



## A Review on Pharmacological Potential of Herbal Extracts in the Treatment of Recurrent Urinary Tract Infections

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Received: November 29, 2024

Published: December 11, 2024

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### Abstract

Urinary tract infections (UTIs) are among the most common bacterial infections globally, causing significant morbidity. With increasing antibiotic resistance, there is a growing need for alternative therapeutic approaches. Herbal medicines offer a promising solution due to their safety, efficacy, and minimal side effects. This study explores the potential of *Cynodon dactylon* (commonly known as Bermuda grass) as a key ingredient in the formulation of herbal suppositories for UTI management.

*Cynodon dactylon*, known for its antimicrobial, anti-inflammatory, and diuretic properties, was incorporated into a suppository base to create a localized delivery system targeting the urinary tract. The formulation was evaluated for physical properties, drug release profile, and antimicrobial efficacy against UTI-causing pathogens. Preliminary results indicate significant inhibition of bacterial growth and enhanced symptom relief compared to conventional treatments.

**Keywords:** Urinary Tract Infections; *Cynodon Dactylon*; Bacteria

### Introduction

Intrauterine adhesions are a defining feature of Asherman syndrome. (I.U.A.) producing pelvic pain among other symptoms irregular menstruation, infertility, miscarriage, and associated mental health symptoms Simon, Santamaria Isaacson (2018) [47,48]. Around 1550 BCE, hysteroscopic lysis of Ancient Egypt was the gold standard for I.U.A. therapy. The Ebers Papyrus talks about a condition that resembles a UTI and has symptoms including stomach ache and scorching urine [46].

UTIs are still a prevalent medical condition, and research into their origins, prevention, and surgical adhesions is still underway. But recurrence is common (Salazar Isaacson Morris 2017), and there are preventative measures like medication [41,42]. Suppositories are solid medication dose forms that are meant to be inserted into bodily cavities. The word "suppository," which meaning "to

place under," comes from the word "hatin." They are employed to provide drugs that have both local and systemic effects. The basic idea is that the suppositories are inserted as solids that dissolve or melt inside the body to distribute the medication to the numerous blood vessels that are present in the area. It has been demonstrated that polysaccharides increase intrinsic antioxidant enzymes, cause cervical cancer HeLa cells to undergo apoptosis, and have an immunomodulatory effect (Li., et al. 2009 Cao., et al. 2010 Xiaoping., et al. 2009) [43,44]. On damaged or irritated epithelial membranes, marshmallow polysaccharides (M.P.) create a bioadhesive layer that promotes healing (Schmidgall schhetz Hensel 2000). Suppositories might profit from eating local food. Various components of A have been reported to exhibit antibacterial, anti-inflammatory, and anti-ulcerogenic properties. Numerous herbal remedies include anti-inflammatory and anti-healing properties, including uterine targeting [45,46]. Consequently, M.P.'s mucoadhesive qualities

make it a suitable option for the vaginal system (Valents, 2005). In the current work, our goal is to create and assess vaginal suppositories that include polysaccharides that have been extracted from the root of *A. officinalis*. Suppositories can also be delivered vaginally, which is where the term “suppositorium” originates. It is frequently called pessaries. The Greek word pessarium, which means pesos, or oval stone, is whence the name pessaries originated [39]. But in recent years, especially in Europe and a few American research centers, work has already started. The highest acceptability is seen in eastern Europe, particularly France and Italy, whereas countries such as the United Kingdom and the United States have not been using suppositories or are hostile to them, particularly when it comes to the delivery of rectal medication [48].

Any infection affecting the kidneys, ureters, bladder, or urethra is referred to as a urinary tract infection (UTI). UTIs are widespread, especially in women, and typically manifest as cystitis in a normal urinary tract. In their lifetime, 50% of all women will get a UTI. They can happen in an uncomplicated host situation, when the patient’s genitourinary tract has no underlying structural or functional abnormalities, or in a difficult host setting, where they do. When diagnosed, it frequently happens in an aberrant urinary tract and is rare in males and children. The majority of UTIs exclusively affect the lower tract’s urethra and bladder (or, in men, the prostate gland). Upper tract UTIs are typically more severe than lower tract UTIs, while being less common.

An estimated 70 to 80 percent of urinary tract infections (UTIs), one of the most significant healthcare-acquired infections (HAIs), are thought to be caused by the use of an indwelling urethral catheter. There were only a few catheters. When organisms are introduced into the bladder during catheter placement, urinary tract infections (CAUTIs) result. The length of an indwelling urethral catheter might range from a few minutes to years. Short-term indwelling catheters are those that remain in place for less than 30 days, whereas long-term (chronic) indwelling catheters are those that remain in place for more than 30 days. Examples of the bacteria that are commonly found in the gastrointestinal (GI) tract and are referred to as enterobacteriales include *Pneumoniae Escherichia coli*, *Klebsiella* and *proteus mirabilis*. Female sex, recent sexual activity, diabetes mellitus, and structural or functional urological abnormalities are risk factors for urinary tract infections. Compared to men, women are more likely to get a UTI. among adults

between the ages of 20 and 50. Women are almost 50 times more likely to get UTIs. Due to the rising prevalence of male instrumentation and prostate enlargement, the female-to-male ratio falls as the incidence of UTIs rises in individuals over 50 [45,46]. After respiratory and gastrointestinal infections, urinary tract infections (UTIs) rank third in terms of frequency among human infections. Urinary tract bacterial infections are really the most frequent source of nosocomial infections and community-acquired infections among hospitalized patients in the United States. It is upsetting and can even be fatal at times. Urinary tract infections and their prognosis, however, are contingent upon the infection site and any risk factors. A urinary tract infection (UTI) is characterized by the presence and growth of bacteria in the urinary tract [42,44]. Bacterial demonstration is necessary for diagnosis. Patients with bacteristrial or pyonephrosis are exceptions to this rule. Certain definitions are required for prostatitis, in which the urine may be sterile, since microbial invasion of any extended tissues may produce the urinary tract infection.

This clonal, perennial grass is native to tropical and warm-temperate regions, where it typically grows in open spaces that are frequently disturbed by fire, flooding, drought, and grazing [43]. This species’ genetic makeup is incredibly diverse, and populations of *C. dactylon* can develop resistance to a variety of harsh environmental conditions, such as salinity or high soil concentrations of heavy metals, to produce highly adapted ecotypes. It is frequently used as a lawn grass but has the potential to become an agricultural weed due to its challenging control and rhizome-based spread [41].

## History

- **Ancient Egypt (around 1550 BCE):** The Ebers Papyrus describes a disease resembling UTI, with symptoms like burning urination and abdominal pain [29].
- **Ancient Greece and Rome (around 500 BCE - 500 CE):** Physicians like Hippocrates and Galen wrote about UTI-like conditions, attributing them to imbalances of bodily fluids (humors) [33].
- **Middle Ages (500 - 1500 CE):** UTIs were often attributed to “bad blood” or other mystical causes.
- **19<sup>th</sup> century:** The discovery of microorganisms and the development of the germ theory led to a better understanding of UTIs as infections.

- **Early 20<sup>th</sup> century (1900-1950 CE):** Antibiotics revolutionized UTI treatment, with sulfonamides and penicillin being used to combat UTIs [34,35].
- **Mid -20<sup>th</sup> century (1950-1980CE):** The introduction of trimethoprim-sulfamethoxazole (TMP-SMX) and other antibiotics further improved UTI treatment [36].
- **Present day: (1980CE- present):** UTIs remain a common health issue, with ongoing research into causes, prevention, and treatment Some interesting historical notes: [37].
- In ancient Egypt, UTIs were treated with beer and other substances [38].
- In ancient Greece, UTIs were associated with the goddess Aphrodite [39].
- In the Middle Ages, UTIs were sometimes treated with blood-letting [40].

## Disease

### Urinary tract infection

Although urinary tract infections are frequent in both men and women, women are more likely to get them because of their physiology [27,28]. Simply put, it can be described as a disorder that women will undoubtedly experience throughout their lives, with a higher prevalence among pregnant women [26,31]. The urinary tract, which includes the upper and lower urinary tracts, is affected, as the name suggests. The infection is called pyelonephritis (kidney infection) or cystitis (bladder infection), depending on the part that becomes infected [30,32].

The symptoms of kidney and bladder infections differ; for example, when a bladder infection causes cystitis, the symptoms include painful and frequent urination, while situations like excessive. Fever and flank pain are typical symptoms of kidney contagion, also known as pyelonephritis. Uncertainty surrounds the infection's prevalence in children and the elderly, which is presently being investigated [24,25]. Although the majority of the bacteria that cause human infections are bacteria, several fungi and viruses also play a part. On the other hand, UTIs caused by fungal or viral infections are regarded as uncommon occurrences. The patient exhibits a range of symptoms as the illness worsens and, in extreme cases, can be fatal, even if it first appears to be benign. According to research, the most prevalent type of bacterial illness is urinary tract infection [22,23].

Urinary tract infections are considered to be the most prevalent hospital-acquired infections and can result from inadequate diagnosis [18,21]. A wide range of clinical syndromes and diseases are included in the infection, each with its own epidemiology, origin, location, and severity. Along with the previously mentioned variables, there are further variations in the degree of damage, the frequency of recurrence, the expression of local symptoms, the existence of complicating factors, and the risk [19,20].

The incidence of bladder infections is typically followed by kidney infections, which can cause blood-borne infections and, in extreme cases, cause fatalities [16,17]. As a result, UTIs can be fatal in extreme cases, and prompt treatment leads to a speedy recovery from the infection. The infection first appears between weeks six and twenty-four of pregnancy. Pregnancy increases the risk of infection for women, even though the prevalence of bacteriuria during pregnancy is comparable to that of non-pregnant women. Pregnancy is when the illness is most common, and this depends on a number of different variables [14,15].

Although it is not universally acknowledged that pregnant women are more likely to get UTIs, as the idea is now being investigated, and a number of studies are trying to determine the importance of pregnancy in connection with UTIs. The idea that UTIs are more common in pregnant women is a complicated one that has not yet been fully comprehended or proven [13]. Pregnancy is regarded as a critical period that necessitates a number of precautionary measures to protect the expectant mother and unborn child, but numerous researchers have attempted in the past and continue to seek appropriate data to correlate the prevalence of UTI during pregnancy." Sexual activity and family history are also major contributors to UTIs, in addition to pregnancy [12].

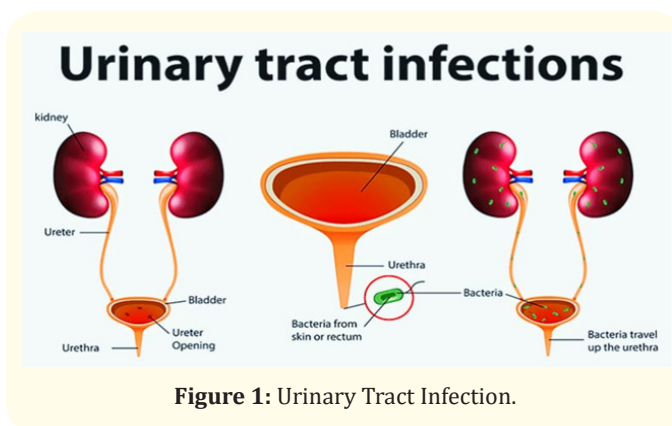


Figure 1: Urinary Tract Infection.

### Types of urinary tract infection

Urinary Tract Infection Types Urinary tract infections come in three varieties. The area of the urinary system that is infected determines the type of infection. Several urinary tract portions, such as the following, may be affected by an infection: [11].

- **Urethritis:** An infection of the urethra, the hollow tube that empties the bladder and sends urine outside the body, is known as urethritis.

- **Cystitis:** A bladder infection caused by bacteria that frequently travels up from the urethra.
- **Pyelonephritis:** An infection of the kidneys, typically caused by an obstruction in the urinary tract or an infection that has travelled up the tract. Urine backflows into the kidneys and ureters when there is a blockage in the urinary tract.

### Classification of urinary tract infection

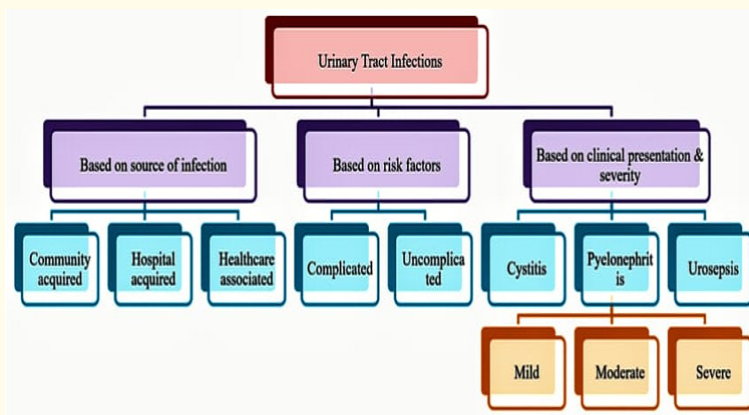


Figure 2

### Sign and symptoms



Figure 3

### Causes of urinary tract infection

The following are the main reasons for urinary tract infections:

- Constipation: This condition causes inflammation and infection in the bladder, which leads to a urinary tract infection [6].
- Diarrhea: The germs from these stools frequently have a tendency to infect the urinary tract
- Diabetes: Inadequate glucose filtration leads to accumulation in some kidney regions, which might result in urinary tract infections [7].
- Dehydration: This prevents the body from eliminating the toxins and even the bacteria. These become stuck and frequently lead to the development of a urinary tract infection.
- Kidney stones are more of a chronic than an acute cause. This results in urinary tract irritation, which is undoubtedly uncomfortable [8].
- Eating meat from unsanitary sources frequently leads to the introduction of the bacteria *E. coli* into the urinary tract, where it quickly multiplies and spreads to cause an illness.

- Not urinating for an extended period of time might drive bacteria back into the urinary tract, which can lead to a UTI. When Should I Get Help for a Urinary Tract Infection [9].

**Dosage form**

A UTI suppository is a dosage form that contains a medication or ingredient that is inserted into the vagina or rectum to treat urinary tract infections (UTIs). Here are some possible dosage forms and strengths for a UTI suppository: [10].

- **Active ingredient:** Methenamine hippurate, Nitrofurantoin, or other UTI-treating medications
- **Dosage form:** Vaginal suppository or rectal suppository
- **Strength:** 100 mg, 200 mg, 500 mg, or other strengths as determined by the manufacturer
- **Dosage:** Insert one suppository every 12 hours for 3-5 days, or as directed by a healthcare professional

**Administration**

- **Vaginal suppository:** Insert into the vagina, pushing gently until it is fully inserted.

- **Rectal suppository:** Insert into the rectum, pushing gently until it is fully inserted.

**New drug**

There are new drug and treatments for urinary for urinary tract infection (U.T.I) that are available or in development including.

- Pivya (pivmecillinam)
- Orlynvah (sulopenem etzadroxil and probenecid)
- Gepotidacin
- Cefepime and enmetazobactam
- Pivmecillinam
- Spero therapeutics SPR994
- Glaxosmithklines GSK252424
- Cidara therapeutics CD101
- Pfizers PF -8730004
- Bacteriophage therapy
- Probiotics

**Patent**

S. no.	Authors	Title	Patent no.	Submission	Publications
01	J. Brian Windor, stan J. Roux alanm. Lioyd, Collin E. Thomas.	Methods and compositions for increasing the efficacy of biological active ingredients	W02005014777A2	2003-10-16	2005-02-17
02	Mahmoud A. Elsohly Waseem. Gul Michae A. Repka, Soumyajit Majumdar, Mohammad Khalid Ashfar,	Compositions containing delta-9-THC-amino acid esters and process of preparation	US9630941B2	2014-08-18	2017-04-25
03	Lekhram Changoer, Gearge ANAS TASSOV,	Suppositories comprising cannabinoids.	US10543190B2	2018-09-05	2020-01-28
04	Ajith Anand, Maren L Arling Arling, Alexandreda silva conceicao,	Methods and composition for rapid plant transfor mation.	US20220124998A1.	2022-01-07	2022-04-28
05	Jheodre.Charles Lamson, Joshua makower, Joseph cataness,	Devices Systems and methods for treating benign prostatic. Hyperplasta and other conditions.	US11471148B2	2021-08-26	2022-10-18
06	Jamesw. Janetka, Zhenfuttam, scott Hultgren. Jerry PINKER, corinne Cusumano.	Compounds and methods for trenting bacterial infections.	US20230033327A1	2022-08- 26	2023-02-02
07	Jamesw. Janetka, Laurel MYDOCK-MCGRANE	Mannose derived antagonists of fimh useful for treating disease	US20220235087A1	2022-04-06	2022-07-06
08	Lekhram CHAGOER, George ANAS TASSOV	Suppositories comprising cannabinods	FP3528784B1	2017-10-19	2023-08 02
09	W. Robert Addington, Stuart P. Miller, Robert E. Stephens, Michael M. Phelipa, Mary W. Briganti	Techniques for evaluating stress urinary incontinence (S. U.I) using involuntary reflex cough test	US8845534B2	2013-10-23	2014-09-30
10	Yaroslav faybishenko, Boris faybishenko.	Health diagnostic systems and methods.	US9131893B2	2013-10-28	2015-09-15

11	Geoffrey H gorres	Device for monitoring a patient for a urinary tract infections.	US8343122B2	2010-04-23	2013-01-01
12	David darling, Jamnes miller suttie mark dalphin, Laimonis Kavalieris, paul O, Sullivan, satish kumar	Method for detecting genetic and phenotypic biomarkers of urothelial carcinoma and treatment thereof	US10131955B2	2016-05-19	2019-07-23
13	Erbey, Jacobl. Upperco, Michael Alan Fisher, Patick William Strane	Negative pressure therapy system	US20220265914A1	2022-05-06	2022-08-25
14	Kevin Weadock, Amit Khanolkar	Methods and devices for preventing catheter related urinary tract infections.	US8911424B2	2011-02-09	2014- 12-16
15	Egbert A. van der MEULEN,Laszlo Balazs Tanko	Methods of treating prostate cancer with Gn RH antagonist	US11826397B2	2022-03-31	2023-11-28
16	David Aaronson sarah Blaschko, Maurice Garcia, Alex Wu	Safety urinary catheter.	US90868B2	2013-01-09	2015-07-21
17	Kevin G. Connors, William L. Pintauro, Sheila K.	Attenuation device for use in an anatomical structure	US10327880B2	2016-08-29	2019-06-25
18	Jamesw Janetka, Zhenfu Han, Scott Hultgren. Jerry Pinkner, corinne cusumano	Mannose derivatives their use in the treatment of bacterial in infections.	ES2959183T3	2014-05-30	2024-02-12
19	James W. Janetk, zhenfu Han, Scott Hultgren, Jerome S, Pinkner corinne cusumano	Compounds and methods for treating bacterial infection.	US10273260B2	2016-12-08	2019-04-30

Table 1

Future prospects

- **Clinical trials:** Conduct clinical trials to evaluate the safety and efficacy of the suppository in humans [5].
- **Standardization:** Standardize the extraction and formulation processes to ensure consistency and quality.
- **Combination therapy:** Explore the potential of combining Cynodon dactylon with other herbal extracts or antibiotics to enhance efficacy.
- **Pharmacokinetics and pharmacodynamics:** Study the absorption, distribution, metabolism, and excretion of the suppository.
- **Toxicity and safety:** Conduct toxicity studies to ensure the safety of long-term use [4].
- **Pharmaceutical applications:** Develop the suppository into various pharmaceutical forms, such as tablets, capsules, or injectables.
- **Patent protection:** Consider patenting the formulation and extraction processes [3].
- **Commercialization:** Scale up production and market the suppository as a natural remedy for UTI management.

- **Research expansion:** Explore the potential of Cynodon dactylon in addressing other health concerns, such as kidney stones or prostate issues.
- **International collaboration:** Collaborate with researchers globally to advance the development and use of herbal suppositories for UTI management [2].

Conclusion

Urinary tract infections (UTIs) are common, particularly in women, and can affect various parts of the urinary system. While antibiotics are the primary treatment, the rise of antibiotic resistance has led to interest in alternative therapies, including new drugs like Pivya and bacteriophage therapy [1]. Vaginal and rectal suppositories, such as those containing methenamine hippurate or nitrofurantoin, offer targeted treatment and may reduce the need for systemic antibiotics. Additionally, natural remedies like polysaccharides from Althaea officinalis (marshmallow root) show promise for preventing recurrence and promoting healing. Continued research into both conventional and natural treatments holds promise for more effective UTI management.

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