum arvense* [Horse tail]**

**[FAMILY:** Equisetaceae]

**Part used:** Stem and leaves

Horsetail's UTI activity is due to its astringent, diuretic and anti-inflammatory properties are due to equisetin and flavone glycosides. Ancient Romans, Greeks, as well as native North Americans used it for kidney stones and bladder problems [49].

**Chemical constituents:**

The volatile constituents of the sterile stems of *Equisetum arvense* (Equisetaceae) were investigated for the first time using GC, GC/MS and C-13 NMR. Twenty-five compounds were identified. Hexahydrofarnesyl acetone cis-geranyl acetone thymol and trans -phytol were the major constituents. According to a study, having horsetail tea 3time/day healed people having kidney stones and allow people to effectively fight a urinary tract infection. Rate crystals and UTIs [50]

**Other uses:**T.B, kidney problem and heal wounds [50].

**g. *Berberine:***

**[Family:** Berberidaceae]

**Part used:** The whole plant

**Chemical constituents:**

It includes *C.chinensis* spp.(Coptis or golden thread), *Berberis aristata* (tree turmeric), *Berberis aquifolium* (Oregon grape), and *Berberis vulgaris* (barberry) in which berberine exist in roots, leaves, rhizome etc. some bacteria, fungi, viruses and helminthes also contain berberine. Mechanisms of antimicrobial effects of berberine is not reported and understood, still it is reported to have an influence on FtsZ protein that is involved in the early stage of bacterial cell divisions [51].

**Other uses:** Used as an antioxidant, antimicrobial property, heart problems [51].

**h. *Vaccinium myrtillus* [Bilberry; Blueberry]**

[Family: Ericaceae]

**Part used:** Berries and leaves.

**Chemical constituents:**

Myrtillus extracts are reported to have same constituents as those found in Cranberry extracts. Most effect against UTIs after cranberry. Anti microbial activities of blue berries are not reported yet but are thought to decrease adhesion of uropathogenic bacteria [52].

**Other uses:** used for digestion, anti oxidant [52].

**i. Trans-cinnamaldehyde from cinnamon bark:**

[Family: Lauraceae]

**Part used:** Bark

Cell and UPEC invasion Amalaradjou *et al* (2011) showed that Trans-cinnamaldehyde reduces the adhesion to uroepithelial by major genes inhibiting that are associated to its adhesion and invasion to human cell tissue [53]

**Other uses:** Tooth decay, antifungal, bad breath [53].

**j. *P. granatum* [Pomegranate]:**

[Family: Punicaceae]

**Part used:** Juice

**Chemical constituents:**

In India UTIs and food borne diseases are treated with PoPx, however , punicalagin ,ellagitannins, and gallic acid plus ellagic acid present in the skin of pomegranate are natural antimicrobial are effective against *S. aureus* as well as *E.coli*, as they precipitate membrane proteins ,causing lysis by blocking enzymes (glycosyltransferase) and higher dose of PoPx like 24.7 mg/ml is less effective bactericidal against *L. monocytogene* [54].



Extracts of *p.granatum* was found to be effective against three types of UTIs by *Al-Wazni et al* and compared the extract inhibition activity to ciprofloxacin against *E.coli* and *S.aureus* [55].

**Other uses:** Cough, sore throat, arthritis etc [55].

**k. *Zea mays* [Maize]:**

**[Family:** Poaceae or Gramineae]

**Part used:** Dried stigmata

**Chemical constituents:**

Corn silk (*Zea mays*) is a herbal remedy made from stigmas, the yellowish thread-like strands found inside the husks of corn. In China, Turkey, US and in France maize is use of cystitis, kidney stones, as a diuretic, disorders of prostate ,UTIs, bedwetting and obesity [56-58]. It is believe to soothe and relax the bladder's lining as well as urinary tubes, so reducing UTI related irritation and increasing the secretion of urine [59]. However, modern researches showed no antibacterial activity [60].

Chinese consider it as an important herb for of prostate problems [61]. Native Americans make use of it to treat UTIs as well as malaria and used for cardiac problems [62]. Corn silk tea has been believed to have good effects on human health like decreasing BP, prostate inflammation, for diabetes and urinary tract infection, large weight and relaxation of the urinary bladder. There have been many commercially available products of maize for medicinal and for therapeutic uses in the market [63].

**Other uses:** Anticancer, anti-inflammatory, hypotensive, hypoglycemic etc [63].

**l. *Juniperus communis* [Juniper]**

**[Family:** Cupressaceae]

**Part used:** Oil

**Chemical constituents:**

Schilcer reported Juniper oil to be effective against many gram negative and gram positive bacteria [64]. Leaf and berries shows effectiveness against urinary tract infections. Terpinen-4-ol, a volatile oil, which is anti-bacterial, is main principle in the treatment of UTIs [65].

**Other uses:**

Relieve stress, natural antiseptic, improves skin condition [65].

**m. *Urtica dioica* [Stinging nettle]**

**[Family:** Urticaceae]

**Part used:** Whole plant

**Chemical constituents:**

Extracts of nettle is effective against gram positive as well as gram negative bacterial pathogens but it is mostly effective for gram positive bacteria [66,67]. Diuretic activities of the herb may be responsible for its effectiveness in UTIs [68].

**Other uses:** Promote lactation, hair growth and to control blood sugar [66].

**n. *Armoracia rusticana* [Horseradish]**

**[Family:** Brassicaceae]

**Part used:** Root

**Chemical constituent:**

Isothiocyanates of *Armoracia rusticana* is responsible for antibacterial activities. It was demonstrated that it can block the penetration of uropathogenic *E.coli* in human cell [69].

**Other uses:** Anti oxidant, good for skin, and improve nervous system [69].

**o. *Solidago Canadensis* [Goldenrod]**

**[Family:** Asteraceae]

**Part used:** Flowers and leaves

**Chemical constituents:**

Goldenrod supplies many beneficial plant compounds, including saponins and flavonoid antioxidants like quercetin and kaempferol (3). Saponins are plant compounds linked to many health benefits. It is effective for UTIs, prostate diseases, Urolithiasis., Rheumatic arthritis and eczema [70,71]. It is reported that Essential Oils of *S. canadensis* were tested for its effectiveness against fungi and bacteria, which remained successful [72].

**Other uses:** Reduce pain, swelling, diuretic etc [72].

### **3. Discussion**

Natural products due to their safety are gaining popularity with the passage of time. These alternative medicines are used and practiced in different countries of the world. Most of the world population considers these alternative medicines as free of side effects and economical. Due to these problems most of the patients switching from the synthetic medicines toward the alternative medicines. The synthetic medicines are notorious for their side effects which leading to poor patient compliance and lack of therapeutic regimen failure. To improve the patient compliance the use of natural products is the best option. One golden aspect of the consumption of natural products is the reduction of polypharmacy, because due to the presence of agonist and antagonistic substances these plants-based medicines work in many disorders at a time (the same plant act as an antibiotic, analgesic, anti-inflammatory etc) which reduces the practice of polypharmacy. The available treatment for UTIs is comprised of synthetic antibiotics, analgesics, and anti-dysuria substances which are responsible for a variety of side effects. These three therapeutic substances might be replaced with a single medicinal plant acting against UTIs. This review article encourages pharmaceutical manufacturers to formulate and develop these plants in suitable dosage forms for clinical practices like most of the plants are in clinical practice. It is suggested to screen these documented plants for all possible acute and chronic toxicological aspects and then convert these alternative remedies to suitable dosage forms. These types of research work will create a linkage between academia and pharmaceutical industries in Pakistan.

### **4. Conclusion**

Fifteen plants that are discussed above for treatments of UTIs had shown great scientific and practical evidences against UTI with same or different mechanisms. Treatment with non-antibiotic agents is a good approach to reduce the risk, incidence of UTIs and symptoms of the illness. In depth knowledge of chemical constituent and their interaction with each other plus interaction with other drugs is essential. Most of these have shown greater diuretic as well as anti-bacterial effectiveness nearly comparable to allopathic and antibiotic system of treatment. Some are not anti-bacterial but are proven effective in current and future UTIs as well as for resistant UTIs as well.

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