

HERBAL MEDICINE AS PREVENTION AND MANAGEMENT OF URINARY TRACT DISORDER

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ABSTRACT

Urinary tract infection (UTI) is one of the most severe public health problem affecting both sexes but females are more susceptible due to the differences in urogenital and reproductive anatomy, physiology and lifestyle. It is also known that the bacteria causing infection can develop resistance to the existing antibiotics that have been prescribed, if the medication is used for a long time. These issues have led to a continuous exploration of different modes of treatment and alternate therapies. Herbs have a long history and proven to be very effective in preventing and treating urinary tract infections. This review gives a bird's eye view on the updated information on urinary tract infections and the potential of some medicinal plants to be used in the management of UTI, including plants that have been approved for the treatment of urinary infections and promising, but less studied but with anti-uropathogenic activity.

Keywords: Herbal medicine, UTI, Phytochemicals, Plant extract, Plant extract.

INTRODUCTION

Urinary Tract Infection (UTI) is the invasion and subsequent multiplication of microorganisms anywhere in the urinary tract. The urinary tract consists of the organs involved in collecting and storing urine and releases it from the body including, urethra, urinary bladder, ureters, kidneys and other auxiliary parts. Anatomically, UTI is categorized into upper UTI involving the kidney, pelvis and ureter and lower UTI comprising the bladder and urethra. The ratio of urinary tract infection between female and males stands at 8:1. Urinary tract infections are very frequent bacterial infections in women. They usually occur between the ages of 16 and 35 years, with 10% of women getting an infection yearly and more than 40% to 60% having an infection at least once in their lives. Recurrences are common, with nearly half getting a second infection within a year. Urinary tract infections occur at least four times more frequently in females than males. Worldwide, about one-third of adult women have experienced symptomatic cystitis

disease at least once in their life and one half have experienced recurring UTI as a result of previous UTI infection (Belete and Saravanan, 2020; Vasudevan, 2014).

Pathophysiology of urinary tract infection

Uropathogens are pathogens which are present in the gut and contaminate the peri-urethral area during uncomplicated UTIs. Such pathogens present in urethra move to the bladder where adhesion molecules and pili help them to invade and colonize the superficial umbrella cells. Host immune response in the form of inflammation and neutrophilic infiltration in the infected area helps to phagocytose the microbes. However, some microbes multiply and make biofilms in the urinary bladder upon the evasion of the immune system. Different types of toxins and proteases from bacteria stimulate the host cell damage, and survival of bacteria during the release of vital nutrients which promote the movement of microbes to the kidneys. Colonized bacteria in the kidneys cause host tissue destruction due to the release of toxins from bacteria and bacteremia might occur if the pathogen crosses the tubular epithelial barrier in the kidneys. On the other hand, in complicated UTIs, uropathogens reach the bladder as in uncomplicated UTI. But during complicated UTI, the bladder defensive environment must be compromised to cause the infection (Johansen *et al.*, 2011; Shaheen *et al.*, 2019).

Catheterization is the most common reason for a compromised bladder. In catheterization, fibrinogen makes a house on the catheter and acts as the source of pathogen attachment. Then, microbes multiply and promote epithelial damage infecting the kidneys by bacteria resulting in bacteremia. The infecting bacteria in UTI may enter the urinary tract from the rectum during sexual activity and then ascend towards the urinary bladder. Literature reports indicated that vaginal environment, when changed due to any cause or especially the loss of H₂O₂-producing Lactobacilli, then females become prone to developing E. coli related UTI which causes 80% of infections in healthy individuals. However the Escherichia coli may have entered the body through the urethra, it is cleared naturally by the body defense system after a few months but in individuals with low immunity, it may persist for some months and can cause infection in individuals with low immunity (Walsh and Collins, 2020; Flores-Mireles *et al.*, 2019).

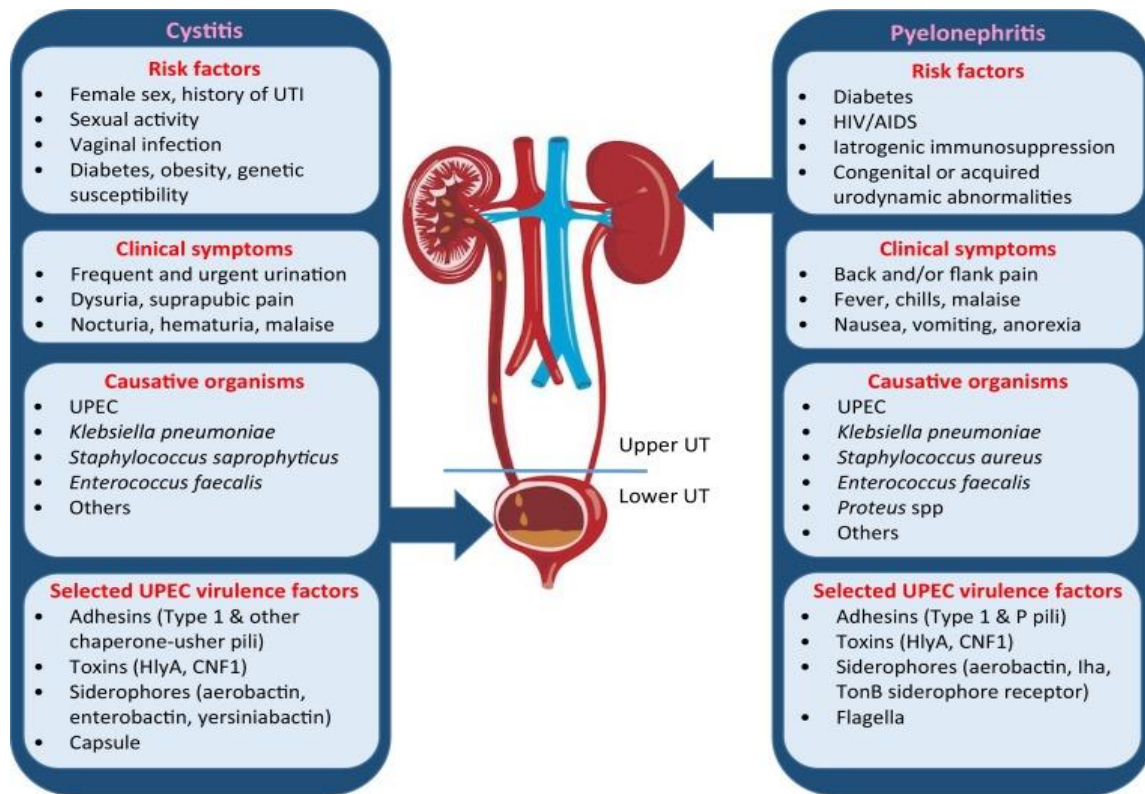


Figure 1: Pathophysiology of urinary tract infection

CLASSIFICATION

Urinary tract infections are divided into two types; complicated and uncomplicated. In uncomplicated cases of UTI, the urinary tract system function is normal. In complicated UTI, urinary tract is not normal systematically. Infections are further categorized as follows.

Isolated infection An isolated infection means that there is a gap of 6 months between two episodes of infection. It mostly involves women under 30–40 years age.

Unresolved infection Unresolved infections mean one attempt has been made to kill microorganism, but the microorganisms did not respond to therapy

Re-infection As indicated that in this type, re-infection is common in patients who have cleared the previous infection with different types of antibiotics but again suffered from infection.

Symptoms of UTI

- Frequent urge to urinate
- Incontinence
- Painful, burning feeling in the area of the bladder or urethra during urination
- Fatigue, lethargy
- Women feel an uncomfortable pressure above the pubic bone.
- Some men experience a fullness in the rectum.

- Despite the urge to urinate, only a small amount of urine is passed
- Milky, cloudy or reddish urine
- Foul-smelling urine
- A fever, which may mean that the infection has reached the kidneys
- Pain in the back or side below the ribs
- Nausea and/or vomiting (Rushton *et al.*, 1997; Kaur and Kaur, 2021).

Current treatments

In most cases, UTIs are relatively easy to treat with a course of broad-spectrum antibiotics, although fluoroquinolones (including ciprofloxacin) are generally avoided as the side effects are often regarded as outweighing the benefits. The most common treatments include trimethoprim/sulfamethoxazole, fosfomycin, nitrofurantoin, cephalexin, and ceftriaxone. However, due to overuse and misuse of commonly used clinical antibiotics, the emergence of antibiotic-resistant pathogens is increasingly common, resulting in the failure of the main antibiotic chemotherapy options. Antibiotic resistance has been a driving force of new drug development initiatives, and implementation of alternative treatment identification and new antibiotic therapies are urgently required (Wagenlehner and Naber, 2006)

The development of antibiotic-resistant bacteria is increasingly resulting in antibiotic therapy failures, and chronic UTIs are becoming more frequent. Additionally, the relatively high rate of UTI recurrence poses a challenge to the effective treatment of these infections. Indeed, that study estimated that approximately 24% of people contracting a UTI will develop a recurrent infection within six months of the original infection. Of further concern, approximately 5% of people who develop a UTI will experience more than three recurrences per year (Lüthje and Brauner, 2016; Stamm, 1982).

Medicinal plants for treatment of UTI

Herbs are generally a safe way to strengthen and tone the body's systems. Herbal treatments for UTIs have been used for centuries. Herbal remedies may relieve urinary tract infections by combating the bacteria, decreasing irritation and healing urinary tract tissues. Some herbs also help prevent future occurrences. Urinary tract infection is commonly treated with prescription antibiotics. However, it is increasingly recognized that using antibiotics frequently may contribute to recurring UTIs and increased dependency on antibiotic use may further weaken the immune system. Natural remedies can provide an effective alternative to prescription medications and their side effects (Bag *et al.*, 2008; Arsene *et al.*, 2021).

The exact mechanism of herbal medicines used to treat UTI is still not well understood due to lack of research, but it was reported that phytochemical constituents acted as nutraceuticals and

immunomodulators, boost body oxidant status or provided antioxidant compounds, prevent attachment of microbes as well as halt the proliferation or multiplication of microorganisms and some might act as microcidal. These diverse properties of medicinal plants are due to the presence of various phytochemical constituents including alkaloids, anthraquinones, flavonoids, glycosides, phenols, saponins, steroids, sterols, tannins, terpenoids, triterpenoids, phytosterols, hydrocarbons, mono and sesquiterpenes, phlobatannins and many other medicinal plant secondary metabolites. Flowers, leaves, bark, fruit, seeds and even whole parts of medicinal plants were ingested to treat UTI and these parts or their extracts are consumed orally as sole preparation or might be mixed with different other foods or drinks (Beydokthi *et al.*, 2017; Dietz *et al.*, 2016).

Commonly used medicinal plants to treat urinary tract infection

Arctostaphylos Uva-Ursi

The primary compound in uva ursi is arbutin, the hydroquinone derivative. The stomach absorbs it and changes it into a substance with disinfectant, antimicrobial and astringent properties. Arbutin fights infection, soothes irritation and reduce inflammation during urination. The tea or tincture can be used in treating bed wetting as well. Bearberry has been reported to be effective against E. coli. The antimicrobial effect appears to be in part due to the capacity of aqueous uva ursi extracts to change microbial cell surface characteristics (Trill *et al.*, 2017; Moore *et al.*, 2019)..

Echinacea purpurea

Echinacea strengthens the immune system and acts as an anti-inflammatory providing immediate relief to the burning sensation that often accompanies a UTI.^{94,95} According to Medline Plus, echinacea signals the immune system to attack the infection and flush the bacteria out of the body by speeding up the urine flow. The key to using echinacea effectively is to take it immediately following the onset of symptom (Kligler, 2003).

Juniperus communis

It belongs to family Cupressaceae. The common name is Juniper. It is diuretic and antibacterial. It contains oxygenated sesquiterpene, monoterpene hydrocarbons, β -pinene, limonene, sabinene and myrcene (Al-Roubaeay *et al.*, 2006).

Agathosma Betulina

The leaf is a diuretic and urinary tract antiseptic, the latter activity is considered to be due to its essential oil content. The underside of Buchu leaves have oil glands containing an essential oil which consists mainly of the monoterpene, diosphenol that smells like black currants and has the unglamorous attribute of being able to clear up urinary tract infections (Mavimbela *et al.*, 2014).

Mentha piperita

It belongs to family Lamiaceae. The common name is Peppermint. It is antispasmodic and antibacterial. It contains menthone, menthol, limone, menthofuran and pulegonen (Jamshed and Jabeen, 2022).

Vaccinium Macrocarpon

The major clinical use of cranberry is to prevent recurrent urinary tract infections. Taking cranberry juice or pills by mouth may help prevent infections and may particularly work against the bacteria *Escherichia coli*. Many years, researchers believed that the ability of cranberries was partly related to its strong acidity. Recent research has shown that it's not the acidity of the cranberries, but the unusual nature of their proanthocyanidins (PACs) that is related to prevention of UTIs (Pérez-López *et al.*, 2009; Davidson *et al.*, 2014).

Taraxacum officinale

It belongs to family Asteraceae. The common name is Dandelion. It is diuretic and antibacterial. It contains nitriles, norisoprenoids, methyl branched aliphatic acids, phenylacetic acid and dehydrovomifoliol (Díaz *et al.*, 2018).

Moringa oleifera

It belongs to family Moringaceae. The common name is Sohanjna. It is antipyretic, anti-inflammatory, and antibacterial. It contains thiocarbamate glycoside, acetylated carbamate, amino acids, tocopherol, moringine, spirochin and kaempferol (Maurya and Singh, 2014).

Terminalia chebula

It belongs to family Combretaceae. The common name is Hareer, har. It is hypolipidemic, antibacterial. It contains chebulin, tannic acid, gallic acid, beta sitosterol, fatty acids and betulinic acid (Bag *et al.*, 2010).

Hydrastis Canadensis

The main healing compound of goldenseal as urinary tract infection remedy is the berberine. Berberine is a plant alkaloid with a long history of medicinal use. The extracts and decoctions of berberine demonstrate significant antimicrobial activity against a variety of organisms, including bacteria, viruses, fungi, protozoans, helminths and *Chlamydia* (Edwards *et al.*, 2015)

Allium sativum

It belongs to family Amaryllidaceae. The common name is Lehsan. It is hypolipidemic and antimicrobial. It contains volatile oil, allicin, alliin, acrolein, phytocidin, diallyl-disulphide and diallyl-trisulfide (Lionel *et al.*, 2020).

Zingiber officinale

It belongs to family Zingiberaceae. The common name is Adrak, Sondh. It is antibacterial, digestive and anti-inflammatory. It contains zingiberene, zingiberol, α -zingiberene, shogaols, gingerols and dihydroparadol (Mohamad, 2019)

Boerhavia diffusa

It belongs to family Nyctaginaceae. The common name is Biskhapra. It is antibacterial, antioxidant and antidiabetic. It contains arachidic acid, behenic acid, saturated fatty acids, vitamins C, lignin, phenolics, steroids, glycosides and boeravinone B (Sahu *et al.*, 2013).

Equisetum Arvense

The plant is one of the best herbal remedies for UTI. Horsetail has astringent, diuretic and tissue healing properties that allow it to effectively fight a urinary tract infection. The diuretic property is believed to be due to equisetin and flavone glycosides. Because of horsetail's diuretic activity, the patients' urine discharge increased, enabling them to flush out the kidney stones, also relieving them of the UTI symptoms (Lemus *et al.*, 1996).

Agropyron repens

Strongly diuretic with a soothing, anti-inflammatory healing effect on the lining of the bladder. It is useful when there is mucus discharge from the bladder with painful and frequent urination (Hautmann *et al.*, 2000).

Galium aparine

Soothing diuretic which is useful for acute or chronic cystitis with swollen lymph nodes and uterine inflammation (Korkmaz *et al.*, 2021).

Urtica dioica

Mild diuretic which is useful if there is a possibility or history of kidney infection. It builds the blood and is a nutrient rich herb (Mirtaghi *et al.*, 2016).

Herbal therapy is one of the most common ways people are utilizing for taking care of their urinary tract infections, whenever it is safe. Each of the herbs discussed above can benefit the urinary tract health drastically. Some will increase the production of urine, others will fight against the bacteria and will soothe the discomfort caused by them. The issue with urinary tract infections is that they tend to be chronic in nature. One urinary tract infection clears just in time for another infection to begin. The first infection weakens the urinary tract and makes it easier for bacteria to move in and cause the second urinary tract infection. The third makes it even easier for the fourth and so on.

Many of effective phytotherapies are on the drug market as whole extracts, and doctors have believed that synergistic interactions between the components of individual or mixtures of herbs are a vital part of their therapeutic efficacy. Until recently there has been little clinical evidence to demonstrate

conclusively that this is the case, and it very often it is argued that the dose of supposed active constituents is too low to exert any therapeutically significant effect at all. In fact the mechanism of action is still unknown and there are several cases of a whole herbal extract showing a better effect than an equivalent dose of an isolated compound. In the past, it was difficult to meet this requirement because of the lack of analytical methods. Many drug preparations at that time were not yet appropriate for controlled clinical studies. Synergistic interactions are of importance, to explain difficulties in always isolating a single active ingredient, and explain the efficacy of apparently low doses of active components in a herbal product.

Therefore, screening medicinal plants with therapeutic potential for UTI cure should be conducted, as well as further studies at the molecular level to reveal the chemical composition of all potential compounds responsible for pharmaceutical activities and their mechanisms. The results sustain the opportunity for further studies with these plant extracts that could improve the current treatment, but more scientific evidence and large-scale well-designed clinical trials are required.

The innovation in prophylactic plant-based treatment strategies should target the bottleneck points from UTI pathogenesis and search for molecules that reduce UTI symptoms without antibiotics and those that increase the host's immune response. Further progress in developing plant-based products to cure UTI will be supported by the advances in UTI pathogenesis and human-based models to understand their pharmacological activities better.

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