

Research Article

## Antimicrobial Activity of Medicinal Plants and Urinary Tract Infections

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### ABSTRACT

Medicinal plants are part and parcel of human society to combat diseases from the dawn of civilization. According to World Health Organization (WHO), about 80% of the world population rely chiefly on plant based traditional medicine specially for their primary health care needs and there has been a worldwide move towards the use of traditional medicines due to concerns over the more invasive, expensive and potentially toxic main stream practices. This review gives a bird's eye view on the updated information on urinary tract infections (UTIs), different categories of urologic herbs, historical use and modern scientific investigations on some important urologic herbs, clinical studies, some isolated chemical compounds and their possible side effects.

**Keywords:** Medicinal plants, Urinary Tract Infections, Historical use, Scientific analysis, Clinical studies, Bioactive constituents, Possible side effects.

### INTRODUCTION

The urinary system, also known as the renal system, It is a system that maintains the volume and composition of body fluids within normal limits. It consists of the kidneys, each one consists of millions of functional units called nephrons. which filter the blood, remove the end products of metabolism and excrete the wastes in the urine; ureters carry the urine away from kidneys to the urinary bladder, which is a temporary reservoir and urethra transports the urine from the urinary bladder to the outside (Figure 1)<sup>1</sup>. The purpose of the renal system is to eliminate wastes from the body, regulate blood volume and blood pressure, control levels of electrolytes and metabolites, and regulate blood pH. The kidneys have extensive blood supply via the renal arteries which leave the kidneys via the renal vein. Following filtration of blood and further processing, wastes (in the form of urine) exit the kidney via the ureters, tubes made of smooth muscle fibers that propel urine towards the urinary bladder, where it is stored and subsequently expelled from the body by urination (voiding). The female and male urinary system are very similar, differing only in the length of the urethra<sup>2</sup>. 800–2,000 milliliters (mL) of urine are normally produced every day in a healthy human. This amount varies according to fluid intake and kidney function<sup>2</sup>.

1. Human urinary system 2. Kidney, 3. Renal pelvis, 4. Ureter, 5. Urinary bladder, 6. Urethra. (Left side with frontal section) 7. Adrenal gland *Vessels*: 8. Renal artery and vein, 9. Inferior vena cava, 10. Abdominal aorta: , 11.

Common iliac artery and vein with transparency 12. Liver, 13. Large intestine, 14. Pelvis.  
*The order of impurities being excreted from the kidneys:*

kidneys → Ureters → Urinary Bladder → Urethra  
*Urinary tract infection (UTI)*

Urinary tract infection (UTI) is a term applied to a variety of clinical conditions ranging from asymptomatic presence of bacteria, or fungi in the urine to severe infection of the organs of the system with resultant sepsis<sup>3</sup>. UTI is defined also as the growth of a known bacterial pathogen more than 10000 cfu/ml tested with a positive dipstick or urinalysis<sup>4</sup>. According to the National Institute for Health and Clinical Excellence (NIHCE) guidelines, urinary tract infection is defined by a combination of clinical features and the presence of bacteria and/ or fungi in urine. About 150 million people developed a urinary tract infection each year<sup>5</sup>. They are more common in women than men<sup>6</sup>. In women, they are the most common form of bacterial infection<sup>7</sup>. Up to 10% of women have a urinary tract infection in a given year and half of women having at least one infection at some point in their lives. They occur most frequently between the ages of 16 and 35 years. Recurrences are common<sup>6</sup>. Urinary tract infections have been described since ancient times with the first documented description in the Ebers Papyrus dated to c. 1550 BC<sup>8</sup>.

### *Epidemiology*

Urinary tract infection is among the most common bacterial infections encountered in clinical practice and

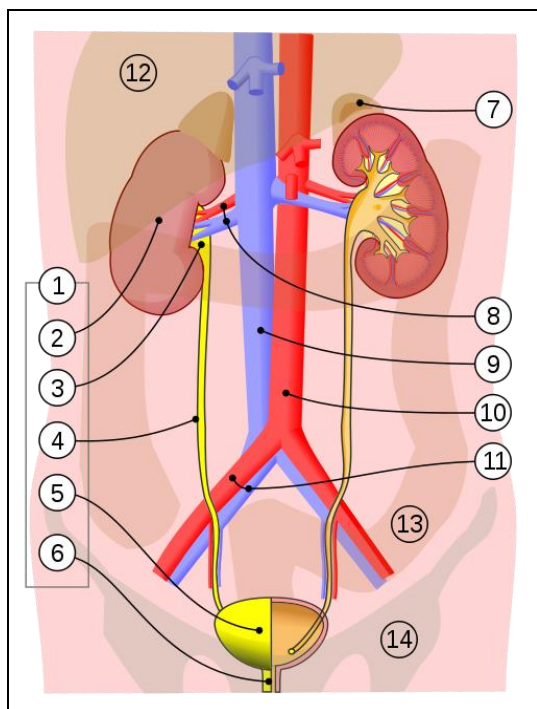


Figure 1: Anatomy of Human Urinary System.

account for the significant morbidity and severe health problem in persons of all ages (Figure 2). Both genders male and female are susceptible to infection, but because of their anatomy and reproductive physiology women are more vulnerable to the infections. Urinary tract infections are the most frequent bacterial infection in women<sup>8</sup>. They occur most frequently 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 some point in their lives<sup>6,9</sup>. Recurrences are common, with nearly half of people getting a second infection within a year. It is estimated that 20% of women develop a UTI during their lifetime; the incidence increases at puberty and remains high throughout adult life, only after the age of 50 years is a similar incidence seen in males<sup>10</sup>. Urinary tract infections occur four times more frequently in females than males<sup>6</sup>. Pyelonephritis occurs between 20–30 times less frequently<sup>9</sup>. They are the most common cause of hospital acquired infections accounting for approximately 40%<sup>11</sup>. Frequent or recent sexual activity is the most important risk factor for urinary tract infection in young women. Nearly 80% of all urinary tract infections in premenopausal women occur within 24 hours of intercourse. UTIs are very rare in celibate women. Other aging-related urinary conditions, such as urinary incontinence, menopause and pregnancy can also increase the risk for recurrent urinary tract infections in women. Asymptomatic bacteriuria occurs in 2–10% of all pregnancies and its prevalence is closely related to socioeconomic status<sup>9</sup>. Rates of asymptomatic bacteria in the urine increase with age from two to seven percent in women of child bearing age to as high as 50% in elderly women in care homes<sup>12</sup>. Rates of asymptomatic bacteria in the urine among men over 75 are between 7-10%<sup>13</sup>. Asymptomatic bacteria in the urine occurs in 2% to 10%

of pregnancies<sup>12</sup>. Urinary tract infections may affect 10% of people during childhood<sup>6</sup>. Among children urinary tract infections are the most common in uncircumcised males less than three months of age, followed by females less than one year<sup>14</sup>. Estimates of frequency among children however vary widely. In a group of children with a fever, ranging in age between birth and two years, two to 20% were diagnosed with a UTI<sup>14</sup>.

#### Etiologic agents

Etiologic agents of UTIs refer to the presence of microbial pathogens within the urinary tract. Although UTI may be caused by any pathogen that colonizes the urinary tract (e.g., fungi, parasites, and viruses), most causative agents are bacteria of enteric origin. There are many bacterial genera that cause urinary tract infection. The bacteria that cause urinary tract infections typically enter the bladder via the urethra. However, infection may also occur via the blood or lymph. Any source of possible infection occurs through urethra which initiates the incidence of the infection. It is believed that the bacteria are usually transmitted to the urethra from the bowel, with females at greater risk due to their anatomy<sup>13</sup>. Urine is generally considered to be sterile and is believed to be germ free. Any source of possible infection occurs through urethra which initiates the incidence of the infection. Urinary tract infections are caused when microbes manage to get past the body's natural defenses. Members of the *Enterobacteriaceae* are the most common organisms isolated from uncomplicated UTI and the most frequent uropathogen is *E. coli* which constitutes up to 80-85% and is followed by *Staphylococcus saprophyticus* which accounts to 5-10%<sup>15,16</sup>. In addition to above mentioned bacterial species *Proteus mirabilis*, *Proteus vulgaris*, *Providencia stuartii*, *Morganella morganii*, *Enterobacter cloacae*, *Enterobacter aerogens*, *Klebsiella pneumoniae*, *Staphylococcus aureus*, Coagulase negative *Staphylococcus*, *Pseudomonas aeruginosa*, *Streptococcus faecalis*, *Acinetobacter calcoacticus*, and *Citrobacter freundii* are also associated with the infections (Vasudevan, 2014). Urinary tract infection due to viral and fungal causes is rare<sup>17</sup>.

*Escherichia coli* are a bacterial organism that belongs to the family *Enterobacteriaceae*. *E. coli* is one of the main causes of both nosocomial and community acquired infections in humans. The organism is therefore of clinical importance and can be isolated from various clinical specimens. It is one of the organisms most frequently isolated from urine and blood<sup>18</sup>. According to Tsao, after *E. coli*, Salmonella was the second most common pathogen<sup>19</sup>. Salmonella UTI do occur in healthy children and adolescents, especially in the presence of gastroenteritis<sup>20</sup>. *Salmonella* has been postulated to enter the urinary tract either hematogenously or by direct invasion of the bladder via the urethra<sup>21</sup>. *Klebsiella species* have account for a smaller proportion of uncomplicated urinary tract infections<sup>22</sup>.

*Pseudomonas aeruginosa* is an aerobic gram- negative bacterium belonging to the bacterial family *Pseudomonadaceae*, that is an important cause of both community-acquired and hospital-acquired infections<sup>17</sup>.

Table 1: Microbial etiology of urinary tract infection.

| Organisms                           | Clinical Characteristics                      |
|-------------------------------------|---|
| Gram-negative bacteria              |   |
| <i>Escherichia coli</i>             | Typical                                       |
| <i>Klebsiella pneumoniae</i>        | Often reinfection                             |
| <i>Enterobacter spp.</i>            | Often reinfection and/or nosocomial infection |
| <i>Proteus spp.</i>                 | May indicate tumor or calculi                 |
| <i>Providencia stuartii</i>         | Often reinfection and/or nosocomial infection |
| <i>Morganella morganii</i>          | Often reinfection and/or nosocomial infection |
| <i>Serratia marcescens</i>          | Often nosocomial infection                    |
| <i>Acinetobacter baumannii</i>      | Often nosocomial infection                    |
| <i>Burkholderia spp.</i>            | Often nosocomial infection                    |
| <i>Pseudomonas aeruginosa</i>       | Often nosocomial infection                    |
| <i>Stenotrophomonas maltophilia</i> | Often nosocomial infection                    |
| Gram-positive bacteria              |   |
| <i>Staphylococcus saprophyticus</i> | Most common during summer                     |
| <i>Staphylococcus aureus</i>        | May indicate focus outside the genitourinary  |
| Enterococcus spp.                   | Often reinfection                             |
| Other Gram-positive bacteria        | In most cases contaminants                    |
| Fungi                               |   |
| <i>Candida spp.</i>                 | May indicate focus outside the genitourinary  |

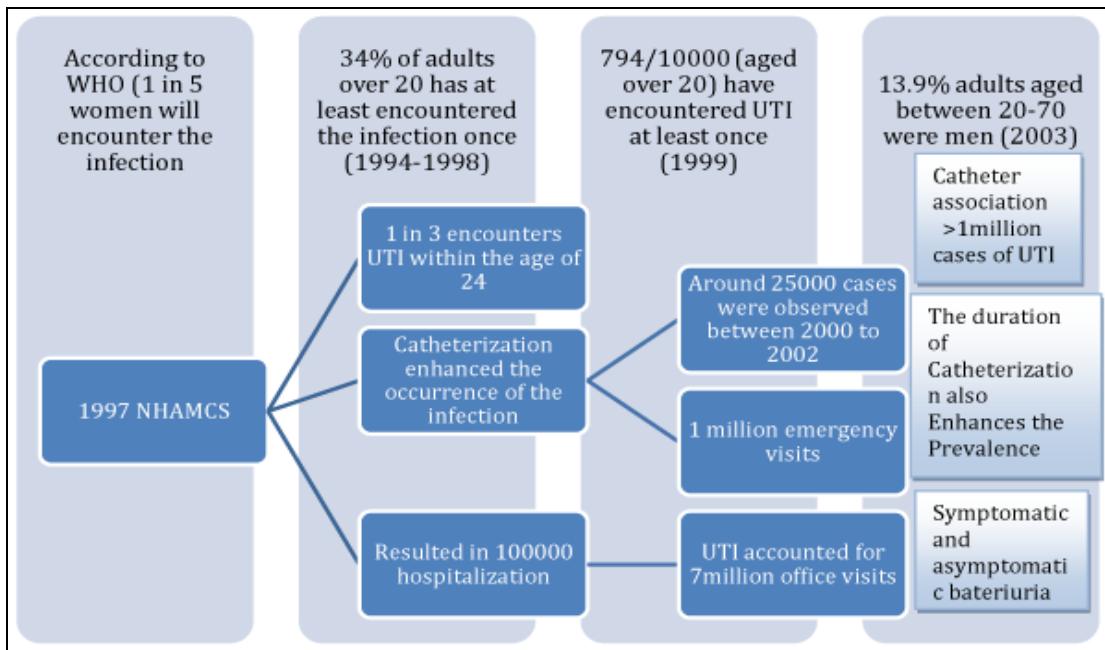


Figure 2: Globally prevalence of UTI among different groups of people over the last few years (Vasudevan, 2014)  
 NHAMCS:-National hospital ambulatory medical care survey.

Among the species of *Serratia* genus, *S. marcescens* plays a significant role as etiological factor in the infections in man. It is a gram-negative bacillus classified as a member of the *Enterobacteriaceae*, has been recognized as a cause of hospital-acquired infection for the last two decades<sup>23</sup>. *S. marcescens* strains were most often isolated from urine collected from intra-vesical catheter as well as from physiologically passed urine<sup>24</sup>. In complicated UTIs, *Staphylococci* and *Enterococci* are the main gram-positive uropathogens. These organisms have become common in hospitals, nursing homes and chronic care facilities. UTIs caused by these organisms are associated with serious underlying illness and institutionalization<sup>25</sup>.

*Chlamydia* and *Mycoplasma* bacteria can infect the urethra but not the bladder.

Urinary tract infection may be caused by Fungi and viruses. Fungi, such as *Candida*, are the second most cause of nosocomial UTI in children. It can be spread systemically and can be life threatening. The prevalence of UTI due to *Candida* increased gradually by the duration of hospitalization, with a prevalence rate 27.2%<sup>26</sup>. Fungi infections are seen in infants and children who are on long-term antibiotics, patients who are immuno-compromised, or patients using invasive devices like IVs, drains and catheters. Viral UTI can be caused by Adenoviruses types 11 and 21, polyoma virus BK, and herpes simplex viruses<sup>27</sup>. The relative frequency of the

pathogens varies depending upon age, sex, catheterization, and hospitalization<sup>28</sup>. The microbiologic etiology of a UTI depends on several factors. Table 1 summarizes the most common findings.

#### Treatment

The standard treatment for a UTI is a course of one or more antibiotics. No single antibiotic is recommended for treating every UTI, but nitrofurantoin (Furadantin®), trimethoprim-sulfamethoxazole (Bactrim™), pivmecillinam (Selexid®), fosfomycin trometamol (Monurol®), fluoroquinolone (eg, Cipro®), and beta-lactam (eg, Augmentin®) may all be used<sup>29,30</sup>. Although many antibiotics can be used to treat UTIs, one of the main factors that determines which antibiotics are chosen is the bacterial resistance pattern. There are strains of *E. coli* that are resistant to antibiotics and are found throughout the world<sup>31,32</sup>. Other strains of bacteria that cause UTIs, including species of *Proteus* and *Klebsiella*, have also developed resistance to specific antibiotics<sup>31</sup>. As a result, the choice of antibiotic is usually governed by susceptibility of the pathogenic organism responsible for an individual's case and/or community history of microbial antibiotic resistance<sup>32</sup>. This is typically determined by regional rates reported by local hospitals, although this information can overestimate the prevalence of resistance among bacteria in a region<sup>33-57</sup>. Some guidelines recommend avoiding a particular antibiotic if local resistance rates to that antibiotic are greater than 20%. Plant medicines have been used for many thousands of years in many different cultures. Today medicinal plants have become a growing alternative for establishing a healthy body environment. They play an important role for the treatment of different types of diseases and disorders since antiquity including urinary tract infections<sup>58</sup>. They can affect the urinary tract infections as disinfectants, analgesics, diuretics or narcotics. Some have been shown to have antimicrobial effect against *Escherichia coli* and other organisms that cause urinary tract infections (UTIs). Medicinal plants can be very effective in programs for resolving UTIs<sup>59-70</sup>.

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